



Bases neurales et multisensorielles du soi corporel: Approches électrophysiologiques et comportementales

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Zoé DARY

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2. Dary Z., Kobliska P., Léonard J., Toupet M., Hautefort C., Pergandi J-M, Denise P., and Lopez C., **Influence of a bilateral vestibulopathy on the bodily self measured by the full-body illusion**, GDR vertige, Marseille, France, Octobre 2023.
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4. Dary Z., Lagarde S., Medina Villalon S., Léonard J., Bartolomei F., and Lopez C., **Neural bases of the bodily self as revealed by electrical brain stimulation in 354 patients with epilepsy**, FENS (Federation of European Neuroscience Societies), Paris, France, Juin 2022

Résumé

Le soi corporel, forme préréflexive du soi, repose sur plusieurs expériences corporelles, telles que la localisation du soi, le sentiment d'appartenance, l'agentivité et la perspective en première personne. Ces expériences se fondent sur l'intégration multisensorielle de signaux (vision, toucher, intéroception, proprioception, vestibulaire). Les études de neuroimagerie fonctionnelle chez des sujets sains ou l'étude de lésions chez des patients neurologiques (tumeur, épilepsie) ont commencé à identifier les bases cérébrales des expériences corporelles sous-tendant le soi corporel. Nous avons exposé, dans un article d'opinion, les principales avancées de ces dix dernières années et les défis majeurs dans l'étude des bases cérébrales du soi corporel. Cette thèse a pour objectif de répondre à trois de ces défis : 1) Identifier causalement le réseau du soi corporel. 2) Décrire la connectivité fonctionnelle de ce réseau. 3) Etudier les bases multisensorielles qui sous-tendent le soi corporel.

Une revue systématique de la littérature sur les bases neurales du soi corporel étudiées par stimulations électriques intracérébrales, nous a permis d'identifier 121 cas de patients issus de 42 études réalisées entre 1937 et 2022. Six régions ont été rapportées comme étant impliquées de façon causale dans le soi corporel : le précuneus, l'insula, le cortex cingulaire moyen, le lobule pariétal inférieur, l'aire motrice supplémentaire ainsi que le complexe amygdalo-hippocampique.

Une étude rétrospective chez 354 patients atteints d'une épilepsie pharmaco-résistante, porteurs d'électrodes profondes, explorés par stéréo-électroencéphalographie (SEEG), nous a permis d'analyser plus de 2 500 réponses évoquées par des stimulations électriques à haute fréquence (50 Hz) du cerveau. 4 % des réponses concernaient une modification du soi corporel. Cette étude corroborait une partie des résultats de notre revue systématique tout en révélant l'implication du cortex cingulaire antérieur. Elle décrivait également le réseau fonctionnel du soi corporel. L'analyse du signal SEEG enregistré pendant que les patients rapportaient une modification du soi corporel a révélé une diminution significative de la connectivité fonctionnelle du lobule pariétal inférieur, du sillon temporal supérieur, des gyrus temporaux moyens et inférieurs et une augmentation de la connectivité de l'insula. Enfin, nous avons montré une diminution de la connectivité entre les régions temporales et le complexe amygdalo-hippocampique associée aux modifications du soi corporel.

Notre troisième axe de travail portait sur le rôle du système vestibulaire dans le soi corporel. Nous avons réalisé une illusion du corps entier (full-body illusion) en réalité virtuelle chez des patients avec une vestibulopathie bilatérale et des sujets contrôles appariés. Aucune illusion n'a été observée chez les patients, ce qui suggère que des mécanismes compensatoires permettraient de réduire le conflit multisensoriel lié à leur déficit. Cette étude suggère un effet de l'âge sur la sensibilité à l'illusion du corps entier.

Cette recherche revêt une importance particulière car elle permet une meilleure compréhension des bases cérébrales et multisensorielles du soi corporel, mettant en lumière causalement son réseau cérébral, sa connectivité fonctionnelle et son interaction avec le système vestibulaire.

Mots clés : Soi corporel, stimulation électrique intracérébrale, SEEG, connectivité fonctionnelle, épilepsie, système vestibulaire, intégration multisensorielle

Abstract

The bodily self, a pre-reflective form of self, relies on several bodily experiences such as self-location, sense of ownership, agency, and first-person perspective. These experiences are based on the multisensory integration of signals (vision, touch, interoception, proprioception, vestibular). Functional neuroimaging studies in healthy subjects or lesion studies in neurological patients (tumor, epilepsy) have begun to identify the brain bases of bodily experiences underlying the bodily self.

We have outlined, in an opinion article, the major advances of the past decade and challenges in studying the neural bases of the bodily self. This thesis aims to explore three of these challenges: 1) Causally identifying the network of the bodily self. 2) Describing the functional connectivity of this network. 3) Studying the multisensory bases underlying the bodily self.

A systematic review of the literature on the neural bases of the bodily self studied by electrical brain stimulations (EBS) allowed us to identify 121 cases from 42 studies conducted between 1937 and 2022. Six regions were reported to be causally involved in the bodily self: the precuneus, insula, middle cingulate cortex, inferior parietal lobule, supplementary motor area, and amygdalo-hippocampal complex.

A retrospective study in 354 patients with drug-resistant epilepsy, carrying deep electrodes, explored by stereo-electroencephalography (SEEG), allowed us to analyse over 2,500 responses elicited by high-frequency (50 Hz) EBS. 4% of the responses involved a disturbance of the bodily self. This study corroborates some of the results of our systematic review while revealing the involvement of the anterior cingulate cortex. It also describes the functional network of the bodily self. Analysis of the SEEG signal recorded while patients reported a modification of the bodily self revealed a significant decrease in functional connectivity of the inferior parietal lobule, superior temporal sulcus, middle and inferior temporal gyri, and an increase in insula connectivity. Finally, we show a decrease in connectivity between temporal regions and the amygdalo-hippocampal complex associated with disturbances of the bodily self.

Our third study focuses on the role of the vestibular system in the bodily self. We conducted a full-body illusion in virtual reality in patients with bilateral vestibulopathy and their matched controls. No illusion was observed in patients, suggesting that compensatory mechanisms may reduce the multisensory conflict related to their deficit. This study suggests an age effect on sensitivity to the full-body illusion.

This research is particularly important as it allows a better understanding of the brain and multisensory bases of the bodily self, causally highlighting its brain network, functional connectivity, and interaction with the vestibular system.

Keywords: Bodily self, electrical brain stimulation, SEEG, functional connectivity, epilepsy, vestibular system, multisensory integration

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Préambule

“ (...) Elle est toute seule dans le cercle de lumière, elle ne voit personne. Elle danse sur le rythme lent de la musique électrique, et c'est comme si la musique était à l'intérieur de son corps. (...) Hawa danse pieds nus sur le sol lisse, ses pieds longs et plats frappent au rythme des tambours, ou plutôt, c'est elle qui semble dicter avec la plante de ses pieds et ses talons le rythme de la musique. (...) Mais elle, elle peut bouger, enfin, elle est libre, elle tourne sur elle-même, les bras écartés, et ses pieds frappent le sol, du bout des orteils, puis du talon, comme sur les rayons d'une grande roue dont l'axe monte jusqu'à la nuit.”

(Le Clézio, Désert)

Si j'entame le début de cette thèse par cette citation, c'est qu'elle donne un sens à la démarche personnelle et intellectuelle qui m'a menée jusqu'à ce moment. Etudier le corps, étudier le soi, étudier la relation entre les deux n'est pas uniquement un objet d'intérêt de ces quatre dernières années. Cet attrait remonte à bien des années, où âgée de seulement 8 ans, j'entamais ma première révolution personnelle : celle de poser un pied sur un parquet de danse. Pour la première fois, je pouvais exprimer ce qu'il y avait de plus personnel en moi, ce qui constituait mon être, ma puissance d'exister. Je le faisais par mon corps. Ce corps qui à travers la danse *« se meut, où le mouvement se déploie. Il n'est pas dans l'ignorance de soi, il n'est pas aveugle pour soi, il rayonne d'un soi »* (Merleau-Ponty 1964). Ce soi qui est mon corps. Le chemin de mes études m'a ensuite menée à la littérature, où grâce à mes années de classe préparatoire, j'ai pu expérimenter la multiplicité des corps : de différentes époques, de différents âges, de différents sexes. Pour reprendre les mots d'Olivier Rolin, la littérature m'a permis d'éprouver *« mille façons que l'humanité a eues d'être humaine »*. En même temps que cette littérature incarnée faisait son cheminement en moi, mon corps propre se transformait, marqué par les rouages du labeur. Pour la première fois, j'éprouvais une forme de dualité entre mon corps, livré à l'inertie de l'apprentissage, et mon esprit enivré par la sollicitation intellectuelle.

Mon unité corporelle, je l'ai retrouvée quand j'ai repris la danse à Paris en même temps que j'entamais mon master de Philosophie des Sciences. C'est d'ailleurs au cours de ces années que je me suis plongée dans la phénoménologie, courant philosophique qui allait guider tout le reste de mes études. Ce mouvement qui place le corps au cœur même de l'expérience d'être. Ma réflexion sur le corps rencontrait un autre versant. Des questionnements théoriques qui mêlaient la danse, la philosophie du corps, l'art théâtral et pictural et les neurosciences cognitives. Mon attrait pour cette discipline me conduisit à suivre des cours à l'ENS, institution tant convoitée pendant mes années de classes préparatoires.

Puis est arrivée une maladie pernicieuse, celle qui déclencha mon attrait pour cet organe qui à l'heure actuelle me passionne. Cette maladie d'Alzheimer, qui est apparue chez l'une et chez l'autre. Cette maladie où l'identité de la personne se retrouve réduite au corps propre. Ce corps qui, malheureusement, n'est plus sollicité et qui oublie comment il

fonctionne. Ce rapport entre le corps et l'identité m'a intriguée. Dans la littérature philosophique et scientifique, une des thèses les plus défendues est que le soi se définit comme la continuité psychologique de l'être dans le temps « *pour être nous-mêmes, nous devons avoir une biographie – la posséder, en reprendre possession s'il le faut. Nous devons nous « rassembler », rassembler notre drame intérieur, notre histoire intime. Un homme a besoin de ce récit intérieur continu pour conserver son identité, le soi qui le constitue* » (Sack 1985). Or, que reste-t-il de la personne quand sa mémoire autobiographique, siège de son identité, se distord ? Que reste-t-il de ce corps qui nous regarde ? Un corps qui a vécu.

Ma décision était prise, je voulais faire des neurosciences cognitives. De manière évidente, je me suis tournée vers le domaine des neurosciences qui traitait des sens, de la perception et du corps. Et me voici, 45 mois plus tard, à écrire une thèse en neurosciences cognitives sur le corps. Thèse emprunte de cette réflexion interdisciplinaire qui m'a stimulée intellectuellement jusqu'ici.

Introduction

Nombreux sont les philosophes qui à travers l'histoire ont questionné la relation entre le corps et l'esprit (Berthoz 1999), proposant diverses approches et théories. La philosophie dualiste de Descartes, héritière de celle de Platon ou d'Avicenne, est souvent la plus citée et la plus discutée (Descartes 1637). Pourtant, de nombreux philosophes tels que Thomas d'Aquin, Nietzsche ou encore Husserl se sont opposés à cette vision en soutenant que le corps et l'esprit ne sont pas des entités distinctes. Un courant de la philosophie qui défend cette thèse est la phénoménologie, porté en autre par Merleau-Ponty (1945, 1964). De manière succincte, ce dernier défend qu'une expérience n'est pas uniquement mentale mais qu'elle est également corporelle. Le monde, la conscience et le corps font, pour lui, partie d'un unique système. Le corps est pour le philosophe un corps-vécu. Cette conception du rôle du corps dans l'expérience et de son lien avec l'esprit a permis de renouveler la pensée scientifique notamment dans les sciences cognitives. La relation entre le corps et l'esprit est devenue la relation entre le corps et le cerveau. En parallèle, les progrès scientifiques, notamment en neuroimagerie, ont également permis de questionner ce dualisme corps-esprit, dans la mesure où des mécanismes cognitifs tels que la pensée sont désormais appréhendés.

Cependant, la recherche en neurosciences cognitives ne doit pas entrer dans un réductionnisme ontologique qui réduirait toute explication à un seul organe, le cerveau. Au contraire, ce débat sur la relation corps-cerveau est fécond parce qu'il y a de nombreuses disciplines des sciences humaines et sociales qui s'y intéressent également. Même si, dans le cadre de cette thèse, nous nous plaçons dans le champ disciplinaire des neurosciences cognitives, nous ne perdons pas de vue la complexité du phénomène étudié et les différents facteurs psychologiques ou sociaux sous-jacents.

Ce travail de thèse s'affilie donc au champ des neurosciences cognitives qui étudie la subjectivité de l'expérience (Gallagher 2000; Blanke et Metzinger 2009; Faivre et al. 2017). Certaines approches s'intéressent davantage aux aspects conceptuels et sémantiques de l'expérience subjective (mémoire, langage) (Gauthier et al. 2020; Bréchet 2022), d'autres, aux aspects moteurs et sensoriels. Nous nous inscrivons dans ce second courant, en articulant notre propos autour d'un concept clé, celui du *soi corporel*. L'ensemble de cette thèse se focalisera sur les bases neurales et multisensorielles du soi corporel.

L'introduction de cette thèse se compose de trois chapitres. Le premier chapitre proposera un bref cheminement interdisciplinaire partant de la philosophie de l'expérience du corps à son étude en neurosciences cognitives. Le second chapitre de cette introduction portera sur les bases neurales du soi corporel. Si l'un des enjeux de cette thèse est d'approfondir notre connaissance sur le lien entre le corps et le cerveau, il serait intéressant de déterminer les relations causales qui existent entre le soi corporel et les régions cérébrales émergentes. Pour cela, nous aborderons les bases neurales du soi corporel par des approches causales, notamment des techniques de stimulations électriques intracérébrales. Enfin le troisième chapitre portera sur les mécanismes multisensoriels qui sous-tendent le soi corporel. Nous nous focaliserons sur le rôle d'un sens encore trop peu étudié dans le champ du soi corporel : le système vestibulaire.

Chapitre 1 : Qu'est-ce que le soi corporel ?

« Derrière tes pensées et tes sentiments, mon frère, se tient un puissant maître, un inconnu montreur de route – qui se nomme soi. En ton corps il habite, il est ton corps »

Nietzsche, *Ainsi parlait Zarathoustra* (1883)

I. Subjectivité et conscience de soi

La conscience de soi a largement été étudiée à travers l'histoire que ce soit par l'intermédiaire de la philosophie de l'esprit, de la philosophie sociale, de la psychologie développementale ou encore plus récemment des neurosciences cognitives. Cependant, ces approches pluridisciplinaires ont entraîné une variété de définitions et de concepts, notamment autour de la notion du soi (Northoff et al. 2006; Legrand et Ruby 2009). Cette première partie définira un ensemble de concepts que nous utiliserons dans l'ensemble de cette thèse.

Un point majeur discuté dans ces différentes disciplines est que la subjectivité, c'est-à-dire le fait d'être un sujet d'expérience, est fondamentale dans la constitution du soi. En philosophie, Descartes est un des premiers à introduire la notion de subjectivité dans l'expérience consciente. Une expérience émerge seulement si un sujet vit cette expérience. Selon lui, le sujet prend conscience de lui-même en tant que chose qui pense « *je connus de là que j'étais une substance dont l'essence ou la nature n'est que de penser et qui, pour être, n'a besoin d'aucun lieu, ni ne dépend d'autre chose matérielle* » (Descartes 1637). Le soi, pour le philosophe, serait par essence une substance, c'est-à-dire « *une chose qui existe en telle façon qu'elle n'a besoin que de soi-même pour exister* » (Descartes 1644). Or, même si cette implication de la subjectivité dans l'expérience consciente est précurseur à l'époque, Descartes est à l'origine d'une forme de dualisme entre l'esprit et le corps. Pour le philosophe, le corps n'est que le support de l'âme : « *l'âme par laquelle je suis ce que je suis est entièrement distincte du corps et même qu'elle est plus aisée à connaître que lui et qu'encore qu'il ne fut point, elle ne cesserait point d'être tout ce qu'elle est* » (Descartes 1637). Cependant, comme le soulignait Strawson, il n'y a pas « *d'expérience sans expérimentateur* » (Strawson 2011) ou encore Merleau-Ponty qu'un « *cartésien ne se voit pas dans le miroir : il voit un mannequin, un "dehors"* » (Merleau-Ponty 1964). La subjectivité de Descartes est dénuée d'un corps sentant ou d'un corps émotionnel (Damasio 1994).

Les sciences cognitives se sont emparées de cette réflexion sur la subjectivité de l'expérience du soi au milieu du XX^e siècle. Le concept renvoie désormais non seulement à l'idée que toute expérience est l'expérience d'un sujet, mais désigne également le contenu de l'expérience même (Zahavi 2005). Cette double dimension de la subjectivité a

été conceptualisée sous le terme de conscience phénoménale. La conscience phénoménale désigne le ressenti d'un sujet, « *l'effet que cela fait* » d'être au monde (Nagel 1974). La conscience de soi est au cœur de la conscience phénoménale. En sciences cognitives, un des critères essentiels de la conscience de soi est la capacité de se reconnaître. Par exemple, en psychologie développementale, la capacité qu'un enfant a de se reconnaître dans un miroir est un des tests majeurs de l'émergence de la conscience de soi (Nielsen et al. 2006; Rochat et al. 2012). Si l'enfant reconnaît que l'image devant lui le désigne bien, il accède à la conscience de soi. L'enfant découvre dans un premier temps une image de lui qui lui est étrangère. Lorsqu'il se reconnaît comme un lui-même, il accède à sa conscience de soi. Le soi apparaît en ce sens comme un objet de la conscience. Il est le contenu de cette dernière ; il est son objet intentionnel. Le sujet projette sa conscience vers un soi qui le désigne. Cette visée intentionnelle de la conscience vers le soi est désignée sous le terme de « **soi-objet** ». Ainsi, lorsque le soi est expérimenté en tant qu'objet, l'individu attribue au soi des caractéristiques physiques ou mentales. Cependant, la conscience de soi n'est pas limitée à cette reconnaissance de soi. En effet, le soi est avant tout le sujet de l'expérience consciente. Par exemple, lorsqu'un sujet se regarde dans le miroir, ce soi observant fait l'expérience même du soi en tant que sujet. Il est implicitement conscient d'être le sujet de l'expérience. Le « **soi-sujet** » désigne ce mode d'être de conscience. Il s'agit de la conscience de la subjectivité de l'expérience.

Partant de cette idée qu'il y a deux modes d'être de la conscience de soi, une conscience orientée vers un soi-objet et une conscience d'un soi-sujet. Dorothée Legrand a proposé quatre formes de conscience de soi : une conscience de soi réflexive, pré-réflexive, réflexive et préréflexive (Legrand 2007, 2010a) (Figure 1). La conscience de soi préréflexive et pré-réflexive correspond à une perception du soi non-intentionnelle (Legrand 2007). La conscience de soi réflexive et pré-réflexive s'applique uniquement au soi-objet, tandis que la conscience de soi réflexive et préréflexive s'applique au soi-sujet. La *conscience de soi réflexive* détermine l'ensemble des états cognitifs de haut niveau tels que le fait de penser sur soi-même, de juger sa personnalité ou son aspect physique. Elle s'apparente également à ce que certains auteurs appellent le soi-narratif (Gallagher 2000), le soi-autobiographique (Damasio 1999) ou le soi-cognitif (Schaller et al. 2021). Ce soi-objet implique des fonctions cognitives telles que le langage, la mémoire, l'imagerie mentale, etc. Dans un tel état mental, l'objet intentionnel dont on est conscient est soi-même. La *conscience de soi pré-réflexive* correspond aux états qui a posteriori atteignent la conscience. Par exemple, un sujet peut sentir un mal être sans arriver à le verbaliser et ce n'est qu'à posteriori qu'il sera apte de dire qu'il était angoissé.

Il y a également deux façons d'être conscient de soi en tant que sujet. Dans un premier temps, on peut être *conscient de soi de manière réflexive*, c'est-à-dire que notre intention est dirigée vers le soi-sujet. Legrand (2007) prend l'exemple suivant : lorsqu'on se saisit d'une rose, on s'intéresse à la rose que l'on saisit et non à notre main qui est en train de la saisir. Pourtant, notre main est bien le sujet de l'expérience. Enfin, la *conscience de soi préréflexive* définit l'expérience consciente avant toute conscience intentionnelle. Il s'agit d'une conscience de soi implicite qui serait au fondement de toutes les autres expériences de conscience de soi (Gallagher 2005; Zahavi 2005). Elle renvoie également aux notions de proto-soi (Damasio 1999) ou de soi minimal (Gallagher 2005; Blanke et Metzinger 2009).

Dans le cadre de cette thèse, nous nous référons seulement à deux formes de conscience : la conscience réflexive du corps-objet et la conscience pré-réflexive du corps-sujet. Nous souhaitons par le développement ci-dessus, souligner la complexité de la conscience de soi.

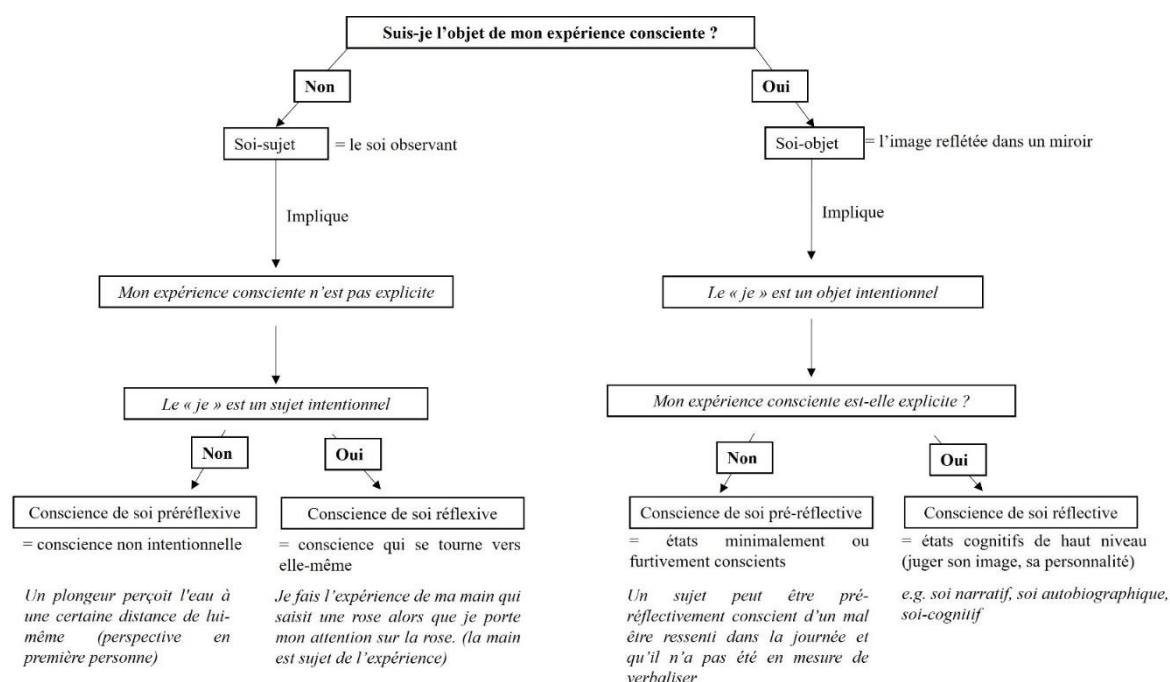


Figure 1 : Les quatre formes de consciences de soi. Lorsqu'une personne fait référence, parle ou pense à soi, elle peut faire l'expérience du soi en tant qu'objet – soi-objet – ou en tant que sujet – soi-sujet. Quatre formes de conscience de soi peuvent être distinguées : la conscience pré-réflexive, réflexive, pré-réflexive et réflexive. Adapté de (Legrand 2007).

II. Expérience du corps : corps-objet et corps-sujet

L'expérience du soi en tant que sujet ou objet repose ainsi sur l'expérience d'être un corps au monde (Merleau-Ponty 1945). Dans la lignée de cette réflexion, de nombreuses études en sciences cognitives s'accordent sur le rôle crucial du corps dans la constitution du soi (Gallagher 2005; Zahavi 2005; Blanke et Metzinger 2009; Faivre et al. 2017). Dans cette thèse, nous nous inscrivons dans cette dynamique en soutenant l'idée que le soi est le corps (ou une partie du corps) (Merleau-Ponty 1945; Legrand 2005). En d'autres termes, l'expérience de soi reposerait sur l'expérience d'être un corps.

Cependant, l'expérience du corps brouille la distinction du sujet et de l'objet (Barbaras, 1998). En effet, comme le souligne Merleau-Ponty, « *la perception externe et la perception de son propre corps varient conjointement car elles sont les deux facettes d'un même acte [...] toute perception externe est immédiatement synonyme d'une certaine perception de mon corps* » (Merleau-Ponty, 1945). Conceptuellement, pourtant, nous pouvons distinguer au même titre que le soi-objet et le soi-sujet, deux modes d'être de la

conscience corporelle : le corps-objet et le corps-sujet (Figure 2). Le **corps-objet** désigne le corps qui est pris comme un objet intentionnel d'un acte de conscience. L'image corporelle est souvent considérée comme exemple pour traduire cette idée. En effet, le sujet tourne son intention vers les propriétés structurales et matérielles de son corps (sa taille, sa couleur, sa morphologie), c'est-à-dire en tant qu'objet matériel. Il s'agit donc d'une conscience corporelle réflexive. A l'inverse, le **corps-sujet** représente l'expérience du corps non-intentionnelle, c'est-à-dire l'expérience du corps toujours présente, avant même de se poser ou de réfléchir sur l'état dans lequel on se trouve (Gallagher 2005). Le corps-sujet constitue le centre de référence des expériences dans la mesure où le sujet perçoit le monde à travers son corps. Le corps fait l'expérience même d'être un corps qui voit, touche, sent, entend, etc. Le corps-sujet est donc une forme préréflexive de la conscience corporelle. Il s'agit d'un « *avant même que nous le sachions* » (Gallagher 2005), ou encore c'est « *une représentation non-conceptuelle et préréflexive des informations relatives au corps* » (Aspell et al. 2012).

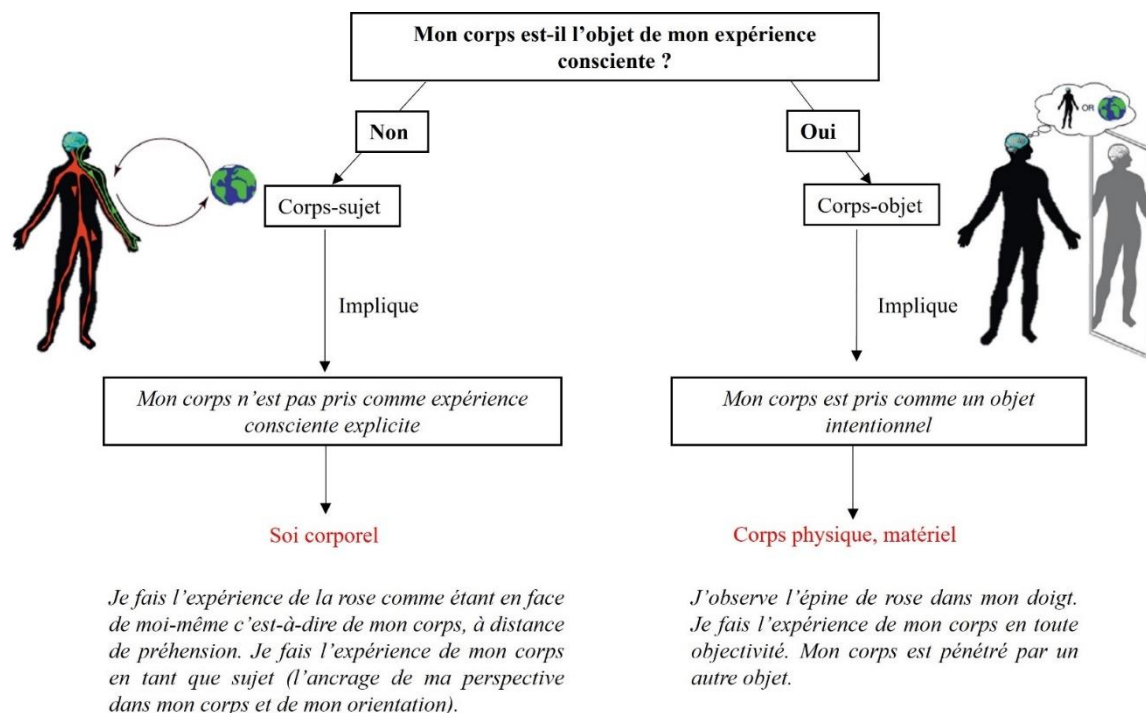


Figure 2 : L'expérience du corps. Image adaptée de (Legrand 2005, 2007). Images issues de (Christoff et al. 2011)

Conceptuellement il est facile de distinguer le corps-objet et le corps-sujet. Qu'en est-il expérimentalement ? Prenons l'exemple décrit par Paillard (1983), d'une patiente avec une neuropathie sensorielle périphérique. Cette dernière n'était pas capable, lorsqu'elle n'avait aucun retour visuel, de localiser une stimulation thermique délivrée sur son bras gauche. Cependant, lorsqu'on lui demandait de localiser la stimulation sur une

image d'un corps, elle en était parfaitement capable (Paillard et al. 1983). Il s'agit bien ici d'une dissociation entre le corps-objet et le corps-sujet. Le corps-objet (image du corps) semble préservé, à l'inverse du corps-sujet. De même, Blanke et collaborateurs (2002) ont appliqué des stimulations électriques au niveau de la jonction-temporo-pariétale chez une patiente lors de l'évaluation préchirurgicale d'une épilepsie pharmacorésistante. Lors de la stimulation (à 3 mA), lorsque la patiente portait son attention vers ses bras ou ses jambes, elle avait la sensation que ces derniers étaient déformés. Cependant, lorsque son attention n'était pas portée sur ses membres, c'est-à-dire sans retour visuel, et que la stimulation était plus élevée (3,5mA), elle avait une expérience de sortie du corps, c'est-à-dire une sensation de flotter et de voir son corps d'un point de vue surélevé (Blanke et al. 2002) et donc une modification du corps-sujet. Cette étude révèle bien les deux formes d'être du corps : lorsque la patiente porte son attention et qu'elle a un retour sensoriel visuel de ses membres, elle transforme son corps en un corps expérimenté, c'est-à-dire en objet intentionnel de la conscience. À l'inverse, lorsqu'elle ne porte pas attention à son corps, elle expérimente son corps en tant que sujet de l'expérience.

Pour aller plus loin, analysons ce qu'il se passe lorsqu'un sujet expérimente une sortie du corps. Une expérience de sortie du corps est caractérisée par une sensation de décorporation dans laquelle le soi est perçu comme étant extérieur au corps. De plus, le sujet peut potentiellement observer son propre corps depuis une perspective visuo-spatiale élevée (depuis son corps illusoire surélevé) (Blanke et al. 2004; De Ridder et al. 2007; Bos et al. 2016). Lors de cette expérience, d'une part, le sujet fait l'expérience d'un corps qui est situé en face de lui, couché sur son lit. Ce corps couché est pris comme objet intentionnel ; il voit ce corps en troisième personne. Cependant, le sujet reconnaît ce corps comme le sien et donc s'identifie à lui. D'autre part, le sujet fait également l'expérience de son corps avec une perspective en première personne depuis ce corps surélevé, même s'il ne sent pas physiquement ce corps. Le sujet « regarde en bas » vers son corps matériel. Ainsi, dans une expérience de sortie du corps, le sujet fait l'expérience de son corps comme étant dans un certain volume, localisé dans un espace et orienté vers un monde qu'il perçoit, sans pour autant faire l'expérience de la matérialité de son corps (Legrand 2010b).

Dans le quotidien, l'expérience du corps est caractérisée par l'union entre le corps-sujet et le corps-objet. L'unité du corps et donc, du soi, résulte de cette imbrication entre les différents modes d'être du corps. Pourtant lors de l'analyse des situations pathologiques que nous venons de décrire, ou lors d'expérimentations en laboratoire (Dieguez et Lopez 2017), ces deux modes d'être sont souvent étudiés séparément (par les chercheurs et les médecins) pour mieux les comprendre (Legrand 2010b). Comme le souligne Legrand (2010b), dans le prisme des pathologies et de l'expérimentation, « *le sujet vit alors des corps comme différents les uns des autres bien que tous siens* » (ibid). Les neurosciences cognitives se sont d'ailleurs longtemps concentrées sur l'étude du corps-objet (Legrand et Ruby 2009). Leurs paradigmes et leurs méthodes d'expérimentation ne permettaient pas d'inclure le corps-sujet dans leur champ de recherche. Depuis une quinzaine d'années, des changements de paradigmes ont été entrepris pour inclure l'étude du corps-sujet.

III. Le soi corporel, un objet d'étude pour les neurosciences cognitives

Dans cette thèse, nous serons souvent confrontés à ce chevauchement entre corps-sujet et corps-objet, ce qui ajoute un niveau de complexité à notre propos. L'utilisation de stimulations électriques intracérébrales, par exemple, révèle une zone grise entre ce qui s'apparente à des expériences corporelles préréflexives (la sensation de flottement par exemple) et le fait de rapporter cette sensation, qui renvoie le corps à sa dimension réflexive et donc objectivée. Par voie de conséquence, nous prenons le parti de conceptualiser ce chevauchement sous le concept de **soi corporel**. Le soi corporel désignerait donc cette expérience subjective implicite et préréflexive d'être le sujet corporel d'une expérience, tout en prenant en considération que dans son étude, il existe nécessairement un moment où le corps-objet est impliqué¹. Par l'intermédiaire de ce concept de soi corporel, les neurosciences cognitives attribuent au corps-objet des aspects subjectifs. L'objectif de ces disciplines sera ainsi d'étudier ces aspects subjectifs soit explicitement par l'intermédiaire de questionnaires où le sujet rapporte ce qu'il a vécu, soit de façon implicite par l'étude des changements physiologiques, électrophysiologiques ou comportementaux lors de tâches spécifiques.

On considère souvent que le soi corporel repose principalement sur quatre expériences corporelles : la localisation du soi, le sentiment d'appartenance du corps, la perspective en première personne et le sentiment d'agentivité. La *localisation du soi* peut être définie comme l'expérience subjective d'occuper un espace donné à un moment donné, généralement dans les limites physiques du corps (Lenggenhager et al. 2007; Blanke et Metzinger 2009). Le *sentiment d'appartenance* est l'expérience que les parties de notre corps nous appartiennent (Tsakiris et al. 2007). La *perspective en première personne* est la perspective spatiale du soi sur le monde (Vogeley et Fink 2003). Enfin, l'*agentivité* fait référence à l'expérience d'être à l'origine de nos actions et pensées (Jeannerod 2007). Ces quatre expériences corporelles cependant varient selon les auteurs. L'agentivité ou la perspective en première personne sont parfois omis (Dobricki et de la Rosa 2013). Le *sentiment d'identification*, défini comme l'expérience subjective que le corps dans sa globalité nous appartient, est également présent dans de nombreux articles utilisant des paradigmes sur le corps entier (Lenggenhager et al. 2007; Park et Blanke 2019; Nakul et al. 2020b; Wu et al. 2024). Dans cette thèse, nous incluons également l'image du corps², définie comme l'expérience subjective de la taille, du poids ou de la forme du corps.

Un courant de recherche en neurosciences cognitives s'intéresse aux mécanismes qui sous-tendent le soi corporel et ses différentes composantes (Blanke 2012). Deux

¹ Notons que notre définition du soi corporel est légèrement différente que celle exposée dans la [Figure 2](#) (p. 16) qui d'un point de vue phénoménologique, est une expérience différente de celle du corps-objet.

² Dans nos articles, nous avons utilisé le terme de *perceptual body image* pour traduire cette même idée.

paradigmes expérimentaux ont été majoritairement utilisés : l'illusion de la main en caoutchouc (Botvinick et Cohen 1998) et l'illusion du corps entier (Ehrsson 2007; Lenggenhager et al. 2007). L'expérience de l'illusion de la main en caoutchouc (*rubber hand illusion*) manipule la congruence des informations visuelles et tactiles, dans le but d'induire une illusion d'appropriation d'une fausse main en caoutchouc. Les participants observent une main en caoutchouc être touchée, de façon synchrone ou asynchrone (avec un délai temporel et/ou un décalage spatial), en même temps que leur vraie main dissimulée. Les participants s'approprient, dans la condition synchrone, la fausse main et relocalisent leur main vers la main en caoutchouc. Cette expérience a été adaptée au corps entier (*full-body illusion*) (Lenggenhager et al. 2007). Les participants reçoivent une stimulation tactile pendant qu'ils observent à travers un visiocasque, leur corps filmé par une caméra placée derrière eux. L'expérimentateur touche le dos des sujets afin de créer une stimulation visuo-tactile : le participant visualise devant lui l'image de son propre dos être touché au même endroit qu'il est touché par l'expérimentateur. La stimulation visuo-tactile est synchrone (le toucher ressenti sur le dos est observé sur le dos du corps au même endroit et au même moment), ou asynchrone (il y a un délai entre le moment où l'expérimentateur touche le dos du sujet et où celui-ci le voit sur le dos virtuel). Ces deux paradigmes permettent d'étudier la localisation du soi, la perspective en première personne, le sentiment d'identification ou d'appartenance. Pour étudier l'agentivité, d'autres paradigmes ont été mis en place. Par exemple, des participants exécutent un mouvement devant une caméra reliée à un écran, ce qui leur permet de voir leur propre main ou celle d'un expérimentateur qui porte un gant identique. L'expérimentateur effectue soit un mouvement différent, soit le même mouvement et le participant doit juger si l'action réalisée est la même que celle effectuée (Sirigu et al. 1999; Haggard 2017).

Des mesures explicites et subjectives par des questionnaires ou des mesures implicites, plus objectives, permettent de quantifier la force de l'illusion. Pour reprendre l'exemple sur l'agentivité, une mesure explicite consiste à demander aux participants de juger si une vidéo qu'il regarde montre leurs propres mouvements de main ou ceux d'une autre personne. Un exemple de mesure explicite pour étudier la localisation du soi a été développée dans un article princeps de l'illusions du corps entier (Lenggenhager et al. 2007). Après la stimulation synchrone ou asynchrone, l'expérimentateur reculait à petits pas le participant d'un mètre les yeux fermés. Ce dernier devait alors retourner en marchant à la position où il estimait avoir été pendant la stimulation visuo-tactile. La différence entre leur position initiale et la position à laquelle les participants retournaient permettait de calculer l'erreur de localisation du soi pendant l'expérience (Lenggenhager et al. 2007, 2011).

Ces paradigmes expérimentaux ont permis de mettre en évidence les bases multisensorielles du soi corporel. En effet, les différents paradigmes utilisés reposaient à l'origine sur la congruence multisensorielle et notamment sur la congruence spatio-temporelle entre une stimulation visuelle et tactile (Botvinick et Cohen 1998; Ehrsson 2007; Lenggenhager et al. 2007). D'autres études ont mis en évidence que des stimulations visuo-motrices (Maselli et Slater 2013), visuo-vestibulaires (Preuss et Ehrsson 2019), visuo-respiratoires (Allard et al. 2017) et visuo-cardiaques (Aspell et al. 2013; Park et al. 2016, 2018) pouvaient également induire l'illusion. L'ensemble de ces études a révélé le rôle des informations visuelles, tactiles, vestibulaires et intéroceptives

dans le soi corporel. Ensemble, ces études mettent en évidence l'importance des informations sensorielles en provenance à la fois de l'extérieur (visuelle, tactile, auditive, etc.) et de l'intérieur du corps (proprioceptive, vestibulaire, intéroceptive, etc.) dans la construction du soi corporel (Park et Blanke 2019).

IV. Ce qu'il reste à faire

- 1) Approfondir l'interdisciplinarité dans l'étude du soi corporel que ce soit entre les disciplines des neurosciences, mais également de la philosophie et de la psychologie cognitive afin de comprendre les mécanismes sous-jacents au soi corporel.
- 2) Approfondir notre connaissance sur les bases multisensorielles du soi corporel notamment sur le rôle de signaux sensoriels encore peu étudiés, comme les signaux vestibulaires.
- 3) Approfondir notre connaissance sur la relation entre les différents composants du soi corporel et les mécanismes neuronaux sous-jacents à ces différentes expériences corporelles.

Chapitre 2 : Bases neurales du soi corporel

Les paradigmes décrits précédemment ont pu être combinés avec des méthodes de neuroimagerie chez des participants sains afin de mettre en évidence les bases neurales qui sous-tendent les différentes expériences corporelles (Ehrsson et al. 2005; Farrer et al. 2008; Lenggenhager et al. 2009; Ionta et al. 2014, 2014; Harduf et al. 2023). En étudiant les bases neurales du soi corporel, les neurosciences intègrent au sein de la cognition la dimension subjective de l'expérience du corps. Récemment, des études ont également combiné des stimulations électriques intracrâniennes à ces différents paradigmes expérimentaux et ont permis d'étudier l'activité électrophysiologique intracérébrale qui sous-tend le sentiment d'appartenance du corps (Guterstam et al. 2019).

I. Approche par la neuroimagerie fonctionnelle non invasive (IRM, PET)

Comme évoqué dans le chapitre précédent, les études en neurosciences s'appuient sur différents types de paradigmes expérimentaux chez des sujets sains (pour plus de détails, voir l'introduction de Dary et al. 2023) pour manipuler les différentes expériences du soi corporel (voir chapitre 1, section III).

Les études en neuroimagerie sur le sentiment illusoire d'appartenance d'une main en caoutchouc ou l'expérience d'identification à un corps virtuel ont mis en évidence l'implication du cortex prémoteur, du cortex somatosensoriel primaire, de l'insula, de l'aire corporelle extrastrée et du sillon intrapariétal (Ehrsson et al. 2004; Ionta et al. 2011a; Limanowski et al. 2014; Chancel et al. 2022a). D'autres études ont montré que la jonction temporo-pariétale, le cortex somatosensoriel primaire, le cortex prémoteur, le cortex cingulaire et le gyrus temporal supérieur postérieur sont liés à des changements illusoires dans la localisation du soi (Ionta et al. 2011b; Guterstam et al. 2015b). Les études en neuroimagerie sur l'agentivité ont montré une implication de l'insula et du lobule pariétal inférieur (Farrer et Frith 2002; Farrer et al. 2008; Chambon et al. 2013). Des modifications dans l'image du corps, telles que la perception d'un changement de la forme et la taille ou de la posture du corps, ont été liées au sillon postcentral, au sillon intrapariétal, à l'insula et au lobule pariétal inférieur (Ehrsson et al. 2005; Kavounoudias et al. 2008; Naito et al. 2017) ([Figure 3](#)).

Les études de neuroimagerie chez les sujets sains sont fondamentales pour comprendre les bases neurales qui sous-tendent le soi corporel. Une autre approche étudie cette question par l'intermédiaire des stimulations électriques intracérébrales.

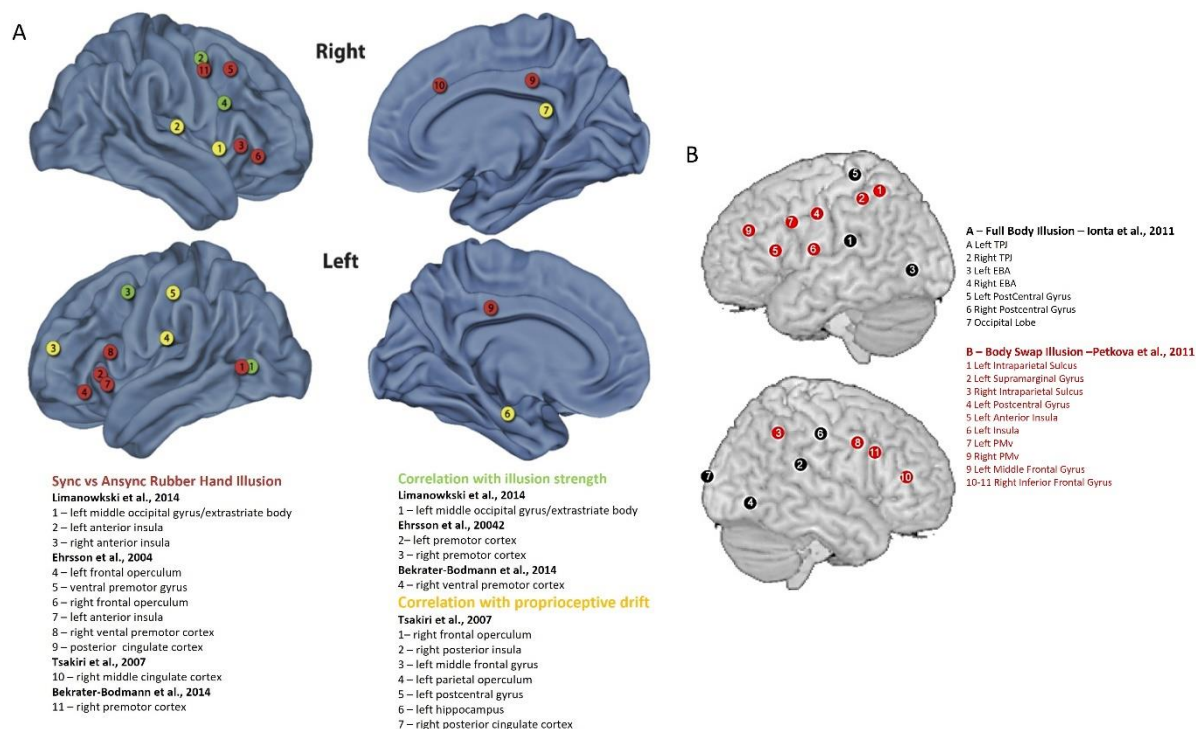


Figure 3 : Bases neurales du soi corporel révélées par des études de neuroimagerie fonctionnelle non invasive. (A) pendant une illusion de la main en caoutchouc. D'après Lenggenhager et Lopez (2014). (B) pendant une illusion du corps entier. D'après Serino et al., (2013).

II. Approches par stimulations électriques intracérébrales

La stimulation électrique est une technique de plus en plus utilisée pour étudier les bases neurales de certains mécanismes cognitifs. Par exemple, les stimulations électriques ont permis de mettre en évidence des réseaux cérébraux impliqués dans la production de la parole (Afif et al. 2010), dans la représentation de scènes visuelles complexe (Schulz et al. 2007), dans la perception des émotions positives (Villard et al. 2023), dans la mémoire autobiographique (Bartolomei et al. 2017a) ou encore dans la localisation perçue du soi (Blanke et al. 2002).

II.1. Aperçu historique des approches par stimulations électriques intracérébrales

L'idée d'utiliser des stimulations électriques pour étudier les fonctions cognitives ou pour traiter de certaines douleurs remonte à l'Antiquité. Dès cette époque, les raies Torpedo, connues pour leurs décharges électriques puissantes, sont préconisées pour soigner certains maux de tête (*Compositiones medicamentorum*, de Scribonius Largo, 46 après J-C). Plus tard, ces poissons sont utilisés dans le traitement des crises d'épilepsie ou de la dépression (Schwalb et Hamani 2008). Au début du XIX^e siècle, des premiers tests utilisant le courant galvanique sont employés pour stimuler le cortex des animaux. Ces études ont mis en évidence que la stimulation électrique de certaines régions corticales entraîne des contractions musculaires chez les chiens (Sironi 2011). Les premières études de stimulation électrique chez l'humain sont réalisées à la même époque. Jean Aladini, professeur de physique et neveu de Galvani, est l'un des premiers à stimuler le cortex cérébral de prisonniers récemment décapités (Figure 4). Pour cela, il enlevait la boîte crânienne, et à l'aide de pile voltaïques, stimulait les méninges ou la surface corticale. Dans son « *Essai théorique et expérimental sur le galvanisme* », Aldini montre que de telles stimulations entraînaient des réactions faciales dans la moitié droite du visage lorsque que la stimulation était appliquée au niveau de l'hémisphère cérébral gauche. De ses expériences, il conclut que la surface corticale est électriquement excitable (Aldini 1804). Ce n'est qu'en 1874, qu'un médecin américain, R. Barthallow, prodigue pour la première fois des stimulations électriques chez l'humain lors d'une chirurgie éveillée (Figure 4). Sa patiente est une femme de 33 ans atteinte d'une tumeur érosive crânienne causant un trou de 2 pouces de diamètre dans le crâne au niveau des lobes pariétaux et temporaux droits. Des stimulations appliquées à cet endroit entraînent une déviation de la tête vers la gauche et une contraction du bras et de la jambe gauche (Zago et al. 2008).

Bien que ces recherches soient prometteuses, il faut attendre le début du XX^e siècle pour que les premières études utilisant des stimulations électriques intracérébrales fournissent une cartographie fonctionnelle du cerveau. Les études pionnières du neurochirurgien W. Penfield permettent pour la première fois de délimiter les aires motrices, visuelles ou encore auditives (Foerster et Penfield 1930; Penfield et Boldrey 1937; Penfield 1947). De plus, Penfield et ses collaborateurs mettent en évidence le rôle majeur des techniques d'enregistrement électroencéphalographique combinées avec les stimulations électriques intracérébrales dans la délimitation de la zone épileptogène. Dans ses rapports d'étude, Penfield décrit l'ensemble des modifications comportementales induites par les stimulations (Penfield 1955) dans les cortex pariétaux, temporaux, frontaux mais également insulaires (voir partie stimulation invasive) lors de chirurgie éveillée chez des patients atteints d'épilepsie focale ou de tumeurs cérébrales.

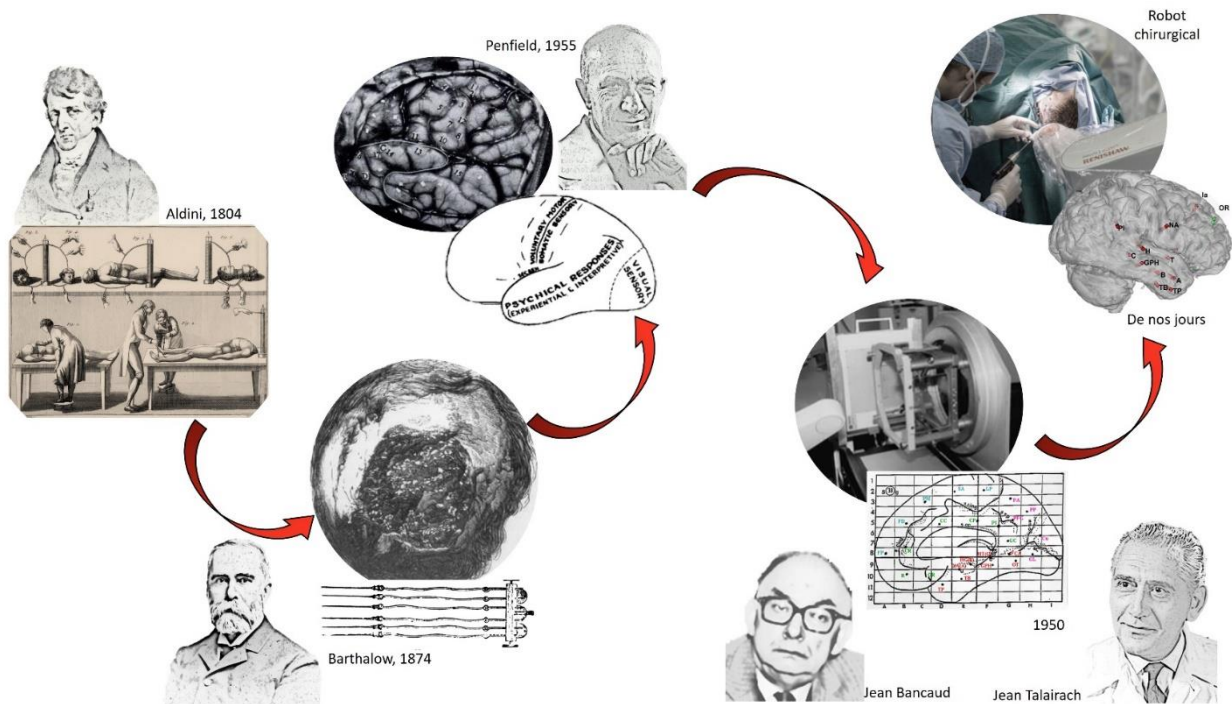


Figure 4 : Evolution de la stimulation électrique chez l'homme.

Au-delà de son importance en neurologie et neurochirurgie, l'intérêt de la recherche en neurosciences pour les stimulations électriques invasives a régressé dans les années 1980 avec l'avènement des techniques de neuroimagerie cérébrale fonctionnelle non invasives comme l'IRM (Figure 5). Contrairement à la stimulation électrique cérébrale, la neuroimagerie fonctionnelle permet de cartographier de manière non invasive le fonctionnement du cerveau chez les patients avec des lésions comme chez les sujets sains. Cependant, de nombreuses critiques ont été faites à l'égard de ces techniques d'IRMf, montrant seulement des corrélations entre un état mental et une activité cérébrale et non un lien de causalité. La stimulation électrique, au contraire, apparaît comme une technique permettant d'établir un lien de causalité. Il faudra ainsi attendre les années 2000 pour que les études de neuroimagerie fonctionnelle se penchent de nouveau sur les techniques de stimulations électriques invasives.

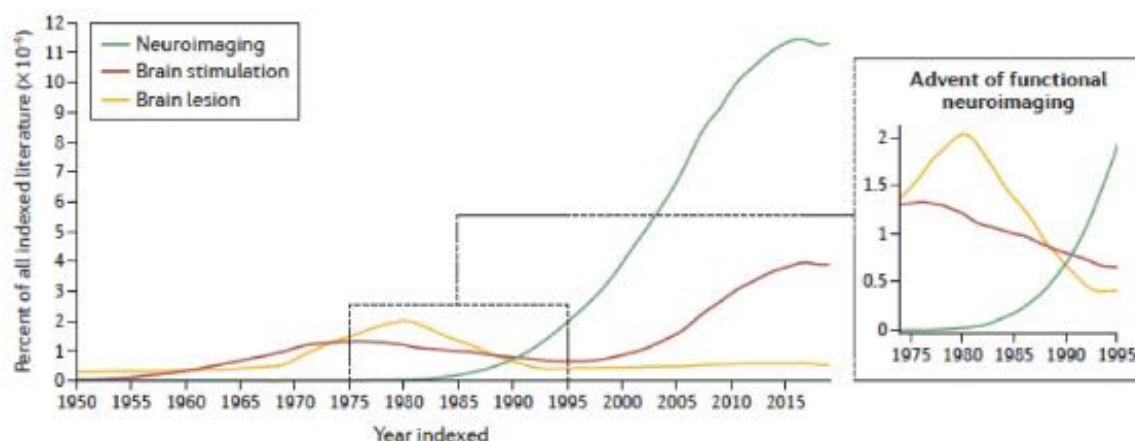


Figure 5 : Évolution de la littérature sur la cartographie fonctionnelle depuis les années 1950. Image issue de Siddiqi *et al.* (2022).

II.2. Comment définir une approche causale dans l'étude de la cartographie cérébrale ?

De grands noms de la philosophie tels qu'Aristote, Thomas d'Aquin ou encore Hume se sont emparés de la réflexion sur la causalité dans les sciences (Ducasse 1966; Gotthelf 1976). Depuis les débuts de la philosophie en Grèce Antique, cette notion est corrélée à l'ambition majeure de rendre intelligible l'origine d'un phénomène, de déterminer la constitution de ce qui est. La définition même de la causalité anime de nombreux débats en philosophie des neurosciences (Ross et Bassett 2024). À l'heure actuelle, il est encore difficile de s'accorder sur une définition précise et consensuelle de la causalité en neurosciences. En 2022, Barack et collaborateurs lançaient un appel à la communauté neuroscientifique pour clarifier le concept de causalité (Barack et al. 2022). Un des problèmes soulevés est que la définition même de la causalité varie en fonction du champ d'application (Barack et al. 2022; Ross et Bassett 2024). Dans cette thèse, nous abordons la causalité appliquée aux méthodes expérimentales dans les neurosciences cognitives et plus précisément les méthodes permettant de cartographier les fonctions cognitives.

Les travaux en neurosciences cognitives tentent de relier une certaine activité cérébrale à une fonction cognitive (Dijkstra et de Bruin 2016; Weichwald et Peters 2021). L'inférence causale consiste à identifier un lien causal entre un symptôme et une région cérébrale afin de comprendre comment les mécanismes cognitifs fonctionnent. Dans le champ des neurosciences cognitives, l'idée selon laquelle les études en neuroimagerie fonctionnelle ne sont pas des approches causales est généralement acceptée (Uddin et al. 2006; Ritaccio et al. 2018). À l'inverse, les études utilisant des stimulations électriques non-invasives ou invasives sont considérées comme étant causales (Siddiqi et al. 2022).

L'objectif de cette partie est de comprendre dans quelle mesure une approche en neurosciences cognitives peut être considérée comme causale.

En philosophie des sciences sur la causalité, plusieurs courants s'affrontent. Parmi ces derniers, une analyse retient notre attention : il s'agit de l'analyse par contrefactuel. Cette dernière consiste à déterminer ce qui se serait passé si une activité avait été différente. En d'autres termes cela vient à proposer que *c* est une cause de *b* si et seulement s'il est vrai que si *c* ne s'était pas produit, *b* ne se serait pas produit. Un raisonnement contrefactuel est donc un raisonnement qui consiste à modifier l'issue d'un événement en agissant notamment sur l'une de ses causes. Une des approches de la causalité par contrefactuel en philosophie des sciences contemporaines est l'interventionnisme. L'interventionnisme stipule que les causes sont des facteurs dont dépendent les événements. Pour qu'une démarche soit considérée comme causale, elle doit être conçue pour estimer ce qui se serait passé si une certaine *intervention* avait conduit à des résultats différents (Woodward 2004; Pearl 2009). Selon cette définition, un événement peut être causal si, toutes choses égales par ailleurs, sa présence ou son absence affecte la probabilité d'un résultat. Pour Woodward, une condition nécessaire et suffisante pour qu'une variable *X* soit une cause directe de *Y* par rapport à un ensemble de variables *Z* est qu'il existe une intervention possible sur *X* qui modifiera *Y* ou sa probabilité (Woodward 2004). De plus, une condition nécessaire et suffisante pour que *X* soit une cause de *Y* par rapport à l'ensemble *Z* est qu'il existe un chemin dirigé de *X* à *Y* tel que chaque lien dans ce chemin est une relation causale directe (Woodward 2004; Dijkstra et de Bruin 2016). Pour résumer, une intervention peut être considérée comme une manipulation qui modifie une variable *X*. Pour que cette manipulation puisse être définie comme causale, elle doit respecter plusieurs caractéristiques : 1) si *I* est une intervention alors, *I* cause *X* ; si *I* atteint une certaine valeur, alors *X* cesse de dépendre des valeurs des autres variables et ne dépend plus que de *I* ; *I* ne cause pas directement *Y* et n'est pas cause de *Y* distinctement de *X* ; et, enfin, *I* est statistiquement indépendant de toute variable *Z* qui cause *Y* sur un chemin qui ne passe par *X* (Woodward 2004; Dijkstra et de Bruin 2016).

En suivant cette analyse par contrefactuel et interventionnisme, nous pouvons être amené à considérer des études en IRMf comme pouvant établir un lien de causalité (Weber et Thompson-Schill 2010; Reid et al. 2019). En effet, certaines expériences en neuroimagerie consistent à comparer les effets d'une tâche cognitive sur l'activité cérébrale et à comparer ces résultats à des conditions contrôles. Ces conditions contrôles permettent d'estimer ce qui se serait passé si la tâche n'avait pas été réalisée ; il s'agit du contrefactuel. Cependant, au lieu de manipuler l'activité cérébrale et d'observer le comportement qui en résulte, ces études manipulent le comportement et observent l'activité cérébrale qui en résulte. C'est pourquoi, certains auteurs considèrent que ce type de méthode ne révèle pas un lien de causalité (Siddiqi et al. 2022). Elles s'appuient uniquement sur les *corrélats* neurophysiologiques ou métaboliques de symptômes ou de comportement (Raichle 2009). Les études de neuroimagerie fonctionnelle (IRMf, PET) ou d'électroencéphalographie sont donc généralement considérées comme reflétant une corrélation entre un état mental et l'activité cérébrale et non un lien de causalité. Un corrélat désigne ainsi des événements qui se produisent ensemble, l'un se produisant si et seulement si l'autre se produit également, sans de réelle explication causale (Havlík et

al. 2023). Comme l'écrit Uddin « *l'imagerie par résonance magnétique fonctionnelle (IRMf) ne fournit que des informations corrélatives sur la relation entre une zone cérébrale donnée et une tâche cognitive particulière. Les relations causales entre le cerveau et le comportement peuvent être testées avec la TMS (stimulation magnétique transcrânienne)* » (Uddin et al. 2006). Bien que la recherche d'un contrefactuel soit nécessaire pour la définition de la causalité, cela ne semble pas une condition suffisante, notamment dans les études de neuroimagerie fonctionnelle (Baumgartner 2009).

Quelles peuvent être les autres conditions nécessaires pour qu'une étude soit définie comme causale dans la cartographie fonctionnelle du cerveau ? À l'heure actuelle, il n'y a pas de réel consensus dans les neurosciences cognitives sur les critères qui permettent d'affirmer avec certitude qu'une relation est causale (Barack et al. 2022). De ce fait, certains auteurs considèrent la force causale d'une étude en fonction de son degré de causalité ou selon son positionnement sur un continuum (Weichwald et Peters 2021; Siddiqi et al. 2022). L'échelle de ce continuum de causalité irait du très improbable au très probable. Pour établir cette dernière, les articles récents en neurologie s'appuient sur neufs points énoncés par Bradford Hill lors de la réunion inaugurale de la Section de médecine du travail en 1965 (Hill 1965). Parmi ces critères, certains points sont particulièrement efficaces pour évaluer la force de l'inférence causale, à savoir :

- La *force de l'association* signifie que plus une association entre l'exposition et l'effet est importante, plus le lien causal est probable ;
- La *relation dose/effet*, traduit la relation entre le niveau d'exposition au facteur (la dose) et le risque observable (l'effet) ;
- La *temporalité* (la cause précède l'effet) traduit l'idée que la cause doit précéder l'effet ;
- La *spécificité* de l'association signifie qu'une cause ne doit entraîner qu'un seul effet
- La *réversibilité* du résultat est un autre critère optionnel, qui désigne la disparition de l'effet lorsque l'intervention est arrêtée ;
- La *cohérence* sous-tend l'idée que l'interprétation de l'association causale trouvée ne se contredit pas ;
- La *preuve expérimentale* critère mal défini par Bradford Hill, peut soit désigner l'existence de données expérimentales chez l'animal qui serviront à comparer avec les résultats obtenus. Elle peut également désigner les données existantes sur les effets d'une intervention.

Ensemble, ces critères révèlent une causalité forte de l'étude. S'appuyant sur ces derniers, Siddiqi et collaborateurs (2022) proposent d'appliquer ce continuum de causalité aux différentes techniques de cartographie cérébrale ([Figure 6.A](#)). L'étude des lésions et les méthodes de stimulations invasives sont celles qui obtiennent des scores de causalité les plus élevés. Lors d'une stimulation invasive un courant électrique est délivré à une certaine intensité dans une région spécifique du cerveau et une réponse est observée. Dans cette situation, le contrefactuel peut être l'absence d'une réponse lorsque la région n'est pas stimulée. On peut également agir sur la dose/effet en modulant l'intensité de la stimulation. La spécificité peut aussi être démontrée lorsque des

interventions faites de façon légèrement différente induisent des résultats différents. Dans le cas des stimulations électriques, il a été démontré qu'une intervention dans l'aire fusiforme du visage entraînait chez des patients une incapacité à reconnaître des visages, alors que des stimulations hors de cette région n'entraînaient aucune perturbation. Ce résultat relie causalement la région fusiforme à la perception des visages (Parvizi et al. 2012) et montre la spécificité de la relation causale. Enfin, les méthodes de stimulation électrique répondent au critère de réversibilité dans la mesure où lorsque la stimulation s'arrête, la modification cérébrale induite est interrompue et revient rapidement à l'état d'avant la stimulation (Figure 6.B). De plus, la stimulation électrique invasive permet également de satisfaire le critère de preuve expérimentale, et ce par exemple en appliquant une stimulation « sham », c'est-à-dire une stimulation placebo dans la même région ou une stimulation non délivrée, ne provoquant pas de réponse. Enfin, il convient de noter que le critère de cohérence est rempli si et seulement si différentes approches convergent vers des résultats similaires. De ce fait, la cohérence nécessite l'implication d'autres techniques de cartographie causale (analyse de recouvrement spatial de lésions cérébrales, etc.). La convergence de différentes techniques de cartographie cérébrale permet ainsi d'inférer une causalité forte. De nombreuses études appliquent cette démarche en combinant différentes méthodes, en particulier l'approche par lésions avec l'approche par stimulations électriques (Darby et al. 2018; Li et al. 2023).

A

	Neuroimagerie sans tâche	Neuroimagerie fondée sur des tâches	Atrophie accidentelle	Neurofeedback	Lésion accidentelle	Stimulation électrique intracérébrale
Contrefactuel	X	✓	✓	✓	✓	✓
Cohérence	X	X	X	X	X	X
Preuve expérimentale	X	X	X	✓	X	✓
Relation dose/réponse	X	X	✓	X	✓	✓
Spécificité	X	✓	✓	✓	✓	✓
Temporalité	X	X	X	X	✓	✓
Réversibilité (optionnel : 0,5pt)	X	X	X	✓	✓	✓
Score	0	2	3	3,5	4,5	5,5



Causalité faible
Causalité forte

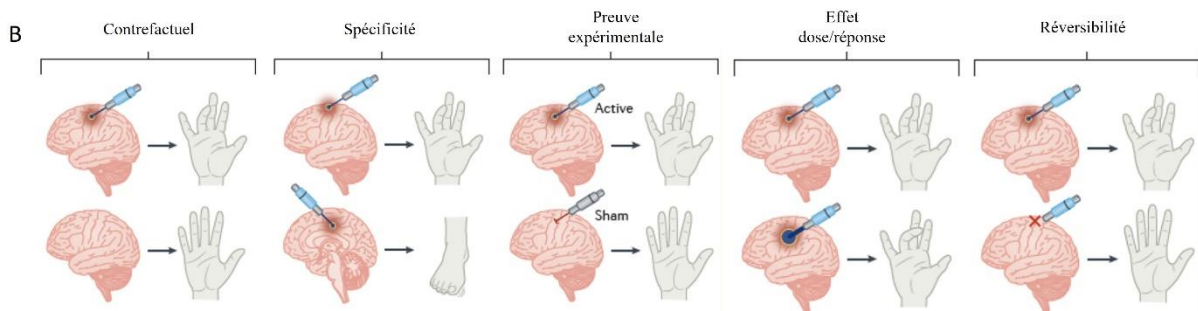


Figure 6 : Évaluation de la force de la causalité dans les études de cartographie du cerveau humain. A) Adaptation du continuum de causalité proposé par Siddiqi et al. (2022) selon les différentes techniques de cartographie cérébrale, allant du moins causal (rouge) au plus causal (vert). ✓ = critère pouvant être évalué par une méthode particulière. ✗ = critère qui ne peut pas être évalué (ou qui n'est pas applicable) à une méthode. B) Exemplification avec la méthode de stimulation électrique intracrânienne de cinq critères de Bradford Hill pour évaluer la causalité.

II.3. *Stimulations non-invasives dans l'étude du soi corporel*

Une des approches de stimulation non invasive que nous n'avons pas mentionnée jusqu'à présent est la stimulation magnétique transcrânienne (TMS). Cette technique consiste à moduler l'excitabilité du cerveau grâce à une stimulation magnétique transcrânienne appliquée sur le cuir chevelu du sujet. Un nombre important d'études en neurosciences cognitives suggèrent que la TMS permet d'induire une inférence causale entre une région stimulée et un comportement observé (Hobot et al. 2021). L'étude des bases neurales du soi corporel n'est pas restée étrangère à cette approche. Des travaux ont appliqué des stimulations magnétiques au niveau du cortex moteur primaire ou du lobule pariétal inférieur pour étudier le sentiment d'appartenance lors d'une illusion de la main en caoutchouc (Kammers et al. 2009; Casula et al. 2022) ou encore de la jonction temporo-pariétale pour étudier le changement de perspective ou le sentiment d'identification (Tsakiris et al. 2008; van Elk et al. 2017; Martin et al. 2020).

Cependant, des études critiques sur la TMS révèlent certaines limites de cette technique dans l'induction d'une inférence causale (Weichwald et Peters, 2021). Par exemple, les effets neurophysiologiques dus à la TMS ne sont pas entièrement compris rendant l'application seule de la TMS insuffisante dans l'inférence causale (Hobot et al. 2021). Le degré de l'inférence causale dans le continuum que nous avons proposé précédemment est donc plus faible que celle des lésions ou de la stimulation électrique invasive. Bergmann et Hartwigsen dans un article récent de 2021 ont mis en évidence de nombreuses limites à l'inférence causale en TMS. Ils fournissent un ensemble de recommandations pour dépasser ces obstacles et améliorer la force de l'inférence causale dans les études de stimulations non-invasives (Bergmann et Hartwigsen 2021).

II.4. Stimulations invasives : focus sur la stéréo-électroencéphalographie

Les stimulations électriques invasives sont généralement utilisées lors de l'évaluation pré-chirurgicale de l'épilepsie ou lors de chirurgies éveillées pour la résection de tumeurs ou de foyers épileptiques (Penfield et Boldrey 1937; Penfield 1947). Il existe différentes méthodes d'implantation d'électrodes et donc de stimulations électriques cérébrales (Figure 7). L'électrocorticographie (ECoG) consiste à insérer des grilles d'électrodes sous-durales ou des bandes d'électrodes à la surface du cortex cérébral permettant de couvrir et d'échantillonner une grande surface du cortex. Cependant, cette méthode ne permet pas d'enregistrer des régions profondes comme l'insula ou le cortex cingulaire. La **stéréoencéphalographie** (SEEG) consiste à insérer des électrodes afin de stimuler et d'enregistrer l'activité électrophysiologique de régions corticales ou sous-corticales telles que le thalamus, l'hippocampe ou encore l'amygdale. Enfin, pendant la chirurgie éveillée, une électrode est stimulée sur la surface corticale. Pendant la stimulation électrique, un courant électrique de quelques mA est directement délivré dans le cerveau pour la SEEG et sur le cortex pour l'ECoG et lors de chirurgie éveillée (Trébuchon et al. 2012). Dans le cadre de cette thèse, nous développerons plus en détails la méthode de la SEEG car elle sera centrale dans nos études expérimentales.

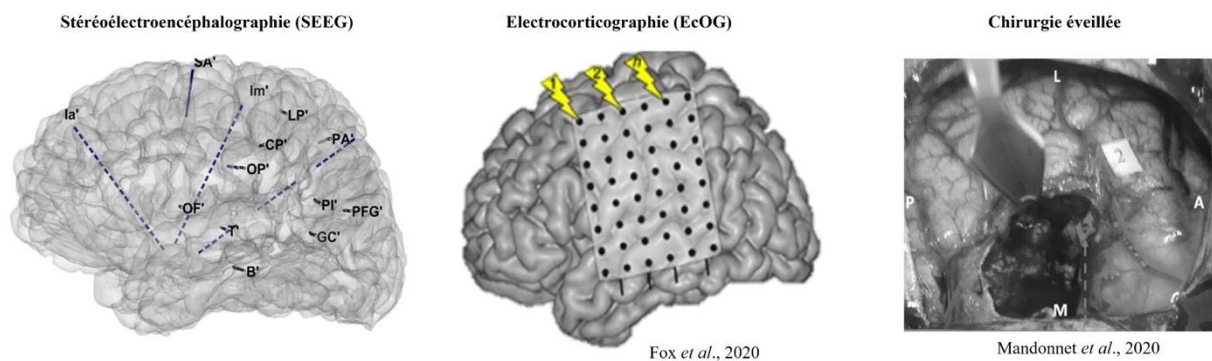


Figure 7 : Différentes techniques de stimulations électriques intracérébrales. La SEEG consiste à insérer des électrodes dans les régions corticales et sous corticales. L'ECoG consiste à insérer des grilles sous-durales ou des bandes d'électrodes à la surface du cortex cérébral. Lors d'une chirurgie éveillée, une stimulation est appliquée à la surface du cortex cérébral à l'aide d'une sonde de stimulation. D'après Fox *et al.*, (2020) et Mandonnet *et al.*, (2020).

La SEEG est une méthode d'enregistrement de l'activité électrique intracérébrale utilisée chez des patients avec une **épilepsie pharmaco-résistante**. En 1949, Hayne et Meyer publient un premier rapport sur l'implantation stéréotaxique d'électrodes chez des patients épileptiques. À la même époque, Jean Talairach et Jean Bancaud développent un outil d'implantation qui améliore les techniques stéréotaxiques chez les patients épileptiques. Le cadre stéréotaxique permet de situer chaque point du cerveau du patient dans un espace de référence. L'implantation d'électrodes en profondeur permet à la fois

d'enregistrer l'activité des structures corticales et sous-corticales, mais aussi d'analyser l'apparition des crises, leur propagation et de corrélérer l'apparition de ces dernières avec des caractéristiques cliniques. De plus, pour les deux neurochirurgiens français, l'objectif est de définir la zone épileptogène, c'est-à-dire la région d'où se propage la crise d'épilepsie (Talairach et Bancaud 1966). La SEEG permet pour la première fois d'étudier les crises spontanées des patients (Reif et al. 2016).

Dans l'atlas de Talairach, les régions cérébrales implantées sont référencées selon un ensemble de coordonnées alphanumériques à partir d'un cerveau post-mortem (Talairach et Tournoux 1988). Un système de lignes est défini et repose sur des repères tels que le troisième ventricule, les commissures antérieure et postérieure (AC-PC), les contours internes du crâne et de structures de référence telles que le sillon sylvien, le sillon temporal supérieur, le sillon rolandique ou encore le sillon frontal inférieur. Ce système permet la normalisation de chaque cerveau individuel sur un référentiel standard (Figure 8). De nos jours, l'implantation des électrodes intracérébrales est réalisée à l'aide d'un robot chirurgical (Faraji et al. 2020) toujours dans un cadre stéréotaxique.

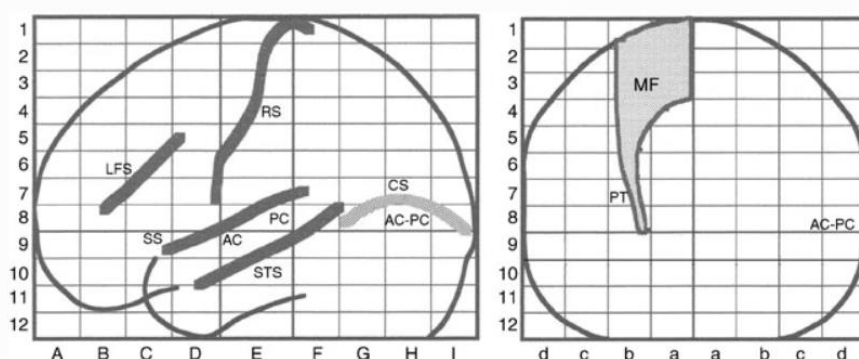


Figure 8 : Système de grilles proportionnelles. Différentes structures sont repérées à l'aide des grilles : AC-PC : commissures antérieure et postérieure ; SS : sillon sylvien ; STS : sillon temporal supérieur ; LFS : sillon frontal supérieur ; RS : sillon rolandique ; CS : sillon calcarin ; MF : fibres motrices, PT : faisceau pyramidal. Image reproduite d'après Benabib *et al.* (2009).

II.4.A. Procédure

Chaque patient possède un schéma d'implantation qui est élaboré en fonction des hypothèses sur la localisation de la zone épileptogène. Ces hypothèses sont issues d'un ensemble de données de neuroimagerie (IRM), de l'examen neurologique et neuropsychologique, des enregistrements vidéo-EEG non invasifs, ainsi que de la sémiologie des crises. Le nombre d'électrodes implantées varie de 8 à 15 en moyenne et chaque électrode de 0,8 mm de diamètre possède 5 à 18 plots espacés de 1,5 mm (Mercier et al. 2022) (Figure 9. A). Après la phase d'implantation, le patient reste à l'hôpital pendant deux semaines environ. L'objectif pour les cliniciens est d'enregistrer le plus de crises

possibles afin d'analyser l'activité électrique enregistrée et de définir la zone épileptogène (Isnard et al. 2018; Trébuchon et al. 2020). Des stimulations électriques bipolaires sont délivrées entre paires de contact d'électrodes adjacents. Les cliniciens délivrent un courant de faible intensité (souvent entre 0,5 et 3 mA) généralement 1 Hz ou à 50 Hz (Mercier et al. 2022). En France, un collectif de cliniciens a publié un article qui énonce, après concertations de 15 centres français, les différentes directives à suivre pour les stimulations intracrâniennes (Isnard et al. 2018). Comme les paramètres de stimulations varient selon les pays, je ne rapporterai ici que ceux utilisés en France.

Les stimulations à 50 Hz (train) durent de 3 à 8 s et chaque pulse dure entre 0,5 et 1 ms (Figure 9.B). Les stimulations par train sont utiles pour déclencher des crises mais également pour réaliser une cartographie fonctionnelle (Trébuchon et Chauvel 2016; George et al. 2020). Les stimulations à 1 Hz (choc) peuvent durer de 20 à 60 s, la durée de chaque pulse dure entre 0,5 et 3 ms et l'intensité peut aller jusqu'à 4 mA. Les stimulation par chocs sont utiles également pour déclencher des crises, en particulier dans l'hippocampe, le gyrus de Heschl ou dans les dysplasies corticales (Trébuchon et Chauvel 2016). La fréquence de stimulation conditionne l'apparition de réponses électrophysiologique dans certaines régions mentionnées ci-dessus (1 Hz) et de réponses cliniques (50 Hz) (Donos et al. 2016; Mohan et al. 2020). Au cours de la séance de stimulations, le patient peut réaliser certaines tâches cognitives (lecture, dénomination, mémorisation, etc.) et le clinicien note les différentes réponses ou comportements observés, comme des mouvements involontaires ou l'arrêt de la parole. Le clinicien consigne également les expériences rapportées par les patients, telles que des hallucinations auditives, visuelles ou émotionnelles (Selimbeyoglu et Parvizi 2010; Drane et al. 2021).

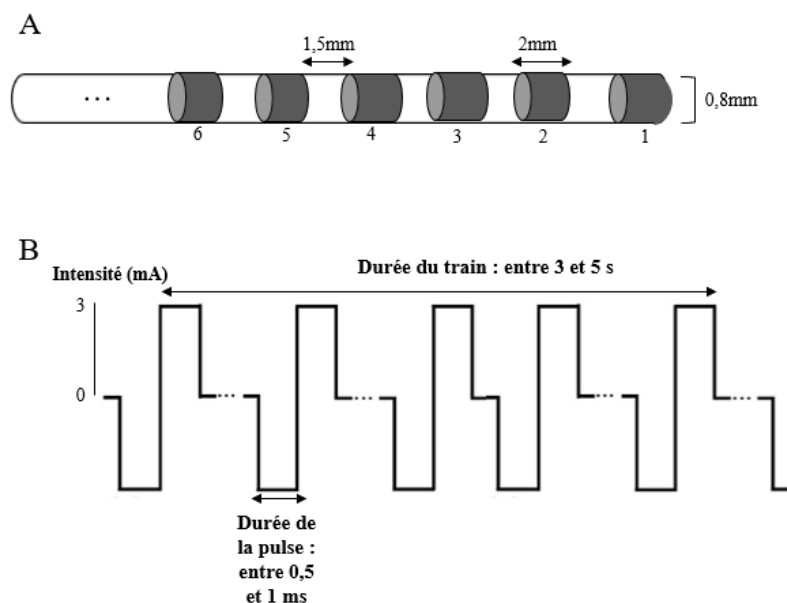


Figure 9 : Configuration des électrodes et paramètres pour les stimulations électriques par train. A) Configuration des électrodes SEEG utilisées pour la stimulation. B) Représentation des paramètres de stimulation d'une pulsation biphasique. Image adaptée de Qi *et al.* (2022).

II.4.B. Résumé de la littérature sur les bases neurales du soi corporel révélées par stimulations électriques intracérébrales

De nombreux auteurs s'accordent sur le fait que la stimulation électrique invasive est le « gold-standard » (Mandonnet et al. 2010) dans la cartographie fonctionnelle cérébrale. Cette technique possède plusieurs avantages. Un premier est que chaque structure répondant à une stimulation sera perturbée électriquement et donc sera impliquée dans un réseau fonctionnel (Mandonnet et al. 2010). L'enregistrement en continu de l'activité cérébrale permet d'identifier l'étendue des réseaux impliqués (Duffau 2015). Un second est que cette technique établit un lien de causalité fort entre une réponse et une région stimulée (Johnson et al. 2020; Siddiqi et al. 2022) (voir partie II.2 p.29). Cette technique semble donc particulièrement adéquate pour étudier les bases neurales du soi corporel.

Dans une revue systématique et méta-analyse de la littérature, publiée en février 2023 dans *Human Brain Mapping* (Dary et al., 2023), nous avons regroupé l'ensemble des études qui utilisent des stimulations électriques intracérébrales lors de chirurgie éveillée ou d'évaluation préchirurgicale de l'épilepsie. Nous avons répertorié 42 études, publiées entre 1930 et 2021. Nous avons identifié 121 cas de patients qui rapportent une modification d'une ou plusieurs expériences du soi corporel à la suite d'une stimulation électrique intracérébrale. L'occurrence de ces modifications à travers ces études s'élève en moyenne à 6,2%. Les expériences corporelles les plus souvent altérées lors de stimulations sont la localisation du soi, qui représente 56% de toutes les réponses, l'agentivité (20%) et l'image du corps (13%).

Des changements dans la localisation de soi, tels que des illusions de mouvement semblables à des sensations vestibulaires, sont évoqués par exemple lors de stimulations de l'hippocampe (Halgren et al. 1978). Ce type d'illusions est également évoqué lors de stimulations du lobule pariétal inférieur (Balestrini et al., 2015 ; Blanke et al., 2000), de l'opercule pariétal (Kahane et al. 2003) ou encore de l'insula (Mazzola et al. 2014). Des modifications de l'agentivité sont rapportés lors de la stimulation au niveau des aires motrices supplémentaires (Fried et al., 1991), du lobule pariétal inférieur (Desmurget et al., 2009), ou encore au niveau du gyrus précentral et du gyrus frontal supérieur (Andelman-Gur et al., 2020). Enfin, des stimulations du cortex cingulaire moyen (Popa et al., 2019), de l'insula postérieure (Hao et al., 2022) ou encore du lobule pariétal inférieur (Blanke et al., 2002) entraînent une modification de l'image du corps.

L'analyse de ces études montre que 32% des réponses sont évoqués dans le cortex pariétal, notamment au niveau du lobule pariétal inférieur. La majorité des altérations de la localisation du soi sont rapportées au niveau du cortex cingulaire moyen, de l'insula postérieure et du complexe hippocampique-amygdalien. Les modifications de l'agentivité sont davantage rapportées au niveau du cortex frontal et pariétal, notamment dans les aires somatosensorielles (gyrus postcentral) ou dans les aires motrices (gyrus précentral). Enfin, les réponses liées à une modification de l'image du corps sont davantage rapportées au niveau du lobe pariétal (lobule pariétal supérieur et inférieur, opercule pariétal). Ensemble, ces données ont mis en évidence six régions clés du réseau du soi corporel, à savoir le lobule pariétal inférieur, l'insula postérieure, l'aire motrice

supplémentaire, le cortex cingulaire moyen, le complexe hippocampique et le précuneus (Figure 10).

Cependant, l'ensemble des études considérées pour cette analyse se focalisent soit sur des régions spécifiques (cartographies fonctionnelles de l'insula ou du cortex cingulaire; Mazzola et al., 2014 ; Oane et al., 2020 ; Sun et al., 2021), soit sur une unique expérience corporelle (Desmurget et al. 2009; Fornia et al. 2020), soit rapportent des études de cas (Blanke et al. 2002; De Ridder et al. 2007; Bos et al. 2016; Yu et al. 2018a). Aucune étude n'a eu pour objectif principal d'étudier le réseau sous-tendant le soi corporel incluant les différentes expériences à la base du soi corporel, et sans a priori sur les régions cérébrales à explorer.

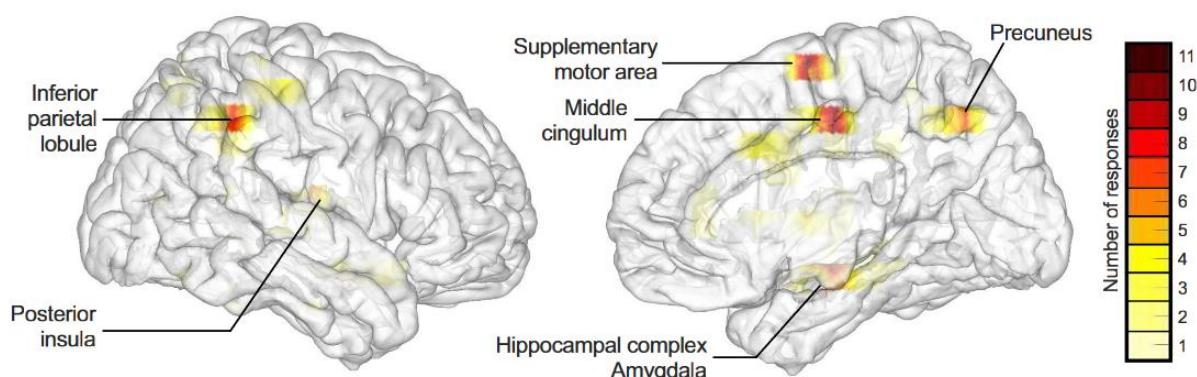


Figure 10 : Cartes de densité montrant le nombre de stimulations électriques intracrâniennes qui évoquent des perturbations du soi corporel. Cette analyse, menée indépendamment de la catégorie de perturbations du soi corporel, a révélé 6 régions principales impliquées dans le soi corporel. D'après Dary et al. (2023).

III. Du localisationnisme au connectome humain

“The functional properties of a nervous system are largely determined by the characteristics of its component neurons and the patterns of synaptic connections between them” (White et al. 1986)

La cartographie cérébrale a reposé pendant longtemps sur le dogme du localisationnisme selon laquelle une région cérébrale a une fonction spécifique. Une lésion au niveau de cette région entraînerait par conséquent un trouble dans la fonction liée. L'exemple souvent cité dans la littérature est l'aire de Broca qui, en cas de lésion, entraîne une aphasie (Broca, 1861). D'autres cas cliniques très célèbres tels que celui de

Phineas Gage de Harlow (Harlow, 1999) ou le patient HM de Scoville et Milner (Scoville et Milner, 1957) montrent également que des déficits comportementaux ou cognitifs peuvent résulter d'une lésion focale. Les travaux par stimulations électriques corticales de Penfield et collaborateurs ont aussi mis en évidence la spécialisation fonctionnelle de régions du cortex chez l'Homme (Penfield, 1947 ; Penfield et Boldrey, 1937 ; Penfield et Jasper, 1954). Cependant, des études sur les mécanismes compensatoires fonctionnels ou sur les mécanismes de déconnexion des réseaux ont remis en cause le concept de localisation fonctionnelle rapporté à une seule région dans le cerveau humain (Gajardo-Vidal et al., 2021 ; Geschwind, 1965). Les études de Geschwind ont montré, par exemple, que l'attention spatiale était liée à un ensemble d'aires corticales fronto-pariétales et de noyaux sous-corticaux interconnectés par des faisceaux de matière blanche. De ce fait, de plus en plus d'études soutiennent désormais l'idée d'une organisation plus distribuée des fonctions cognitives (Duffau, 2021 ; Fox, 2018 ; Thiebaut de Schotten et Forkel, 2022).

Ces nouvelles approches ont ainsi développé un vaste domaine de recherche sur le **connectome humain**. Le connectome désigne une carte qui répertorie l'ensemble des connexions cérébrales. Le développement de cette approche depuis les années 1980 peut s'expliquer d'une part par l'évolution dans le domaine de la physique statistique des réseaux complexes avec notamment le développement de nouvelles méthodes pour quantifier, analyser et modéliser l'organisation et les interactions de larges réseaux complexes (internet, réseau aérien, etc.). Une deuxième explication trouve son origine dans l'évolution des méthodes de mesure et de visualisation du cerveau humain à plusieurs échelles, par exemple, l'IRM pour cartographier les réseaux anatomiques et fonctionnels à l'échelle macroscopique ou encore l'optogénétique pour tracer les voies à l'échelle mésoscopique chez de nombreuses espèces animales (Fornito et al. 2016).

L'analyse du connectome peut s'appuyer sur la théorie des graphes pour modéliser et simplifier l'ensemble des régions interconnectées (Fornito et al. 2016). Dans cette perspective, un réseau est ainsi décrit comme un ensemble de nœuds (régions corticales ou sous-corticales) connectés par des arrêtes (liens). Certains nœuds très connectés sont considérés comme des hubs. La connectomique peut être analysée à différentes échelles, que ce soit au niveau macroscopique, mésoscopique ou microscopique (Fornito, Zalesky, et Bullmore, 2016). L'échelle microscopique désigne l'étude du neurone et de la manière dont il traite et transmet l'information. L'échelle mésoscopique se caractérise par l'étude du circuit local de neurones et de sa connectivité. Enfin, l'échelle macroscopique désigne l'étude de l'organisation cérébrale en un réseau de structures neuronales et de fonctionnelles. Dans le cadre de cette thèse, nous nous focaliserons sur les échelles mésoscopique et macroscopique.

Une première façon d'établir un connectome est d'identifier les voies de connexions constituées des faisceaux de fibres de la matière blanche. Il s'agit là d'établir un connectome structural. Pour cela, les techniques de neuroimagerie comme l'IRM permettent échantillonner l'ensemble du cerveau à l'échelle macroscopique. Le connectome fonctionnel, quant à lui, repose sur la dépendance statistique temporelle entre des signaux enregistrés et des régions cérébrales distantes. Si les méthodes utilisées dans la connectivité fonctionnelle se rapportent à la SEEG ou à l'ECOG, on se situe au niveau mésoscopique. À l'inverse, si le connectome fonctionnel est réalisé grâce à IRMf,

on se place au niveau macroscopique. Enfin, la connectivité effective intègre la notion de causalité : une structure A cause un changement ou non sur une structure B. La [Figure 11](#) représente les différentes méthodes d'analyse de connectivité.

Les relations entre les différents niveaux de connectivité alimentent un débat dans les neurosciences, notamment entre la connectivité structurale et fonctionnelle. De nombreuses études ont mis en évidence le fait que les régions connectées sur le plan structural le sont généralement sur le plan fonctionnel. Cela suggère donc un chevauchement entre la connectivité structurale et fonctionnelle. Des travaux ont d'ailleurs montré que le degré d'activation fonctionnelle d'une région corticale était influencé par des propriétés structurelles de la région en question, notamment par son volume cortical, son épaisseur, ou encore sa surface (Litwińczuk et al., 2022). La densité de connexions locales semble également influencer la quantité d'activité corticale échangée entre les régions. Enfin, l'échange d'activité corticale entre des régions éloignées est plus efficace lorsqu'il est soutenu par des fibres de substance blanche de longue portée (Bullmore et Sporns, 2012). Bien qu'il existe des liens entre connectivité structurale et fonctionnelle, les cartes de connectivité peuvent être différentes (Fox, 2018). Chacune des connectivités présenterait des caractéristiques uniques. Des études ont ainsi montré que des connections fonctionnelles fortes existent entre des régions sans connexion structurelle directe (Honey et al. 2009). De plus, d'autres études ont montré que des régions qui ne sont pas directement connectées par des fibres de substance blanche peuvent présenter des patrons d'activité corrélés, suggérant que ces régions sont indirectement connectées fonctionnellement (Litwińczuk et al., 2022).

Ensemble, ces résultats montrent que l'étude de la connectivité structurale et fonctionnelle apporte des informations complémentaires dans l'analyse des réseaux fonctionnels. Seulement quelques études ont combiné les différentes approches de connectivité pour étudier la localisation du soi (Bratu et al. 2021), l'image corporelle³ (Moayedi et al. 2021) ou encore le sentiment d'appartenance du corps (Mandonnet et al. 2020).

³ Dans leur article, Moayedi *et al.* (2021) définissent l'image corporelle comme une perception dynamique consciente de la représentation du corps.

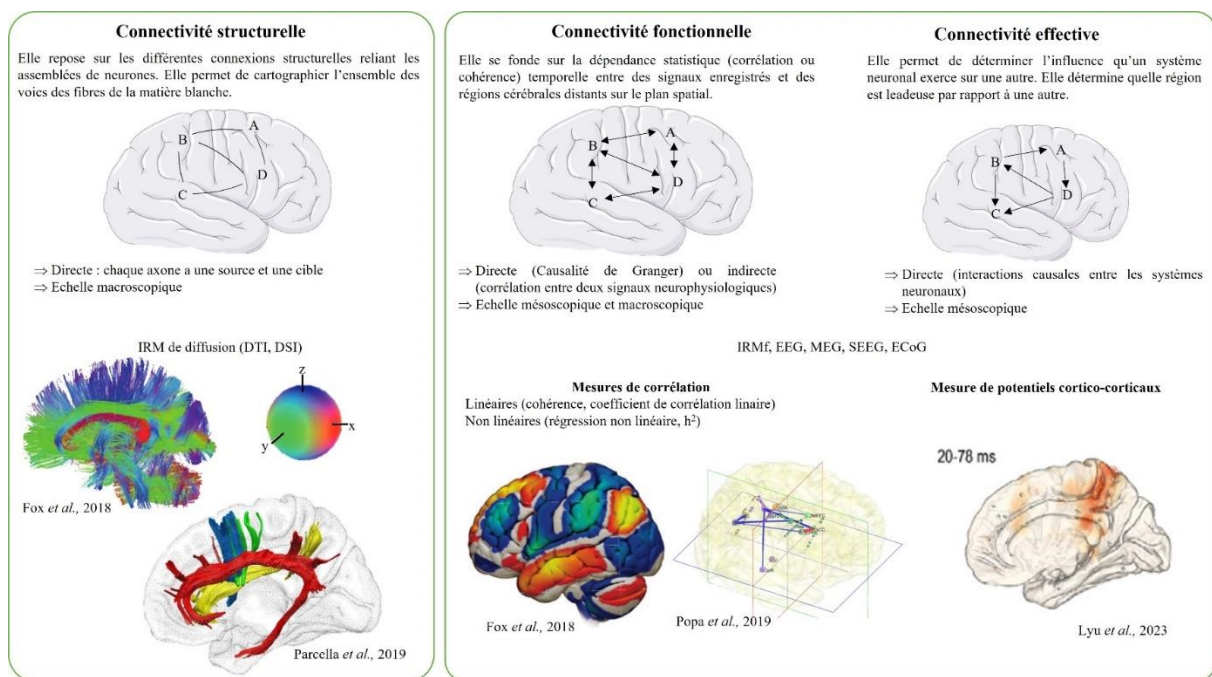


Figure 11 : Les différentes méthodes d'analyse de la connectivité.

III.1. Connectivité structurale et soi corporel

La connectivité structurale repose sur les différentes connexions entre assemblées de neurones ; elle se situe à l'échelle macroscopique. Elle permet de cartographier l'ensemble des voies constituées par les fibres de la matière blanche. Cette méthode est possible grâce à l'imagerie de tenseur de diffusion (DTI). Le principe repose sur l'IRM de diffusion. Cette technique permet d'observer la diffusion des molécules d'eau dans le cerveau humain et ainsi d'étudier la microarchitecture de ses tissus (densité, organisation structurale). Dans le cerveau et dans les différentes structures qui le composent, la diffusion de l'eau n'est pas identique dans toutes les directions ; il s'agit d'un milieu anisotrope. La diffusion de l'eau est contrainte par les axones des neurones de la matière blanche, elle ne peut pas se déplacer dans toutes les directions. Le mouvement des molécules est limité dans les directions perpendiculaires à leur axe d'orientation. La circulation des molécules d'eau est donc plus facile le long des faisceaux d'axone. Ainsi, grâce à la mesure du déphasage lié au déplacement de ces molécules selon plusieurs axes, il est possible d'identifier les directions selon lesquelles ces molécules se diffusent avec le plus de facilité. La connectivité structurale est le résultat de la tractographie obtenue.

Un courant de recherche récent analyse les effets de déconnexions de matière blanche à la suite d'une lésion afin d'identifier les réseaux neuronaux sous-jacents (Thiebaut de Schotten et al. 2020) (Figure 12). Dans un article d'opinion publié dans *Frontiers in Integrative Neuroscience*, nous avons souligné que ce type d'approche est depuis quelques années appliqué à l'étude des bases neurales du soi corporel (Dary et

Lopez 2023). Par exemple, dans un article récent de Pacella et collaborateurs (2019), l'étude des déconnexions des réseaux chez 174 patients ayant eu un AVC dans l'hémisphère droit, montre que le système limbique, le réseau attentionnel ventral et le réseau prémoteur sont impliqués dans la conscience motrice, et donc potentiellement dans le réseau de l'agentivité.

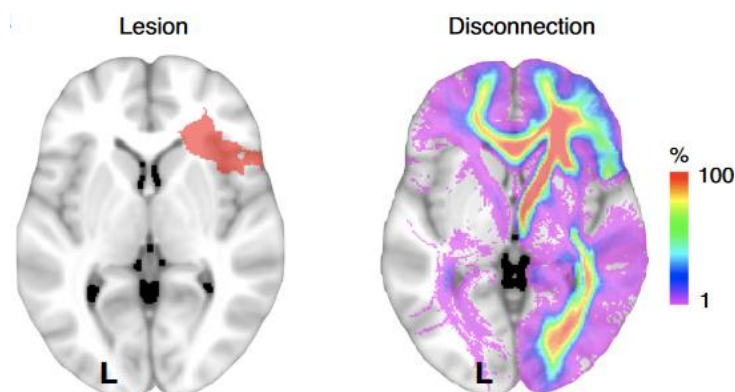


Figure 12 : L'estimation des déconnexions d'une lésion cérébrale. D'après Thiebaud de Schotten *et al.* (2020).

III.2. *Connectivité fonctionnelle et soi corporel*

La connectivité fonctionnelle, concept proposé par Karl Friston en 1994, se fonde sur la dépendance statistique (corrélation ou cohérence) temporelle entre des signaux enregistrés et des régions cérébrales distantes (Friston 1994). Les corrélations temporelles sont considérées comme étant le résultat d'interactions neuronales de régions à distance au sein d'un réseau (Figure 11). La connectivité fonctionnelle peut être étudiée grâce à différentes techniques : l'EEG, la MEG, PET, IRMf (échelle macroscopique) ou encore par SEEG ou ECoG (échelle mésoscopique). Un grand nombre de méthodes permet d'estimer la connectivité fonctionnelle. Un article de Wang et collaborateurs répertorie 42 méthodes et détaille les paramètres les mieux adaptés selon la situation d'analyse envisagée (Wang et al. 2014).

III.2.A. Connectivité fonctionnelle en IRMf et soi corporel

En IRMf, par exemple, il est possible d'enregistrer les variations de concentration en désoxyhémoglobine dans le sang (BOLD). Les variations du signal BOLD sont majoritairement observables dans la matière grise, notamment dans les régions corticales. Il a été en effet montré que sans tâche cognitive effectuée, une variation dans l'activité du signal BOLD est observable dans la matière grise ce qui traduit un fonctionnement par défaut. Cette oscillation du signal BOLD toutes les 20 à 100 secondes est synchronisée dans plusieurs régions plus ou moins éloignées, ce qui permet de

déterminer un réseau fonctionnel du cerveau à l'état de repos. Il existe différents réseaux fonctionnels avec une activité au repos spécifique (Yeo et al. 2011; Raichle 2015). Par exemple, sept réseaux fonctionnels sont généralement décrits : le réseau du mode par défaut (*default mode network*, DMN), le réseau de saillance (*salience network*), le réseau visuel, le réseau somatosensoriel, le réseau dorsal de l'attention, le réseau limbique et le réseau fronto-pariétal (Figure 13.A) (Yeo et al. 2011; Fox et al. 2020). Dans le cadre de cette thèse, nous détaillerons seulement deux réseaux fonctionnels, le DMN et le réseau de saillance, du fait de leur rôle central dans les mécanismes cognitifs liés au soi.

(a) Le réseau du mode par défaut

Le DMN, terme proposé en 2001 par Raichle, est un réseau central dans la cognition (Raichle et al. 2001) (Figure 13.B). Il est présent chez le rat, le primate non humain, le chat et l'Homme (Lu et al. 2012). Il est constitué de régions corticales bilatérales et symétriques dans le cortex pariétal médian et latéral (précuneus, cortex cingulaire postérieur, gyrus angulaire), le cortex préfrontal ventro-médian (cortex cingulaire antérieur) et dans le cortex temporal médian et latéral (cortex enthorinal, hippocampe). Le DMN s'active lorsque le sujet n'effectue pas une tâche qui demande de l'attention ; son activité diminue lorsque des tâches cognitives sont réalisées. Il est souvent considéré comme le réseau du vagabondage mental, de la rêverie éveillée, suggérant l'existence d'une activité cérébrale de repos (Raichle 2015). Cependant, le DMN est impliqué dans des mécanismes cognitifs plus complexes qui sous-tendent par exemple le traitement émotionnel (cortex préfrontal ventromédian), l'activité mentale se rapportant à soi (cortex préfrontal dorso-latéral et le souvenir d'expériences antérieures (précuneus, cortex cingulaire postérieur) (Raichle 2015).

(b) Le réseau de saillance

Le réseau de saillance est constitué du cortex cingulaire antérieur, de l'insula antérieure, ainsi que de certains noyaux de l'amygdale, de l'hypothalamus, du striatum ventral et du thalamus (Figure 13). Il établit une relation entre tout ce qui est relatif à soi et au monde extérieur. En effet, il joue un rôle crucial dans l'identification des stimuli endogènes et exogènes les plus pertinents afin d'adapter le comportement le plus rapidement possible. Il intervient dans les mécanismes cognitifs liés aux émotions, à la douleur, à la motivation, à la récompense ou encore à la conscience de soi, par l'intégration d'informations sensorielles ou émotionnelles (Craig 2009; Menon 2015). Le réseau de saillance est hautement connecté au DMN (Menon et al. 2023) et au réseau fronto-pariétal.

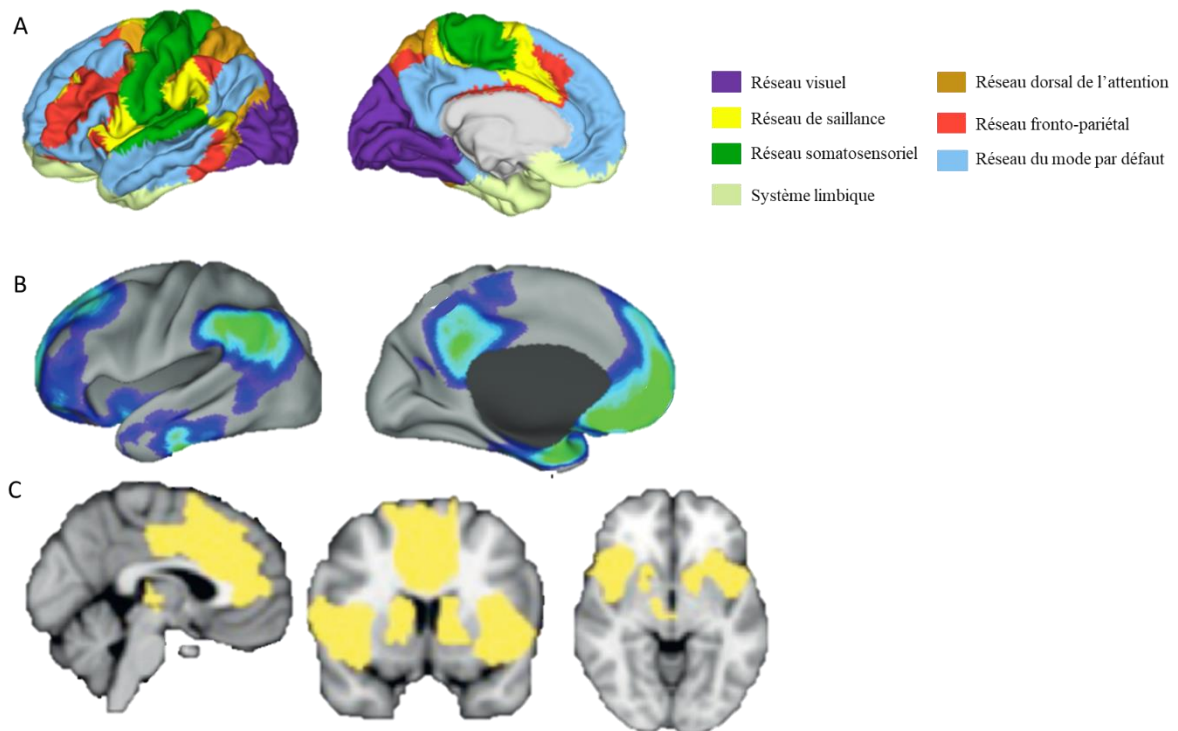


Figure 13 : Les différents réseaux fonctionnels. A) Les sept principaux réseaux fonctionnels du cerveau humain. Image adaptée de Fox *et al.* (2020). B) Connectivité fonctionnelle à l'état de repos du réseau du mode par défaut. Image adaptée de Raichl *et al.* (2015). C) Réseau de saillance. Image adaptée de Menon *et al.* (2011).

Dans l'étude du soi corporel, certains auteurs étudient la corrélation du signal BOLD pendant une expérience d'illusion multisensorielle. Par exemple, Ionta et collaborateurs (2014) montrent que lors d'une illusion modifiant la perspective en première personne et la localisation du soi, la jonction temporo-pariétale est connectée bilatéralement à l'aire motrice supplémentaire, au cortex prémoteur ventral, à l'insula, au sillon intrapariétal et au cortex occipito-temporal (pour plus de détails, voir Dary et Lopez 2023).

III.2.B. Connectivité fonctionnelle en SEEG et soi corporel

La connectivité fonctionnelle peut également être étudiée à partir des enregistrements par SEEG ou ECoG. Dans ce cas, la connectivité est analysée dans l'échelle mésoscopique. L'ECoG, par exemple, permet de calculer des potentiels de champs locaux. Chaque paire de contacts adjacents le long d'une électrode implantée est considérée comme un nœud dans le réseau et les enregistrements correspondent au signal provenant de la population de neurones situées sous l'électrodes et à proximité (Fornito *et al.* 2016). Les seules études de connectivité fonctionnelle utilisant l'ECoG se rapportent au langage ou encore à des tâches motrices (Zhang *et al.* 2010; Rolston et Chang 2018).

En SEEG, pour calculer la force de connectivité des nœuds dans le réseau, des méthodes de corrélation non-linéaire sont utilisées pour calculer des régressions entre les signaux enregistrés par des électrodes implantées dans des régions distantes (Bartolomei et al. 2017b). Les régressions non linéaires telles que la mesure du coefficient de corrélation h^2 permettent d'estimer la force de la connectivité entre des populations de neurones (Wendling et al. 2001). Ce coefficient de corrélation est compris entre 0 et 1. Une valeur de h^2 proche de 0 sera synonyme d'une absence de corrélation entre un signal A et un signal B. À l'inverse, une valeur du h^2 proche de 1 signifiera une forte corrélation entre les signaux. Dans le cas de la connectivité fonctionnelle, le coefficient de corrélation n'est pas orienté. En d'autres termes, il nous indique comment deux signaux A et B sont liés, mais il n'apporte pas d'information sur l'influence d'un signal sur un autre (Fornito et al. 2016).

Dans l'étude du soi corporel, une seule étude a étudié la connectivité fonctionnelle en utilisant la SEEG. Cependant, cette étude s'est focalisée sur la connectivité du cortex cingulaire. Popa et collaborateurs (2019) ont analysé le signal SEEG pendant des stimulations du cortex cingulaire chez 110 patients avec une épilepsie pharmaco-résistante. Parmi ces patients, douze ont rapporté des modifications de certaines expériences corporelles. Ces modifications étaient liées à une diminution significative de la connectivité fonctionnelle entre le cortex cingulaire et l'insula postérieure gauche mais également entre le cortex cingulaire et le cortex préfrontal, l'aire motrice supplémentaire, le cortex somatosensoriel et moteur. Une augmentation de la connectivité fonctionnelle était à l'inverse observée entre le cortex cingulaire antérieur et le cortex préfrontal dorsolatéral (Popa et al. 2019).

III.3 Approche de connectivité effective

La connectivité effective renvoie à l'influence qu'un système neuronal exerce sur un autre (Figure 11). En ce sens, la connectivité effective permet d'établir une causalité ; il s'agit d'une mesure dirigée. Elle détermine quelle région est « leadeuse » par rapport à une autre et donc la directionnalité de la relation entre deux structures. En SEEG la connectivité effective est également estimée grâce à des méthodes de régressions non-linéaire telles que le h^2 . Des indices de directionnalité sont calculés en prenant en compte la propriété asymétrique du coefficient de corrélation non-linéaire h^2 ainsi que le décalage de phase entre deux signaux. En d'autres termes, les valeurs de h^2 sont différentes si le calcul est effectué de A vers B ou de B vers A. Si la valeur de l'indice de directionnalité s'approche de 1 cela signifie que A est leader de B et si la valeur s'approche de -1, cela signifie que B est leader de A (Wendling et al. 2001).

Une autre façon d'étudier la connectivité effective est de calculer des potentiels évoqués cortico-corticaux. Les potentiels évoqués cortico-corticaux sont mesurés grâce à l'enregistrement des réponses électrophysiologiques de l'ensemble des électrodes implantées lors de la stimulation électrique entre deux contacts d'électrodes adjacents. La méthode de potentiels évoqués cortico-corticaux implique de délivrer un courant de 1 à 10 mA pendant 100 à 500 μ s entre une paire d'électrodes adjacentes (Keller et al. 2014).

La stimulation déclenche une réponse électrique locale, au niveau de contacts adjacents ou plus éloignés. La procédure est répétée entre 10 et 50 fois afin de moyenner le signal de la réponse évoquée. La cartographie cérébrale par potentiels évoqués cortico-corticaux repose sur l'analyse de la réciprocité entre les régions. En d'autres termes, elle repose sur la fréquence à laquelle la stimulation d'une région A évoque un potentiel évoqué cortico-cortical au niveau d'une région B et réciproquement. Dans une étude récente, Lyu et collaborateurs (2023) utilisent cette méthode pour étudier le lien causal entre le précuneus et des sensations de dépersonnalisation. Leurs résultats montrent que des stimulations au niveau du précuneus antérieur entraînent des potentiels cortico-corticaux principalement au niveau du cortex cingulaire moyen, du cortex sensorimoteur, du cortex préfrontal médian et du lobule pariétal supérieur et inférieur. Ces résultats suggèrent une forte connectivité entre le précuneus et ces régions qui sont fortement impliquées dans le réseau du soi corporel (Lyu et al. 2023).

IV. Ce qu'il reste à faire

- 1) Aucune étude à l'heure actuelle n'a étudié les bases neurales du soi corporel et ses différentes composantes dans une seule et même étude. La plupart se sont focalisées sur des régions spécifiques liées à des expériences corporelles singulières.
- 2) Aucune étude n'a apporté de preuve causale sur l'existence d'un réseau du soi corporel
- 3) Très peu d'études se sont interrogées sur la dynamique générale du réseau fonctionnel associé au soi corporel
- 4) Seulement deux études, dont une étude de cas (Popa et al. 2019; Bratu et al. 2021), ont analysé la connectivité fonctionnelle du réseau du soi corporel en utilisant la SEEG.

Chapitre 3 : Bases multisensorielles du soi corporel : implication du système vestibulaire dans le soi corporel

Le soi corporel se fonde sur différentes expériences corporelles. Ces expériences reposeraient sur l'intégration de signaux sensoriels provenant du corps et de son environnement. Une étude majeure publiée en 2002 par Blanke et collaborateurs étaye cette hypothèse. Les auteurs ont appliqué des stimulations électriques de plusieurs intensités au niveau du gyrus angulaire droit. Les premières stimulations entre 2 et 3 mA ont induit chez la patiente des sensations vestibulaires telles que la sensation de tomber d'une certaine hauteur ou de s'enfoncer dans son lit. Lorsque l'intensité augmentait (3,5 mA), la stimulation provoquait une expérience de sortie du corps (OBE, *out-of body experience*). La patiente avait alors l'illusion de se voir allongée dans son lit, d'un point de vue élevé. Des stimulations d'une intensité similaire ont entraîné une sensation de flottement et de légèreté. Les auteurs concluent que les expériences de sortie du corps peuvent donc être visuelles, vestibulaires, somesthésiques (Blanke et al. 2002). Ainsi, les expériences de sortie du corps résulteraient d'une perturbation dans l'intégration des informations sensorielles (Nakul et Lopez 2017) et par voie de conséquence, le soi corporel reposerait sur l'intégration cohérente de différents signaux corporels.

Outre les études par stimulations électriques, les travaux sur le soi corporel utilisent divers paradigmes expérimentaux qui reposent sur la manipulation des informations sensorielles pour étudier les mécanismes sensoriels sous-tendant le soi corporel. La majorité de ces recherches s'accorde sur le rôle des informations visuelles, proprioceptives, vestibulaires et intéroceptives dans le soi corporel (Blanke 2012; Faivre et al. 2015; Park et Blanke 2019). Dans un article d'opinion (Dary et Lopez 2023), nous montrons les avancées récentes dans les neurosciences cognitives dans l'étude des bases multisensorielles du soi corporel. Les derniers travaux sur cette thématique se sont longuement penchés sur le lien entre le soi corporel et les signaux intéroceptifs (Aspell et al. 2013; Park et al. 2016), c'est-à-dire les signaux provenant des récepteurs des organes internes et des viscères (cœur, estomac, reins, etc.). Cependant, encore trop peu d'études se sont intéressées à l'influence du système vestibulaire sur le soi corporel (Lopez et al. 2012b; Lopez 2013, 2015, 2016; Pfeiffer et al. 2013; Ferrè et al. 2015; Preuss et Ehrsson 2019). Pourtant de nombreuses preuves soulignent le lien entre le système vestibulaire et le soi corporel, par des réseaux neuronaux qui se recouvrent ou encore par des cas cliniques.

I. Bases anatomiques du système vestibulaire

Naissant dans l'oreille interne, le système vestibulaire périphérique a pour fonction d'encoder les translations et les rotations de la tête dans l'espace. Il fournit également au cerveau des signaux sur la gravité. Il joue un rôle crucial dans les réflexes oculomoteurs (qui permettent aux yeux de compenser le mouvement de la tête et de stabiliser l'image sur la rétine) et posturaux (mouvement qui permettent de stabiliser la posture, maintenir l'alignement de la tête et du corps). Il contribuerait à la cognition spatiale, à la perception et à l'action (Berthoz 1997).

Le système vestibulaire périphérique est composé de trois canaux semi-circulaires qui sont sensibles aux accélérations angulaires, chacun dans une dimension de l'espace, et de deux organes otolithiques, l'utricule et le saccule. L'utricule code les accélérations linéaires horizontales et le saccule les accélérations linéaires verticales. Plusieurs méthodes de stimulations naturelles du système vestibulaire périphérique existent (Palla et Lenggenhager 2014). L'utilisation de chaises rotatives qui tournent autour d'un axe vertical permet de stimuler les canaux semi-circulaires horizontaux chez des participants assis en position verticale et les canaux verticaux chez les participants allongés sur le dos (Furman 2016). Des plateformes de mouvement du corps entier ont récemment été développées pour contrôler avec plus de précision la vitesse, l'amplitude ou l'accélération des mouvements appliqués au corps entier (Lopez et al. 2013). Des stimulations naturelles peuvent également être appliquées uniquement au niveau de la tête grâce à des manipulations actives de la tête (Zangemeister et al. 1986) ou à des mouvements actifs de la tête (Carriot et al. 2014). Cependant, les méthodes de stimulations vestibulaires qui utilisent des fauteuils rotatifs ou des plateformes de mouvements du corps entier sont difficiles à combiner avec la neuroimagerie telle que l'IRMf. De ce fait, des méthodes artificielles pour stimuler le système vestibulaire périphérique ont été mises en place. Une première méthode est la stimulation calorique. Elle consiste à injecter dans le conduit auditif externe de l'eau ou de l'air. Cette méthode stimule essentiellement les canaux semi-circulaires qui sont sensibles aux accélérations angulaires. Une deuxième méthode est la stimulation galvanique qui consiste à envoyer un léger courant électrique dans une paire d'électrodes positionnées sur la peau derrière les oreilles. Cette méthode permet de stimuler l'ensemble des afférences vestibulaires à savoir les canaux semi-circulaires et les organes otolithiques. Enfin, la stimulation acoustique consiste à envoyer des sons brefs capables d'activer les organes otolithiques (utricule et saccule) (Figure 15.A).

I.1. *Rappel des différentes voies vestibulaires*

Les contributions vestibulaires au contrôle sensorimoteur et à la cognition (mémoire, émotions, navigation spatiale, imagerie mentale, cognition sociale, représentations du corps, etc.) reposent sur des voies qui partent de l'oreille interne et se projettent sur les noyaux vestibulaires, le thalamus et le cortex cérébral ainsi que sur le

cervelet et les ganglions de la base. La [Figure 14](#) adaptée de Nakul et collaborateurs (2021) résume les principales voies vestibulaires.

Le nerf vestibulo-cochléaire transmet les informations des récepteurs de l'oreille interne vers le tronc cérébral et le cervelet. Les noyaux vestibulaires se situent dans le tronc cérébral et constituent un premier niveau d'intégration avec les signaux visuels et somesthésiques. Les signaux vestibulaires sont projetés vers les noyaux oculomoteurs et assurent le réflexe vestibulo-oculaire. Cette voie vestibulo-oculaire sert notamment, lors des mouvements de la tête, à stabiliser l'image sur la rétine. La voie vestibulo-cérébelleuse est impliquée dans l'intégration sensorimotrice, le contrôle moteur et la précision des mouvements (Smith et al. 2024). La voie vestibulo-spinale se projette des noyaux vestibulaires vers les motoneurones spinaux et est impliquée dans la posture.

Les noyaux vestibulaires se projettent également vers les noyaux thalamiques. Le thalamus relaie et module le flux d'informations sensorielles vers le cortex cérébral (Lopez et Blanke 2011). Des études électrophysiologiques chez le chat ou chez le singe ont mis en évidence les réponses thalamiques lors de stimulations vestibulaires (Jung et al. 1963; Grüsser et Guldin 1995; Chen et al. 2011; pour une revue plus exhaustive, voir Lopez et Blanke 2011). Chez l'homme, ce sont davantage les données de neurologie qui ont permis de mettre en évidence les voies vestibulaires thalamo-corticales (Lopez et Blanke 2011). Il existe des projections des noyaux thalamiques vers un grand nombre de régions corticales, qui constituent le « cortex vestibulaire ».

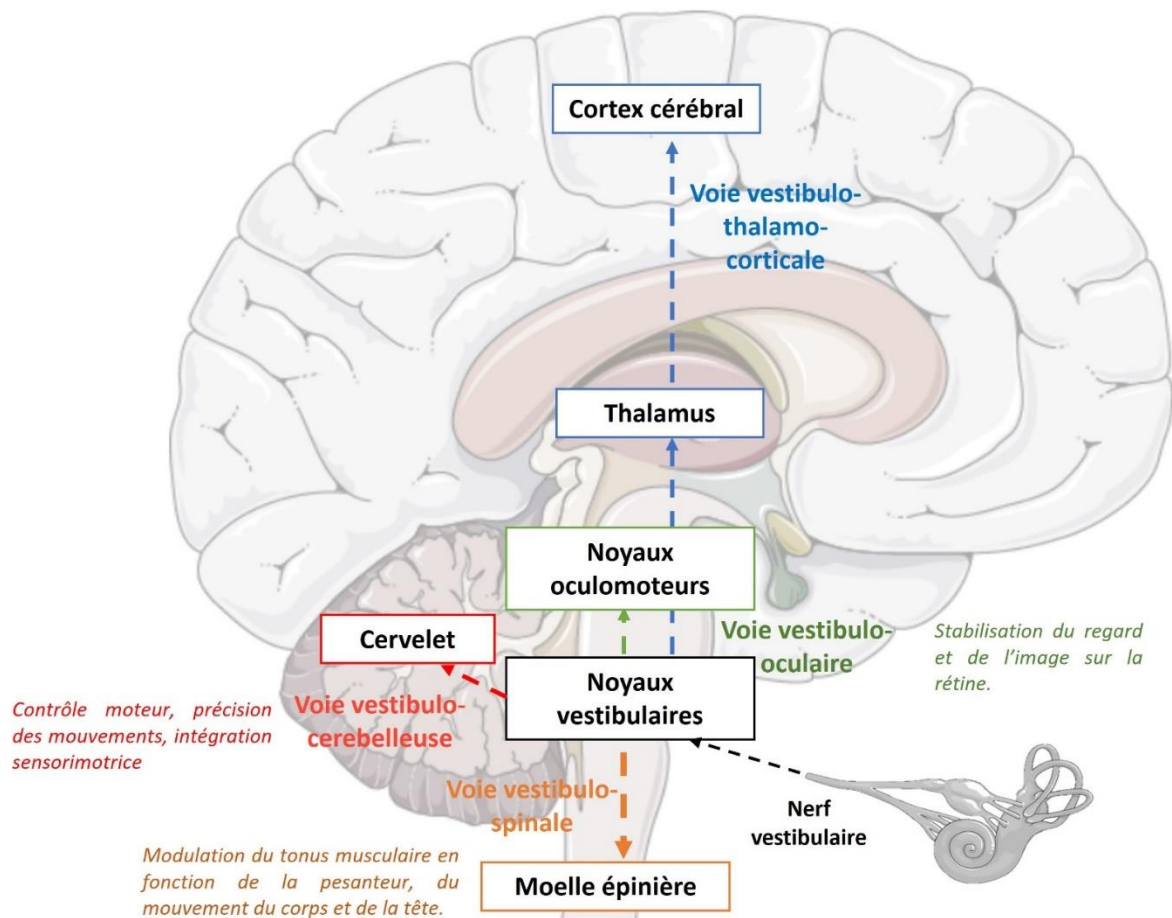


Figure 14 : Les différentes voies vestibulaires et leurs fonctions. Image adaptée de Nakul et al. (2021).

1.2. Cortex vestibulaire

Le cortex vestibulaire désigne l'ensemble des régions corticales multisensorielles qui reçoivent des informations vestibulaires. Les différentes méthodes de stimulations artificielles du système vestibulaire décrites précédemment combinées avec des méthodes de neuroimagerie ont mis en évidence des régions cruciales du cortex vestibulaire. Il a été ainsi observé qu'à la suite d'une stimulation galvanique, l'activation de l'hippocampe, des régions du cervelet, du thalamus, le précuneus et le cortex cingulaire antérieur (Lopez et Blanke 2011; Lopez et Cullen 2024). Le cortex vestibulaire pariéto-insulaire (PIVC), région multisensorielle, qui comprend l'insula postérieure, l'opercule pariétal et proche de la jonction temporo-pariétale est considérée comme une région centrale du cortex vestibulaire (Dieterich et Brandt 2010) (Figure 15).

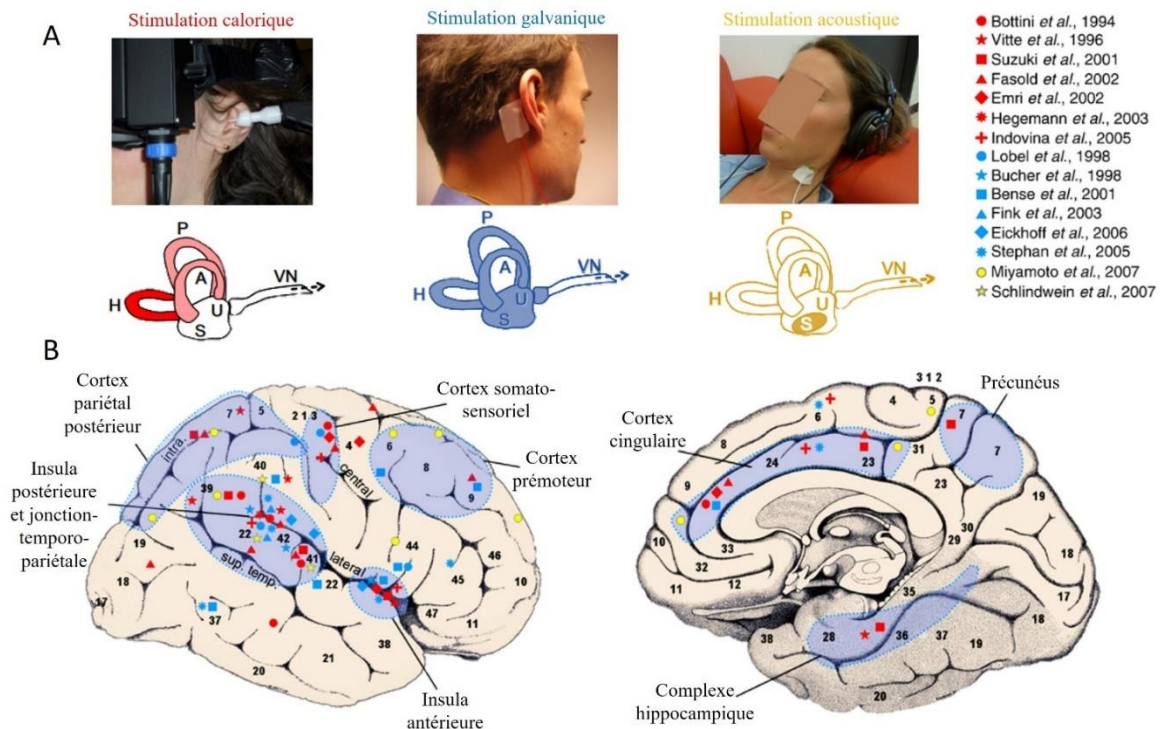


Figure 15 : Cortex vestibulaire révélé par des études de neuroimagerie. A) Les différents types de stimulations artificielles du système vestibulaire et leur principal organe activé. B) Cortex vestibulaire selon les méthodes de stimulations utilisées. Image adaptée de Lopez et Blanke (2011).

Cependant, il faut noter que les stimulations artificielles du système vestibulaire ont tendance à activer d'autres systèmes sensoriels. C'est pourquoi, une autre façon d'étudier les bases neurales du cortex vestibulaire repose sur les stimulations électriques intracérébrales. De nombreuses études ont répertorié des sensations vestibulaires à la suite de stimulations dans des régions spécifiques du cortex. Une analyse rétrospective chez 219 patients avec une épilepsie pharmaco-résistante montre que les sensations vestibulaires telles que des sensations de rotation ou de translation illusoire du corps, des vertiges ou des étourdissements représentaient 7,6% des sensations évoquées par des stimulations au niveau de l'insula postérieure (Mazzola *et al.* 2014). Une autre étude par stimulations intracrâniennes corrobore ces résultats, en montrant que des stimulations au niveau de l'insula postérieure entraînait des vertiges (Yu *et al.* 2018b). D'autres études ont mis également en évidence l'implication de régions du cortex pariétal comme le précuneus, le lobule pariétal inférieur, le cortex cingulaire postérieur, le gyrus postcentral, le sillon interpariétal et le lobule pariétal supérieur dans les sensations de vertige (Balestrini *et al.* 2015; Caruana *et al.* 2018; Oane *et al.* 2020; Lyu *et al.* 2023). Enfin, des études récentes ont mis en évidence l'implication de régions sous-corticales. En effet, des sensations vestibulaires ont été rapportées à la suite de stimulation au niveau des ganglions de la base et plus précisément du putamen et du globus pallidus (Qi *et al.* 2022).

Zhang et collaborateurs (2023) ont récemment décrit que les sensations vestibulaires au niveau de l'amygdale représentaient 6% de toutes les réponses évoquées.

A notre connaissance, il existe seulement deux études de cartographie qui utilisent des stimulations électriques intracérébrales pour étudier le réseau cérébral des sensations vestibulaires (Kahane et al. 2003; Li et al. 2023). L'étude de Kahane et collaborateurs (2003) a mis en évidence chez 260 patients épileptiques que les sensations vestibulaires (sensation de rotation, de translation, de flottement) étaient rapportées lors de stimulation du cortex vestibulaire périsylvien qui comprend le lobule pariétal inférieur (gyrus supramarginal), le gyrus temporal supérieur et médian, et l'opercule pariétal (Figure 16.A). La deuxième étude de Li et collaborateurs (2023) a comparé les données de 23 cas de patients avec des lésions cérébrales qui rapportent des vertiges avec des données de stimulations électriques intracérébrales chez 17 patients présentant des vertiges. Les deux approches ont permis d'identifier un réseau cérébral à l'origine du vertige (Figure 16). Ce réseau implique le cortex prémoteur, l'aire v2 du cortex visuel, l'aire 3aV du cortex somatosensoriel primaire, le gyrus supramarginal, le sillon intrapariétal, le gyrus postcentral, l'opercule pariétal, le cortex insulaire et les aires motrices supplémentaires.

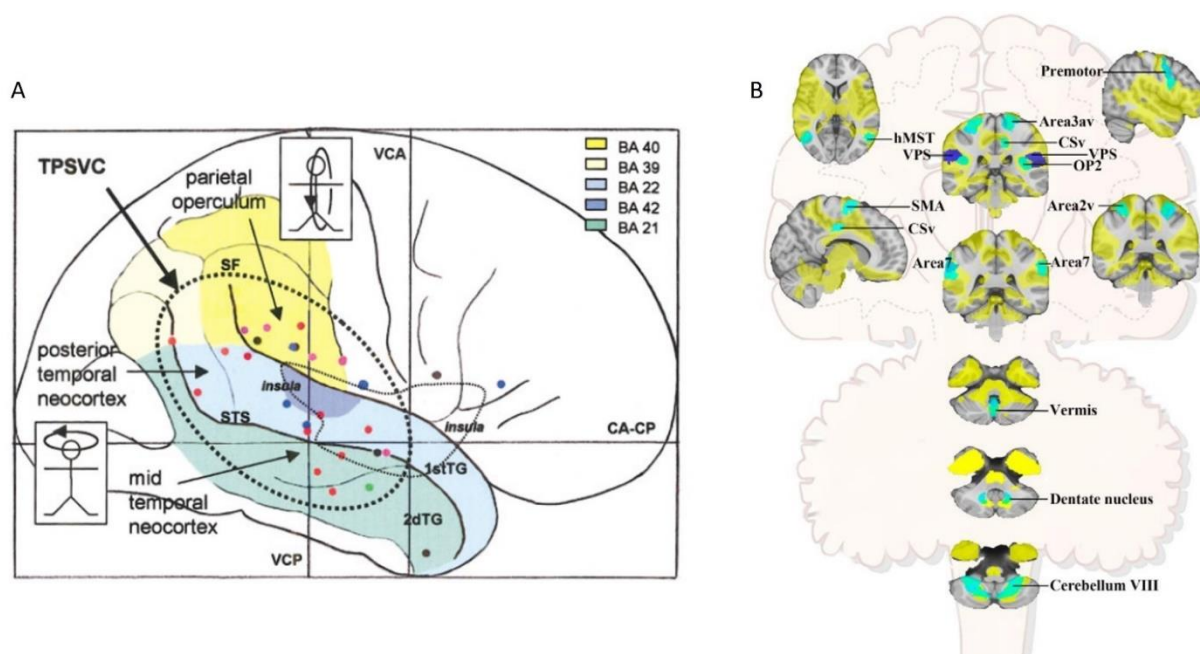


Figure 16 : Cortex vestibulaire. A) Cortex vestibulaire révélé par stimulations électriques intracrâniennes. Image issue de Kahane *et al.* (2003). B) Représentation schématique du réseau vestibulaire révélé par l'étude de lésions. Les régions comprennent l'aire bilatérale 2v, l'aire 3av, le cortex prémoteur, le CSv : aire visuelle du sillon cingulaire, l'aire OP2 : opercule pariétal 2, l'aire 7, l'aire VPS : aire visuelle postérieure de Sylvian (ou PIC, cortex insulaire postérieur), la SMA : aire motrice supplémentaire, l'aire hMST : aire temporale médiane supérieure, le thalamus ainsi que le noyau denté et le cervelet. Reproduit de Li et al, (2023).

Le réseau vestibulaire cortical apparaît donc comme étendu et englobe un grand nombre de régions multisensorielles qui sont fortement interconnectées (Raiser et al.

2020). Il se pourrait que certaines régions multisensorielles impliquées dans le réseau vestibulaire le soient également dans celui du soi corporel. Par exemple, la jonction temporo-pariétale apparaît comme une région centrale à la fois du cortex vestibulaire et du soi corporel (Blanke et al. 2002; Blanke et Arzy 2005). D'ailleurs, les modifications de la localisation du soi rapportées lors de stimulations électriques intracérébrales, telles que les illusions de flottement, les sensations de légèreté, de translation du corps, de chutes sont des illusions vestibulaires otolithiques (Dary et al. 2023). En outre, certains auteurs proposent que les expériences de sortie du corps entraînant une modification dans le soi corporel seraient dues à un trouble d'intégration des informations vestibulaires avec les informations de l'espace personnel et extrapersonnel (Blanke et al. 2004; Blanke 2012). Une des hypothèses proposées est donc que les informations en provenance de l'oreille interne influenceraient des mécanismes à l'origine du soi corporel.

II. Cas cliniques et expérimentaux : rôle du système vestibulaire dans le soi corporel

II.1. Cas cliniques

De nombreux cas cliniques suggèrent un lien entre le système vestibulaire et le soi corporel. Les descriptions de patients retranscrites par Bonnier en 1905 explicitent cette relation : des patients avec des atteintes vestibulaires rapportaient des modifications dans la perception de la forme et de la taille de leur corps. Un patient avait par exemple l'impression de sentir que « *sa tête devenait énorme, immense, se perdant dans l'air ; son corps disparaissait et tout son être se réduisait à son seul visage* » (Bonnier 1905). Une autre description souvent rapportée est celle de Schilder qui décrit également une distorsion de l'image du corps chez des patient atteints de vertiges : « *le cou enflait pendant le vertige* », « *mes extrémités devenaient plus grandes* », « *mes pieds semblaient s'allonger* » (Schilder 1935). D'autres cas cliniques rapportés sont relatifs à d'autres expériences du soi corporel, comme par exemple la dépersonnalisation (Grigsby et Johnston 1989) ou encore un sentiment de présence (Bonnier 1905). Une étude plus récente chez 210 patients atteints de troubles vestibulaires (vertiges, sensations de flottement, déséquilibres, tête qui tourne) montre que 14% d'entre eux rapportaient des expériences de sortie du corps et cette sensation est significativement plus élevée que chez des sujets sains appariés en âge et en sexe (Lopez et Elzière 2018). Cette étude suggère également que des symptômes de dépersonnalisation et de déréalisation sont associés à une plus grande probabilité de rapporter une illusion de sortie du corps. Cette idée est d'ailleurs soutenue par certains travaux qui montrent que différentes pathologies vestibulaires sont associées à des symptômes de dépersonnalisation se traduisant par le sentiment que le soi et le corps paraissent étranges ou irréels (Sang et al. 2006; Jáuregui Renaud 2015; Lopez et Elzière 2016; Lopez et al. 2018; Brandt et Dieterich 2020; Elyoseph et al. 2023).

D'autres études ont mis en évidence le lien entre le système vestibulaire et les émotions ou la cognition sociale (Deroualle et al. 2017; Nakul et al. 2020a).

II.2. *Approches expérimentales*

Outre ces approches cliniques, une autre façon d'étudier le lien entre le système vestibulaire et le soi corporel est par l'intermédiaire des stimulations vestibulaires (chapitre 3, partie I, et [Figure 15](#)). Des travaux ont ainsi montré que des stimulations caloriques ou galvaniques pouvaient entraîner une modification dans la perception de la taille et de la forme du corps (Lopez et al. 2012b, 2018) ou encore dans la localisation du soi (Lenggenhager et al. 2008). Certaines études ont également combiné des stimulations artificielles du système vestibulaire avec des illusions telles que l'illusion de la main en caoutchouc ou du corps entier (Lopez et al. 2010; Ferrè et al. 2015; Preuss et Ehrsson 2019). Par exemple, Preuss et collaborateurs ont combiné une stimulation visuo-vestibulaire congruente avec une full-body illusion à la première personne. Les participants observaient un corps oscillant de droite à gauche en même temps qu'ils recevaient une stimulation galvanique. Les résultats montrent qu'une stimulation visuo-vestibulaire congruente augmentait l'identification à l'avatar (Preuss et Ehrsson 2019). D'autres études ont utilisé des stimulations naturelles avec des illusions (Macauda et al. 2015; Nesti et al. 2018; Thür et al. 2019). De façon générale, ces études suggèrent que lors d'un conflit visuo-vestibulaire, les participants ont tendance à s'identifier plus au corps virtuel. Une étude récente de Wu et collaborateurs étaye ce propos (Wu et al. 2024). Cette étude a combiné la réalité virtuelle dans laquelle les participants observaient leur corps changer de position selon l'axe gravitaire à une plateforme mobile permettant de passer progressivement d'une position allongée à une position élevée retournée. Ce changement de position que ce soit dans la scène visuelle ou de la plateforme simulait une illusion de sortie de corps. L'objectif de l'étude était d'étudier l'interaction visuo-vestibulaire en faisant varier la congruence de direction entre les informations visuelles et vestibulaires. Les résultats de cette étude montrent que la congruence entre les signaux vestibulaires gravitaires et les signaux visuels apparaît primordiale dans l'induction d'une illusion de sortie de corps. Ces résultats corroborent l'idée que le soi corporel est sous-tendu par l'intégration cohérente des informations vestibulaires et plus précisément, dans le cas présent, des informations otolithiques, avec d'autres informations sensorielles (Blanke 2012; Wu et al. 2024).

III. Ce qu'il reste à faire

- 1) Encore trop peu d'études ont étudié le lien entre le système vestibulaire et le soi corporel, et plus précisément le rôle du système otolithique dans le soi corporel.
- 2) Trop peu d'études ont étudié expérimentalement les effets de troubles du soi corporel lié à des troubles vestibulaires périphériques.
- 3) La connectivité fonctionnelle au sein du réseau vestibulaire est encore trop peu étudiée et comprise.

Objectifs

Ce travail a pour but d'étudier les bases cérébrales et multisensorielles du soi corporel. Les chapitres introductifs ont permis de poser les fondements théoriques. Nous avons également relevé plusieurs aspects dans l'étude du soi corporel qui n'ont été que partiellement abordés (Etude 1, article d'opinion publiée dans *Frontiers in Integrative Neuroscience*).

Cette thèse tente donc de répondre à trois objectifs majeurs :

- 1) Un premier objectif est **d'étudier les bases neurales du soi corporel par une approche causale** en utilisant des stimulations électriques intracérébrales.
Premièrement, nous avons réalisé une revue systématique de la littérature sur les bases neurales du soi corporel révélées par la stimulation électrique (Etude 2 publiée dans *Human Brain Mapping*). Nous avons pu constater qu'aucune étude à ce jour n'a conduit de recherche sur les bases neurales du soi corporel sans se focaliser a priori sur une région spécifique ni sur une composante particulière du soi corporel. Ainsi, nous souhaitons dans ce travail de thèse explorer pour la première fois, dans une même étude, les bases neurales de l'ensemble des différentes expériences sous-tendant le soi corporel.
Deuxièmement, nous avons conduit une analyse rétrospective chez 354 patients épileptiques implantés en SEEG dans le cadre d'une évaluation pré-chirurgicale. Nous avons analysé plus de 110 réponses à des stimulations ayant provoqué des modifications d'une ou plusieurs composantes du soi corporel (Etude 3).
- 2) Le second objectif de ce travail est **de décrire le réseau cérébral impliqué dans les différentes expériences corporelles**. Comme nous l'avons développé dans le chapitre d'introduction, la cartographie fonctionnelle se détache peu à peu de l'approche purement localisationniste pour considérer les processus cognitifs comme faisant intervenir des régions plus ou moins distantes au sein d'un réseau. Dans cette thèse, nous utilisons des résultats de connectivité fonctionnelle issue de l'analyse de signaux de SEEG pour déterminer le ou les réseaux qui sous-tendent les différentes composantes du soi corporel (Etude 3).
- 3) Le troisième objectif de ce travail de thèse consiste à **étudier les liens entre le système vestibulaire et le soi corporel, aux niveaux comportemental et cérébral**. Nous analysons le lien entre le système vestibulaire et le soi corporel en étudiant l'influence d'une perte vestibulaire bilatérale dans une illusion multisensorielle induite en réalité virtuelle (Etude 4).

Contributions théoriques et expérimentales

Avancées majeures et principales perspectives dans l'étude des bases neurales du soi corporel

Article 1 : Article d'opinion sur l'étude des bases neurales du soi corporel

Understanding the neural bases of bodily self-consciousness: recent achievements and main challenges

Article publié dans Frontiers In Integrative neuroscience

L'objectif de ce travail n'est pas d'être exhaustif mais de souligner les principaux résultats dans l'étude des bases neurales du soi corporel et les futurs questionnements sur lesquels la communauté neuroscientifique devrait se pencher. Cinq points essentiels retiennent notre attention :

- 1) Les nombreux travaux publiés ces dix dernières années sur la contribution des sens « silencieux », notamment l'intéroception, aux mécanismes neuronaux du soi corporel.
- 2) Les études sur l'imbrication des différents mécanismes neuronaux du soi corporel et des formes du soi de plus haut niveau tels que le soi cognitif.
- 3) La tendance actuelle de travaux récents qui tentent d'apporter des preuves causales plutôt que corrélationnelles aux bases neurales du soi corporel.
- 4) Le développement croissant des analyses de connectivité structurale, fonctionnelle et effective qui mettent en évidence le fonctionnement en réseau des régions cérébrales impliquées dans le soi corporel.
- 5) Le manque d'échanges entre les différents niveaux d'analyses dans le champ des neurosciences pour comprendre la complexité des mécanismes cérébraux liés au soi corporel.

Aux vues de ces différents points, le travail expérimental réalisé dans cette thèse s'inscrit dans les quatre premières tendances.



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Understanding the neural bases of bodily self-consciousness: recent achievements and main challenges

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The last two decades have seen a surge of interest in the mechanisms underpinning bodily self-consciousness (BSC). Studies showed that BSC relies on several bodily experiences (i.e., self-location, body ownership, agency, first-person perspective) and multisensory integration. The aim of this literature review is to summarize new insights and novel developments into the understanding of the neural bases of BSC, such as the contribution of the interoceptive signals to the neural mechanisms of BSC, and the overlap with the neural bases of conscious experience in general and of higher-level forms of self (i.e., the cognitive self). We also identify the main challenges and propose future perspectives that need to be conducted to progress into the understanding of the neural mechanisms of BSC. In particular, we point the lack of crosstalk and cross-fertilization between subdisciplines of integrative neuroscience to better understand BSC, especially the lack of research in animal models to decipher the neural networks and systems of neurotransmitters underpinning BSC. We highlight the need for more causal evidence that specific brain areas are instrumental in generating BSC and the need for studies tapping into interindividual differences in the phenomenal experience of BSC and their underlying mechanisms.

KEYWORDS

consciousness, body representation, self-consciousness, multisensory integration, neuroimaging

1. Introduction

The last decades have seen a surge of interest in the neural mechanisms underpinning self-consciousness. A very productive line of research has investigated the brain mechanisms of bodily self-consciousness (BSC), showing that they rely on several bodily experiences and multisensory integration. BSC encompasses bodily experiences such as *self-location*—the experience of occupying a volume of space, typically localized within the body; *body ownership*—the experience of owning a body; *agency*—the sense of being in control of one's own movements; and *first-person perspective*—the experience of an egocentric perspective on the world and the self (Blanke, 2012).

Pioneer descriptions of patients with stroke or epilepsy associated with disturbances in one or several aspects of BSC suggested that parts of the cortex and thalamus were involved in the experience of being a self, of being embodied, of owning a body, or of having the

control over actions and thoughts (e.g., Lhermitte, 1939; Gerstmann, 1942; Hécaen and de Ajuriaguerra, 1952). For example, seizures and lesions in the temporo-parietal junction have consistently been associated with illusory disembodied self-location (Blanke et al., 2004), and damage to the insula and parietal cortex have consistently been associated with disownership of body parts (Berlucchi and Aglioti, 2010).

Neuroscientists have more recently put BSC under scientific scrutiny by combining pluridisciplinary approaches from experimental psychology, virtual reality, neuroimaging, electrophysiology, physiology and robotics (Blanke et al., 2015; Bernasconi et al., 2022; Monti et al., 2022). A fruitful approach developed during the last 20 years to identify the neural bases of BSC has been to manipulate bodily experiences by creating multisensory illusions, and to explore the neural correlates of these changes in BSC. Two widely used and popular experimental paradigms in cognitive neuroscience were the “rubber hand illusion” (Botvinick and Cohen, 1998) and the “full-body illusion” (Ehrsson et al., 2004; Lenggenhager et al., 2007; Slater et al., 2009), developed to manipulate illusory self-identification with a fake hand or body, a mannequin, or a virtual hand or body. Non-invasive functional neuroimaging combined to these illusions revealed that BSC involves the premotor cortex, middle and inferior temporal cortex, extrastriate body area, inferior parietal sulcus, primary somatosensory cortex, insula, anterior cingulate cortex, and the temporo-parietal junction (e.g., Ehrsson et al., 2004; Tsakiris et al., 2007, 2008; Ionta et al., 2011b; Petkova et al., 2011).

As part of the Research Topic *Insights in Integrative Neuroscience 2022*, the present literature review aims at identifying novel developments, current challenges and future perspectives (see ¹ and Buhusi et al. (2023), in this Research Topic) in the analysis of the neural bases of BSC. We do not intend to be exhaustive in this non-systematic review of the literature, and present a selection of lines of research that, according to us, were particularly important in the field in that they contributed to the multilevel analysis of BSC (i.e., from neurochemistry to neurons, neural assembly, and whole brains, across species and across the lifespan). Relevant references were selected after searching in PubMed articles published in English in the last 10 years about BSC [and the main bodily experiences underpinning BSC: self-location, agency, first-person perspective, body ownership; see Blanke (2012)]. On the basis of this literature search, 60 articles were identified, among which we highlighted results from articles published in mostly the last 5 years, that provided novel developments into the understanding of the neural bases of BSC. We summarized results from studies providing a better understanding of the contribution of silent senses (e.g., interoceptive signals) to the neural mechanisms of BSC, results from studies investigating the overlap between the neural mechanisms of BSC and higher-level forms of self (i.e., the cognitive self), and novel approaches from structural and functional connectivity to decipher the neural network underpinning BSC. We also identify the main current challenges and propose future perspectives that need to be conducted to progress into the understanding of the neural mechanisms of

BSC. In particular, we point the lack of crosstalk and cross-fertilization between subdisciplines of integrative neuroscience to better understand BSC, especially the lack of research in animal models to decipher the neural networks and systems of neurotransmitters underpinning BSC.

2. Recent developments and major accomplishments

2.1. Neural mechanisms of interoception contribute to BSC

Neuroscientific investigations of BSC have increasingly paid attention to the link between BSC and interoceptive signals, i.e., signals from receptors in inner organs and viscera (heart, stomach, blood vessels, kidneys...) contributing to homeostasis. Although interoceptive signals are often processed in a pre-reflective way (we are usually not aware of our heart beats, unless we are very excited or scared), they also contribute to a large range of higher-order functions, such as emotions and decision making (Craig, 2009; Khalsa et al., 2018). There is also evidence that interoceptive signals contribute to BSC (Aspell et al., 2013; Seth, 2013).

A line of research measured the participant's ability to perceive their heartbeats [i.e., using heartbeat counting tasks or heartbeat tracking tasks (Garfinkel et al., 2015)] or their internal bodily states using questionnaires, and correlated these measures of interoceptive sensitivity to several bodily experiences related to BSC. For example, participants with higher interoceptive acuity tended to show lower illusory ownership, i.e., lower self-identification with a fake hand (Tsakiris et al., 2011), or tended to report higher anchoring of their self to their body (Nakul et al., 2020a).

Park et al. (2016) used electroencephalography and a method referred to as heartbeats evoked potentials (HEPs) to analyze how brain activity in response to heartbeats was modulated during experimentally-induced self-identification with a distant body (Figure 1). The authors demonstrated that HEPs amplitude decreased during illusory self-identification with a distant body, for electrodes located over frontocentral scalp regions. In addition, changes in BSC were correlated to HEPs amplitude. Source localization and cluster-based permutation tests indicated that the activity within the left and right posterior cingulate cortex, extending to the supplementary motor area, was associated with changes in BSC (i.e., self-identification with the avatar). The authors noted that using a less conservative statistical threshold, activity in the left insula, a crucial area for interoception, was also related to self-identification with an avatar. Using intracranial electroencephalography in eight patients with epilepsy, a technique characterized by a high spatiotemporal resolution, the same team confirmed that modulation of HEP amplitude during illusory self-identification with an avatar was related to neural activity in the insula (Park et al., 2018).

Altogether, data indicate that, in addition to exteroceptive visual and tactile signals, the brain processing of interoceptive signals contributes significantly to the neural bases of BSC [reviewed in Park and Blanke (2019)]. The data especially point

¹ <https://www.frontiersin.org/research-topics/43343/insights-in-integrative-neuroscience-2022#overview>

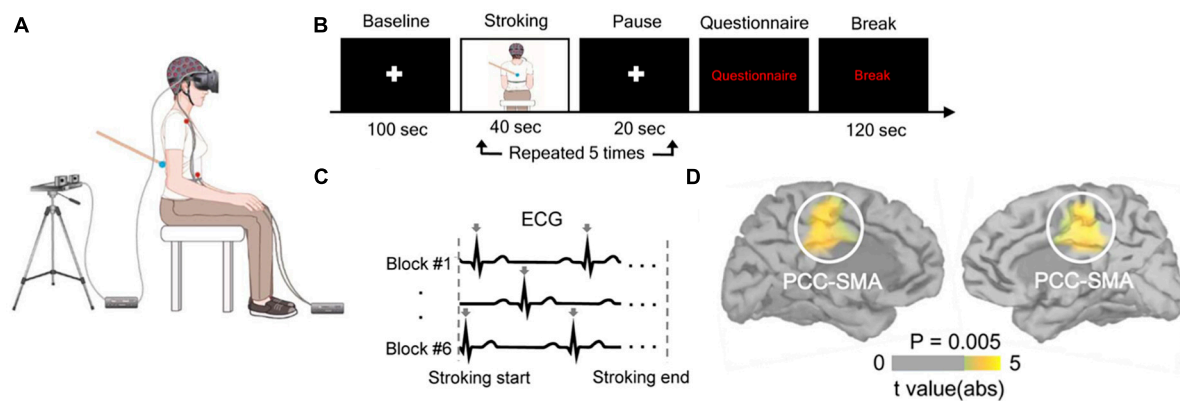


FIGURE 1

Heartbeat evoked potentials and bodily self-consciousness (BSC) in a full-body illusion. (A) Participants received on their back a tactile stimulation either synchronously or asynchronously with a video of their own back being stroked in a head-mounted display. (B) Participants answered a questionnaire about BSC (e.g., self-identification with the seen body) after five exposures to visuo-tactile stimulation. (C) Electrocardiogram was recorded during the visuo-tactile stimulation. Arrows indicate cardiac R-peaks. (D) Difference in activation by heartbeats between synchronous and asynchronous visuo-tactile stimulation was significant in the bilateral posterior cingulate cortex. Reproduced from Park et al. (2016).

to the importance of interoceptive information processing in the insula for BSC.

Another study analyzed the correlation between gut physiology and BSC in 31 healthy male participants (Monti et al., 2022). With a new method based on a wireless capsule ingested by participants, Monti et al. (2022) recorded temperature, pressure and pH across the entire gastrointestinal tract in real-time during a full-body illusion in virtual reality coupled with electrogastric rhythm recordings. The authors used questionnaires to measure illusory self-identification, self-location and agency over a virtual body breathing in synchrony or not with the participants. Results showed a relation between illusory self-location and pH: less acidic pH was associated with a stronger sense of occupying the same place as the virtual body. A lower feeling of disembodiment was also associated with higher gastrointestinal temperature. Electrogastric data indicated a relation between physiological activity of the stomach and self-identification with a virtual avatar.

The data reviewed above have strong implications in that they showed that BSC is directly related to objective physiological measures about the inner state of the body, in line with previous demonstrations of relations between illusory ownership over a fake body part and immune reaction (Barnsley et al., 2011). They open new avenues for clinical neuroscience to investigate whether conditions characterized by an abnormal sense of embodiment and sense of self (e.g., depersonalization) are related to abnormal brain processing of gut interoceptive signals.

2.2. Shared neural networks underpinning conscious experience of sensory events and BSC

Cognitive neuroscientists and clinicians progressed in understanding the neural bases of consciousness by investigating *conscious experience* of sensory events (e.g., conscious perception of visual signals, sounds, touch), that is, “what it is like” to have a sensory experience (Nagel, 1974). An important question was to understand whether brain networks involved in the conscious

experience of sensory events (without self-representation) overlap with those underpinning BSC (the experience of a bodily self). Invasive intracranial electrical stimulation in patients with epilepsy and during awake brain surgery have long shown that stimulation of various cortical and subcortical sites can evoke a variety of conscious experiences (Penfield, 1958; Halgren et al., 1978) devoid of self-representation (e.g., seeing phosphenes; auditory hallucinations: hearing human voice; somatosensory sensations: warmth, paresthesia, tingling, flexion of a finger; pain; vestibular responses: feeling of falling or flying; see Selimbeyoglu and Parvizi (2010), for a comprehensive review), or distortions in the sense of self (e.g., sensation of unreality, out-of-body experience, disownership; see Dary et al. (2023), for a comprehensive review). Fox et al. (2020) conducted an extensive whole-brain mapping of the effects of direct intracranial electrical stimulation in 67 patients with epilepsy (Figure 2A). The authors found that the elicitation rate of conscious experience (mainly devoid of self-representation) was high in rather unisensory parietotemporal and occipital cortices at the base of the cortical hierarchy. By contrast, they reported that electrical stimulation of the heteromodal cortices placed higher in cortical hierarchy, such as the frontal cortex, had a much lower elicitation rate (Figure 2B).

In a more focused investigation of the role of the prefrontal cortex based on the same data sample, Raccach et al. (2021) concluded that, with the exception of electrical stimulation of the orbitofrontal cortex and the anterior cingulate cortex, which can disturb conscious experience, electrical stimulation of the anterolateral prefrontal cortex does not seem to modify conscious “relation to the immediate environment.”

This result is important in that the prefrontal cortex has often been proposed as a crucial region for conscious experience, especially for partisans of the global workspace theory (Dehaene and Changeux, 2011; Boly et al., 2017; Odegaard et al., 2017). According to this theory, conscious experience “occurs when incoming information is made globally available to multiple brain systems through a network of neurons with long-range axons densely distributed in prefrontal, parieto-temporal, and cingulate cortices” (Dehaene and Changeux, 2011, p. 200). However, it appears that a conscious experience was mostly evoked or modified

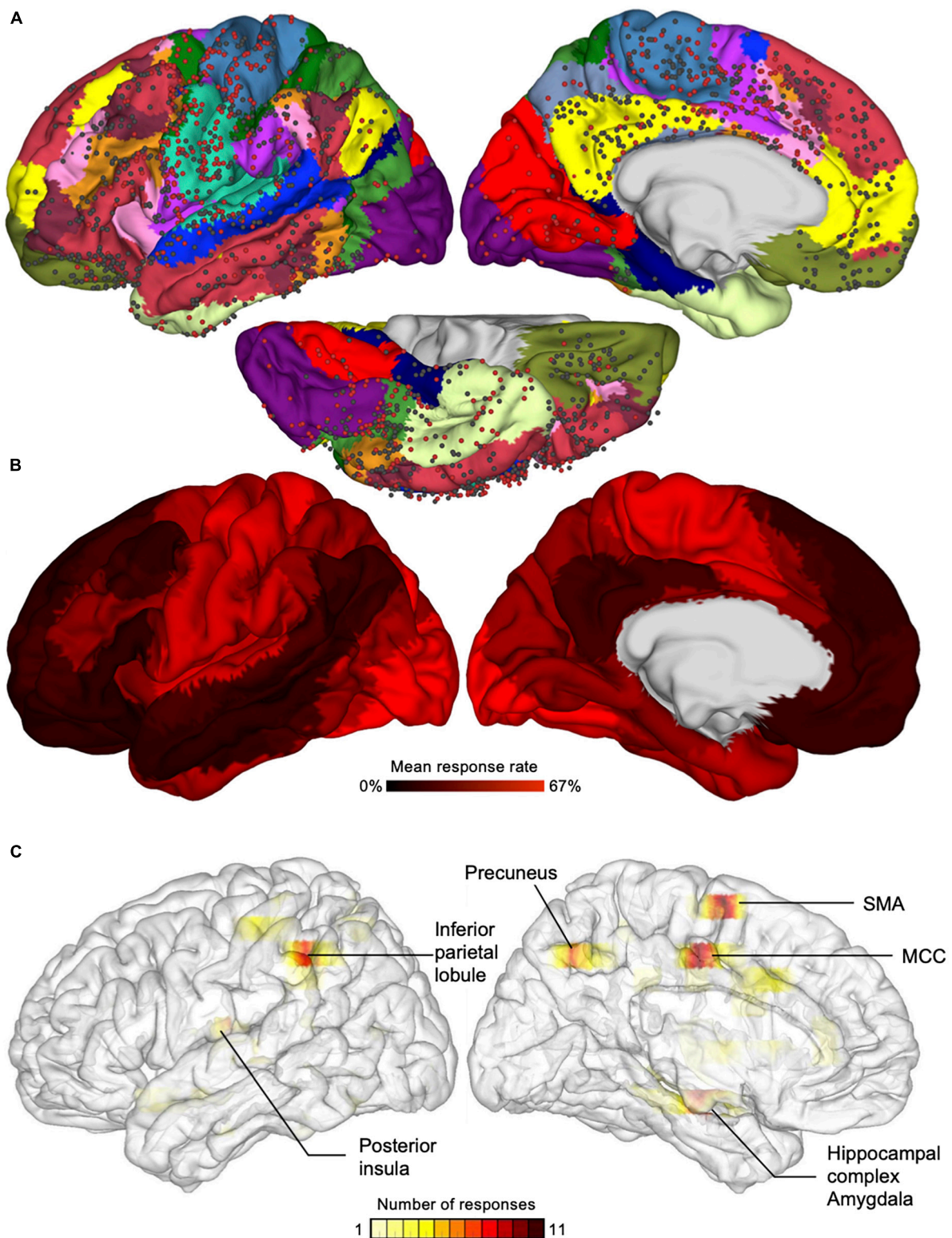


FIGURE 2

Responses elicited by electrical stimulation of the cortex in awake epileptic patients. (A) Circles represent the location of electrical stimulation applied in different epileptic patients. Red circles are sites where electrical stimulation evoked a change in the conscious experience or a motor response, whereas black circles are sites where no response was evoked. (B) The color code represents the mean response rate, showing high response rate in somato-motor and visual networks and low response rate in the default and limbic networks and in other transmodal networks. Reproduced from Raccach et al. (2021). (C) Color-coded density maps showing the number of electrical brain stimulation evoking disturbances of the bodily self in a systematic review of the literature, showing six main areas underlying the bodily self. MCC, middle cingulate cortex; SMA, supplementary motor area. Brain images have been flipped horizontally to allow comparisons with part (B). Reproduced from Dary et al. (2023).

after stimulation of a large posterior network including the sensory cortices, most often not involving the prefrontal cortex (Koch, 2018; Raccach et al., 2021).

As introduced above, BSC is grounded on bodily experiences and the integration of sensory signals from the body and its immediate environment. Accordingly, neural activity within the multisensory and sensorimotor cortices is deemed crucial for the bodily self (Blanke, 2012). **Figures 2B, C** compares intracranial electrical brain stimulation evoking conscious experience not directly related to the self (Koch, 2018; Raccach et al., 2021) with stimulation evoking disturbances of the BSC, such as disembodiment, disownership of a body part, or abnormal sense of agency (Dary et al., 2023). A recent systematic review of the literature between 1937 and 2022 identified a total of 221 patients who reported altered BSC during electrical brain stimulation (Dary et al., 2023). Three-dimensional density maps of stimulation that most consistently altered BSC revealed the crucial contribution of the middle cingulum, inferior parietal lobule, supplementary motor area, posterior insula, hippocampal complex/amygdala, and precuneus (**Figure 2C**). Interestingly, these regions overlap with the cortices where the elicitation rate of conscious experience not directly related to the self was high (**Figure 2B**; Fox et al., 2020).

In conclusion, results from intracranial stimulation studies indicate a strong overlap between brain networks underpinning conscious experience of sensory events devoid of self-representation and those involved in BSC (disturbances of the bodily self). Thus, consciousness of a bodily self may share similar brain mechanisms with conscious experience, mostly grounded in the sensorimotor cortices, emphasizing again the embodied nature of BSC.

2.3. Shared neural networks underpinning the bodily self and the cognitive self

Self-consciousness is a multifaceted aspect of the mind: in addition to BSC (the bodily self), which is mostly pre-reflective and relies on multisensory and motor mechanisms (Blanke, 2012), higher-levels forms of self, sometimes referred to as “cognitive self” (or “narrative self”), are more reflective and involve a sense of self extended in time [Gallagher (2000); reviewed in Schaller et al. (2021)]. The cognitive self involves cognitive processes, such as self-recognition in a mirror, self-recognition of the own voice, autobiographical memory, language (e.g., the use of “I” and “me”), or mental time travel (Schaller et al., 2021). Whereas the bodily self and cognitive self are conceptually different, there are theoretical and experimental arguments to suggest that they cannot be separated (e.g., Zahavi, 2005), overlap partially, and that self-consciousness emerges from interactions between both levels (Gallagher, 2013). Damasio (1999), for example, distinguished a simple level of self (the “protoself,” related to the bodily self) from a more complex form of self (the “autobiographical self,” related to the cognitive self), which depends on cognition. According to Damasio (1999), the relation between these two levels of self is crucial, in that the autobiographical self relies on the foundation of the protoself. Phenomenal approaches of the self have also suggested that pre-reflective self-consciousness serves

as a foundation for all reflective levels of the self (e.g., Legrand, 2007).

Given the conceptual overlap between the bodily and the cognitive self, recent studies endeavored to explore the extent to which BSC may share some mechanisms and neural substrates with high-level forms of self. A line of research investigated the contribution of brain networks supporting memory, as memory involves cognitive processes at the base of a self extended in time (i.e., a self with a past, a present, and a future). Br  chet et al. (2018) specifically tested whether BSC shares neural correlates with episodic and semantic aspects of autobiographical memory. The rationale was that “the subjective sense of self in time that enables us to re-experience ourselves in the past and mentally project ourselves into the future, i.e., *autonoetic consciousness*” (Br  chet et al., 2018; p. 2) (at the base of episodic autobiographical memory), involves core aspects of BSC, such as self-location and first-person perspective. Results from their meta-analysis of functional neuroimaging studies on autobiographical memory, compared to core areas of BSC identified by Ionta et al. (2011a) indicate an overlap between the regions involved in BSC and in episodic autobiographical memory in the bilateral angular gyrus. No overlap was found in other parietal and temporal areas. In addition, there was no overlap between BSC and semantic autobiographical memory. Thus, the angular gyrus appears to be a core region for multisensory processing related to the immediate bodily self experience (experience of perceiving the world from a first-person perspective and of being spatially located) and for later re-experiencing the self in episodic autobiographical memory.

2.4. Structural and functional connectivity to decipher the neural network underpinning BSC

In addition to the identification of the brain areas linked to changes in BSC, neuroimaging studies are now investigating the patterns of structural and functional connectivity which characterize the brain networks underpinning BSC. Rather than a pure localizationist approach as allowed by clinical case reports and case series, these more recent approaches allow predicting and decoding states of BSC as a function of the pattern of activity and connection within brain networks [reviewed in Thiebaut de Schotten and Forkel (2022)].

Structural connectivity refers to the neural fibers pathways connecting distant brain areas, and can be approached using diffusion tensor imaging (DTI) and diffusion spectrum imaging (DSI). A line of research analyzed the effects of brain disconnections on cognitive functions, such as language, to identify the underlying neural networks (Thiebaut de Schotten et al., 2020). These approaches can now be extended to the study of BSC. Pacella et al. (2019), for example, analyzed direct damage and disconnections from neuroimaging data in 174 patients with a right hemisphere stroke. They showed that three neural networks contribute significantly to anosognosia for hemiplegia, indicating that the premotor network, the limbic system and the ventral attentional network were involved in motor consciousness. To identify the brain network underpinning the sense of body ownership, Errante et al. (2022) analyzed structural

brain connectivity in patients with stroke, who misidentified other individual's limb as their own. The authors quantified the probability of disconnection of subcortical tracts in 70 patients with stroke presenting or not abnormal limb ownership and used DTI in a subsample of these patients. They found that altered sense of limb ownership was mainly related to disconnection of the arcuate fasciculus and the third branch of the superior longitudinal fasciculus (**Figure 3**). Thus, deficits in the sense of limb ownership resulted from the disconnection between frontal (ventral premotor cortex), parietal (intraparietal sulcus) and temporal (extrastriate body area) areas (**Errante et al., 2022**). Although ownership for a body part may be less relevant for BSC than global, whole-body ownership, the brain mechanisms involved appear to be similar (**Ionta et al., 2014**).

Functional connectivity is based on statistical dependence (e.g., measure of correlation or coherence) between signals recorded from distant brain areas. For example, functional connectivity can be obtained by calculating the correlation between BOLD signal fluctuations from distant brain regions during experimentally-induced changes in BSC (using full-body illusions modifying global body ownership and self-location). **Ionta et al. (2014)** investigated the network of areas functionally connected with the temporo-parietal junction, a core area encoding the sense of self-location and first-person perspective (**Ionta et al., 2011b**). The authors found that the temporo-parietal junction was bilaterally connected to the supplementary motor area, ventral premotor cortex, insula, intraparietal sulcus, and the occipito-temporal cortex. In addition, the authors reported that the strength of functional connectivity between the right temporo-parietal junction and the right insula reflected more strongly the perceived self-location and first-person perspective. These regions have consistently been related to global aspects (whole-body ownership and self-location) of BSC in previous neuroimaging studies [reviewed in **Blanke (2012)**, **Serino et al. (2013)**].

Functional connectivity can also be assessed from stereo-electroencephalography (intracranial recordings) during

presurgical evaluation of epilepsy, for example by calculating non-linear regressions between EEG signals recorded from distant intracranial electrodes (**Bartolomei et al., 2017a,b**). **Popa et al. (2019)** retrospectively analyzed the responses to electrical stimulation of the cingulate cortex in 110 patients with epilepsy. Twelve patients reported distorted BSC and body image during electrical stimulation of the cingulate cortex. Changes in BSC and body image were associated with a significant decrease in functional connectivity of the cingulate cortex with the left posterior insula (and to a lesser extent the left anterior insula), as well as with the prefrontal cortex, supplementary motor area, premotor cortex, primary somatosensory and motor cortices, and with the frontal and parietal opercula. In addition, changes in BSC were associated with increased functional connectivity between the anterior cingulate cortex and dorsolateral prefrontal cortex, as well as between temporal areas, the right anterior insula and supplementary motor area, or the right posterior insula.

3. Main challenges and perspectives

We focus here on three main challenges that may have hampered progresses in the understanding of the multisensory mechanisms and the neural bases of BSC: the lack of crosstalk and cross-fertilization between different subdisciplines and approaches from integrative neuroscience to decipher the neural bases of BSC; the often correlational rather than causal evidence that specific brain areas are instrumental in generating BSC; and the need for studies tapping into interindividual differences in the phenomenal experience of BSC and their underlying mechanisms. Some perspectives are summarized in **Table 1**.

3.1. Lack of cross-talk and cross-fertilization between subdisciplines of integrative neuroscience to decipher the neural bases of BSC

Integrative neuroscience is characterized by the investigation of brain functions with several levels of analysis, ranging from

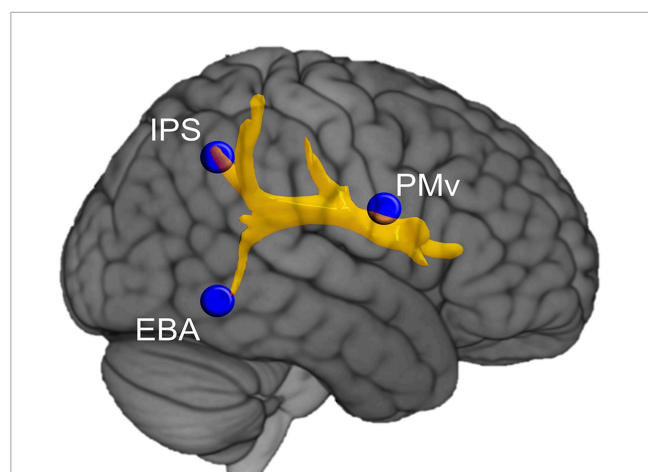
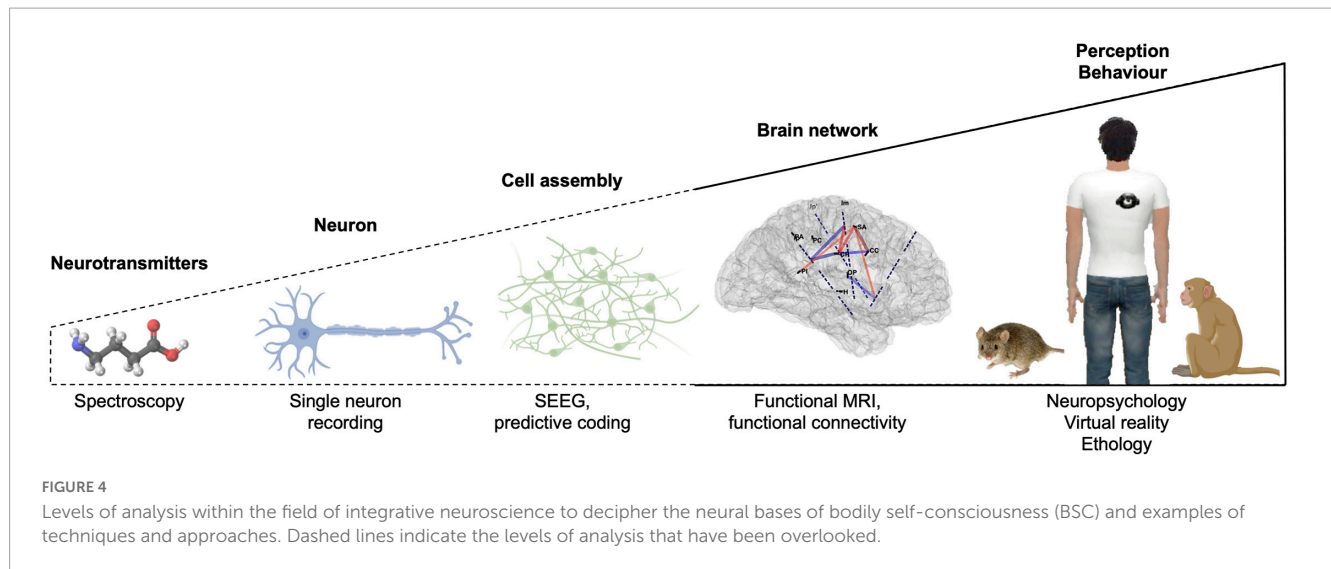


FIGURE 3

Structural connectivity underlying the sense of body ownership. Representation of the tracts damaged more frequently in stroke patients with disturbed sense of body part ownership when compared to patients whose sense of body part ownership was not affected. EBA, extrastriate body area; IPS, intraparietal sulcus; PMv, ventral premotor cortex. Reproduced from **Errante et al. (2022)**.

TABLE 1 Some research perspectives.

- Improve cross-talk and cross-fertilization between levels of analysis of BSC
- Build conceptual bridges to better integrate multiple levels and methods of analyses of BSC
- Provide stronger causal evidence of involvement of neural networks in BSC
- Describe better the evolutionary aspects of BSC and its neural bases
- Describe the systems of neurotransmitters or hormones regulating BSC
- Analyze better interindividual differences in BSC and their neural underpinning, explaining variety in the experience of self from neurotypical to other populations
- Analyze overlap and differences between the neural bases of BSC and high-level aspects of the self
- Investigate further interrelations between the neural bases of BSC and the immune system



molecular (genes, neurotransmitters, receptors) and cell levels (action potentials) to cell assemblies, brain networks (whole-brain imaging) and cognition/behavior (ethology, neuropsychology), using a variety of methods (Figure 4). Multi-level analyses are required to understand complex behaviors, body-mind relations, or the neural bases of BSC. Each level of analysis depicted in Figure 4 can provide important insight into the neural bases of BSC. However, we note that there have been so far little interactions and cross-fertilization between the different levels of analyses within the field of integrative neuroscience, which have focused on the bodily self and their neural bases:

- **Molecular (genes, neurotransmitters, receptors) levels.** Studies into molecular levels are important to understand the biological bases of the neural tissue and its environment (structure and functions of the cells, synapses, receptors, and systems of neurotransmitters) that support BSC. This is important for clinical research as various microdeletions of genes may manifest with intellectual disability, personality disorders and altered sense of self. For example, there is an increased risk of schizophrenia in 22q11.2 deletion syndrome (Goldenberg et al., 2012), characterized by distorted sense of agency (i.e., erroneous attribution of actions to the self) (Salomon et al., 2022). We note that there have been to our knowledge only very few attempts to link BSC to neurochemistry and neuronal mechanisms, despite methods and techniques are available in animal and human research models. For example, Wada et al. (2019) used an original paradigm evoking illusory ownership over a fake body part in mice (the so-called rubber tail illusion). They investigated the intensity of the rubber tail illusion in *Caps2*-KO mice, that exhibit autistic-like phenotypes by reducing brain-derived neurotrophic factor (BDNF) release in the brain. They showed that *Caps2*-KO mice had lower rate of behavioral responses compatible with illusory ownership than the wild-type mice. This indicates that BDNF seems important for plastic events related to BSC in the parietal cortex, in line with observations in non-human primates and in humans (Ishibashi et al., 2002; Hiramoto et al., 2017). Despite this interesting line of research, only few studies directly investigated the systems of neurotransmitters or hormones related to BSC regulation. It would especially be important to demonstrate that the networks

that have been linked to BSC are actually instrumental in the generation of BSC, just as the implication of the dopaminergic ventral tegmental area in consciousness (Spindler et al., 2021). Future studies should endeavor to analyze how different systems of neurotransmitters and neurons support BSC. Functional magnetic resonance spectroscopy, for example, would be a useful, non-invasive approach to provide *in vivo* quantification of brain regional biochemistry (Stanley and Raz, 2018).

- **Neuronal level.** Studies into the neurophysiological activity of neurons (action potentials) is especially important to investigate bodily experiences underpinning BSC as they can reveal the multisensory integration rules of signals from the body and its surrounding. Multisensory integration properties of neurons have been related to experimentally-induced changes in body part ownership or changes in the body schema (Iriki et al., 1996; Graziano et al., 2000). Although results from experimentally-induced changes in BSC in humans have been interpreted in the light of single cell recordings in non-human primates, there have been only little attempts to replicate these illusions in non-human primates, rodents, or other animal species.

- **Cell assembly and brain network level.** BSC and consciousness more generally are not reducible to the functioning of a few neurons or of a given brain area, but are rather seen as an emergent property of the brain, based on the communication of signals across large groups of neurons (cell assemblies) in distant brain regions (Godwin et al., 2015). Studying the synchrony between cell assemblies is deemed essential to understand how functionally and anatomically connected networks of neurons in the cortex and subcortical structures underpin certain behaviors/cognitive states (Oberto et al., 2022). Functional MRI, PET and EEG studies have described some neural correlates of BSC [reviewed in Blanke (2012), Serino et al. (2013)], but causal evidence of implications of certain cell assemblies in BSC need to be consolidated (see section “3.2 Paucity of causal evidence, instead of correlational evidence, in the study of the neural bases of BSC”), together with the description of their connectivity and pattern of communication (Uhlhaas et al., 2009). Just as for the analysis at the neuronal level, it will be important to compare the functioning of cell assemblies in human

and non-human primates to study evolutionary aspects of BSC (Parvizi and Kastner, 2018).

- *Behavioral level: ontogenetic and phylogenetic approaches.* Studies into BSC at the behavioral level can be achieved using approaches from experimental psychology, psychophysics, cognitive neuroscience, or neuropsychology. Combining ontogenetic and phylogenetic approaches of BSC will be especially important to understand the emergence of the self (and its bodily and cognitive components) and self-consciousness. BSC has been investigated in infants (Cowie et al., 2018), in adults, and more rarely in adolescents and aging populations. However, there is to our knowledge no clear description of the patterns of development and changes in the neural underpinnings of BSC that occur throughout the life span. In addition, how developmental aspects of BSC relate to phylogenetic development of BSC has, to our knowledge, not been systematically investigated. Although there is evidence that even invertebrates show representation of the extent of their body (Sonoda et al., 2012), or that non-human primates can adopt the visuo-spatial perspective of other individuals (Karg et al., 2016), there is no clear answer as to how and to what extent BSC (and the neural structures at its basis) developed in vertebrates and invertebrates.

Although multi-level analyses are required to understand complex behaviors, theoretical articles have already highlighted the difficulty to integrate subdisciplines of neuroscience and to synthesize large data sets ranging from neurochemistry to whole-brain imaging (Kotchoubey et al., 2016). It has been pointed that “the usual solely additive combination of methods and levels may not be sufficient to construct a comprehensive picture of neuropsychological phenomena. Only theoretical efforts seem to promise integration by building conceptual bridges. Integration is not a juxtaposition of concepts, but rather their overlap” (Kotchoubey et al., 2016, p. 5; Buhusi et al., 2023). Thus, integrating data from different levels of analysis would be the true challenge for the neuroscientific investigations of BSC and its neural underpinning.

There are examples of successful multi-level approaches within the field of integrative neuroscience (e.g., neural underpinnings of working memory, locomotor behavior, motor control, and social behavior) (Grillner et al., 2005; Cacioppo and Decety, 2011; Kotchoubey et al., 2016; Buhusi et al., 2023). However, integrative approaches of BSC are rather rare and data must often be gathered from related but different research areas. For example, investigations into the neural bases of self-location (the experience of occupying a volume of space) can be linked to studies of the neural bases of spatial navigation and spatial memory, which have been deciphered in several animal models (e.g., Ulanovsky and Moss, 2007; Killian et al., 2012; Cullen and Taube, 2017; Grieves and Jeffery, 2017; Moser et al., 2017), or in humans using intracranial EEG recordings (e.g., Ekstrom et al., 2003). Similarly, understanding the neural bases of the sense of agency – approached to date mostly through correlative studies [e.g., Farrer and Frith, 2002 reviewed in Charalampaki et al. (2022), Abdulkarim et al. (2023)] and a few causal studies (Dary et al., 2023) may require to compile results from studies on motor control, volition, intentional movement and sensory feedback (Haggard, 2017). There is indeed only rare studies in non-human primates or other animal models that directly

investigated the sense of agency (Kaneko and Tomonaga, 2011; Couchman, 2015).

We suggest that the integrative approach was particularly successful for the investigation of the experience of body ownership, as an effort has been made to link various levels, methodologies, and fields, including philosophy (de Vignemont, 2011; Blanke, 2012; de Vignemont and Alsmith, 2017). As noted above, the rubber hand illusion (Botvinick and Cohen, 1998; Tsakiris and Haggard, 2005) has been extensively used as an experimental paradigm to understand the phenomenal and multisensory levels of limb ownership, as well as their neural bases. At a behavioral level, illusory ownership over a fake hand or avatar has been investigated in healthy humans and in various clinical populations. However, only few studies adapted this paradigm to other animal species, including monkeys (Graziano et al., 2000; Fang et al., 2019) and more recently mice (Wada et al., 2016, 2019; Buckmaster et al., 2020), also showing that synchronous visuo-tactile stroking on a body part placed in an anatomically plausible posture can elicit illusory ownership. The paradigm has also been adapted to fMRI, EEG, PET, intracranial EEG, allowing to understand how very large neuronal assemblies contribute to BSC. With the exception of single cell recordings in parietal area 5 in monkeys, showing that response of bimodal visuo-proprioceptive neurons change when a monkey looks at a taxidermized arm being stroked in synchrony with its own arm (Graziano et al., 2000), we do not know to what extent this applies to other brain areas and how is the sense of owning a body part coded at single neuron level and small neurons assemblies. Interestingly, there have been a few pharmacological studies that have shown increased rubber hand illusion intensity in individuals taking ketamine (Morgan et al., 2011) or an interaction between the sense of body part ownership and the immune system (Finotti and Costantini, 2016; Finotti et al., 2018). Similar multilevel approaches should now be extended to all bodily experiences underlying BSC, with a stronger emphasis on phylogenetic aspects of BSC (interspecies), and interindividual differences in BSC (Table 1).

3.2. Paucity of causal evidence, instead of correlational evidence, in the study of the neural bases of BSC

Whereas fMRI and PET are considered to show neural correlates of BSC, a causal demonstration of the involvement of specific brain regions in BSC can be provided by non-invasive and invasive direct brain stimulation (Siddiqi et al., 2022; Elmaleh et al., 2023).

Non-invasive brain stimulation modulates the excitability of the brain using transcranial magnetic stimulation (TMS) and transcranial direct-current stimulation. For example, van Elk et al. (2017) used transcranial direct-current stimulation to investigate the role of the right temporo-parietal junction in perspective taking. The authors found that anodal stimulation of the right temporo-parietal junction reduced the performance when participants mentally simulated being in someone else's shoes (i.e.,

third-person perspective taking). Similarly, [Martin et al. \(2020\)](#) found that anodal stimulation to the right temporo-parietal junction increased the effect of the participant's body position (congruent or not with that of a seen avatar) in a third-person perspective taking task. These studies stressed that the right temporo-parietal junction is causally involved in perspective taking.

A recent TMS study focused on real-time brain activity underlying the sense of body ownership ([Casula et al., 2022](#)). The authors coupled TMS over the hand region in the primary motor cortex with EEG recordings in 19 healthy participants immersed in a virtual environment in which virtual limbs were displayed. [Casula et al. \(2022\)](#) showed a decrease in cortical activity in the hand region of the primary motor cortex contralateral to the virtual hand participants self-identified with. Moreover, this study showed that illusory hand ownership was related to increased connectivity with the posterior parietal cortex, and decreased connectivity with the premotor cortex, indicating plasticity in the fronto-parietal networks associated with the ownership component of BSC.

Invasive brain stimulation is used to map brain functions during presurgical evaluation of focal intractable epilepsy ([Ritaccio et al., 2018](#); [Mercier et al., 2022](#)) and in awake patients during brain tumor resection ([Duffau, 2015](#)). During electrical brain stimulation, a current of several mA is delivered to the brain through implanted electrodes or through subdural grids of electrodes placed at the surface of the cerebral cortex. Recently, several studies have reported the effects of direct electrical brain stimulation on BSC. For example, patients stimulated in the precentral gyrus, superior frontal gyrus, or in the planum temporale, reported disturbance of agency, while stimulation in the inferior temporal gyrus, middle occipital gyrus and middle frontal gyrus evoked changes in self-location, such as a feeling to “get out of his/her body” ([Andelman-Gur et al., 2020](#)). A systematic review of the literature ([Dary et al., 2023](#)) showed that only electrical stimulation of the parietal cortex disturbed all core components of BSC considered in the review article (i.e., body ownership, self-location, agency, first-person perspective) and the proportion of responses evoked by electrical stimulation in the parietal cortex was higher than in any other brain area stimulated. Except for disturbance of body ownership, which was only evoked once by stimulation of the superior parietal lobule, stimulation of the inferior parietal lobule altered all other core components of BSC. The inferior parietal lobule (angular gyrus and supramarginal gyrus) was also the area where the spatial density of electrical brain stimulation distorting the bodily self showed the strongest overlap ([Figure 2C](#)). However, this retrospective analysis of published cases lacked structured questionnaires or interview that are required to describe the complex experience associated with changes in the bodily self. In addition, this analysis included only few studies providing whole-brain mapping, with rare studies of the subcortical structures and no study of the brainstem. Prospective studies should now provide whole-brain mapping (cortical and subcortical) of the structures causally involved in BSC by describing effects of direct electrical brain stimulation in large cohorts of patients with epilepsy or brain tumors, using novel methods to identify the focal and connective organization of brain networks (see [Elmalem et al., 2023](#)).

3.3. Considering interindividual differences in BSC and its neural mechanisms

Although the rubber hand illusion and the full-body illusion have been showed to modify BSC at the group level, studies revealed interindividual differences in the vividness of these illusions. One explanation given to these interindividual differences focused on the role of empathy ([Nakul et al., 2020b](#)), suggesting that participants with higher empathy scores were more prone to experiencing the illusion. Accordingly, individuals with autism spectrum disorders, who are less empathic, were less sensitive to body illusions than control participants ([Mul et al., 2019](#)). In addition to personality traits such as empathy, another explanation takes into account individual differences in how the brain weights tactile, visual, vestibular, interoceptive and proprioceptive information for interpreting bodily experiences underlying BSC ([Pfeiffer et al., 2013](#); [David et al., 2014](#)). Individuals trained to use proprioceptive and interoceptive signals, such as professional dancers ([Ehrsson, 2012](#); [Virtanen et al., 2022](#)), might be less prone to different types of bodily illusion (rubber hand illusion, full-body illusion).

Other studies tried to explain interindividual differences by variations in the cortical thickness in areas underpinning BSC. [Kanayama et al. \(2017\)](#) investigated the relationship between subjective reports about agency, ownership, or the narrative self, and gray matter volume in 96 healthy participants. They found a significant correlation between gray matter volume in the insula and subjective reports. The ownership score correlated with gray matter volume in the postcentral gyrus, insula and angular gyrus. Another study investigated whether cortical thickness correlated with interindividual differences in illusory body ownership during the rubber hand illusion ([Matuz-Budai et al., 2022](#)). Results from this study showed that subjective reports correlated positively with cortical thickness in several areas, such as the insula, precuneus, postcentral gyrus, lateral occipital cortex, middle temporal gyrus and superior temporal gyrus. Altogether, these results indicate that the morphology of some brain structures might explain in part the interindividual differences in the bodily illusion and BSC.

The different factors explaining the interindividual differences in the experience of being a self, including the morphology of the brain, the different patterns of functional and structural connectivity, or the functioning of the metabolic, immune and neurochemistry systems, should be taken into account more systematically in future studies.

4. Conclusion

The investigation of the neural bases of BSC has been a very active and productive field of research during the last 10 years. These studies have extended our understanding of the multisensory contributions to the neural underpinnings of BSC, reinforcing for example the role of interoceptive signals in BSC ([Park and Blanke, 2019](#)). Recent studies have also endeavored to identify

the commonalities and differences between the brain networks underpinning the pre-reflective and immediate bodily self from higher-level forms of “cognitive” self. However, we noted a lack of cross-talk and cross-fertilization between levels of analyses, as well as the paucity of data regarding the molecular and cellular mechanisms underlying the neural bases of BSC (Table 1). This lack of data not only limits the interpretation of studies investigating phenomenal aspects of BSC, but also hampers the understanding of the mechanisms leading to abnormal forms of BSC in neurodevelopmental and psychiatric disorders (Tordjman et al., 2019). A better understanding of the neural bases of BSC will also be especially important for a better assessment of patients with brain lesions, or to understand and predict more accurately the consequences of brain surgery (e.g., resection of glioma or epileptogenic zone) on the various components of BSC (Schaller et al., 2021).

Author contributions

ZD and CL drafted, corrected, and finalized the manuscript. Both authors contributed to the article and approved the submitted version.

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Étudier les bases neurales du soi corporel par une approche causale

Article 2 : Revue systématique et méta-analyse de la littérature sur les bases neurales du soi corporel révélées par stimulations électriques intracérébrales

Neural bases of the bodily self as revealed by electrical brain stimulation: A systematic review.

Article publié dans Human Brain Mapping

Cette étude a pour objectif à la fois de répertorier l'ensemble des travaux qui utilisent des stimulations électriques intracérébrales et d'analyser leurs résultats pour identifier les bases neurales du soi corporel. Pour cela, nous avons suivi la méthodologie d'analyse PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*). Nous avons identifié 42 articles (études rétrospectives, séries de cas, étude de cas) de 1937 à août 2022 dans lesquels nous avons répertorié 121 cas de patients qui, à la suite d'une stimulation électrique, ont rapporté une modification d'au moins une expérience du soi corporel. Nous avons classifié les modifications du soi corporel en cinq catégories : la localisation du soi (à l'échelle du corps entier ou d'une partie du corps), l'agentivité, la perspective en première personne, le sentiment d'appartenance, l'image du corps et des symptômes liés au soi et corps tels que des sensations de dépersonnalisation ou de présence. Nous avons créé un tableau qui récapitule l'ensemble des cas de patients qui ont rapporté des modifications du soi corporel (Tableau 4, matériel supplémentaire). Des modifications de toutes les composantes du soi corporel sont rapportées uniquement dans le cas des stimulations du lobe pariétal et plus précisément au niveau du lobule pariétal inférieur. Une carte de densité 3D, réalisée avec l'aide des ingénieurs de l'INS, révèle six régions centrales impliquées dans le soi corporel : le cortex cingulaire moyen, le lobule pariétal inférieur, l'aire motrice supplémentaire, l'insula postérieure, le complexe hippocampique/amygdale et le précuneus.

Depuis la date de publication de notre revue, d'autres études ont été publiées, que nous résumons ci-dessous. Récemment, nous avons trouvé dans une étude de Qi et collaborateurs (Qi et al. 2022) que cinq patients rapportaient des modifications de la localisation du soi (« Tout mon corps est très léger, comme si je flottais dans l'air, et je suis

en légère transe »), du sentiment d'appartenance (« J'ai l'impression que l'avant du haut du corps gauche et le menton gauche ne sont pas les miens »), ou de l'image du corps (« Je ressens des vertiges, et le membre supérieur gauche et le haut du corps gauche sont très légers », « J'ai l'impression que mon corps est très lourd et qu'il me pèse », « mon corps est lourd ») lors que stimulations au niveau des ganglions de la base (Figure 17.A).

Dans un autre article publié par Duong et collaborateur (2023), nous avons également trouvé un patient qui rapportait, à la suite de stimulations dans l'insula antérieure, des modifications dans la localisation du soi assimilée à des sensations vestibulaires (« sensation que si je tombais en arrière. Mais c'était surtout du côté droit »). Une stimulation dans l'insula postérieure chez un autre patient a modifié la localisation du soi, cette fois-ci similaire à une illusion proprioceptive (« un peu [de tension] dans son bras gauche, comme s'il bougeait alors que ce n'est pas le cas », « impression que la main gauche bouge », « j'avais l'impression de bouger [ma main] mais ce n'était pas le cas en réalité »), ainsi que des modifications dans l'agentivité (« tension dans la jambe gauche, comme s'il était impossible de la bouger ») (Figure 17.B).

Enfin, un dernier article que nous avons précédemment mentionné dans l'introduction de cette thèse (section connectivité effective), publié par Lyu et collaborateurs (2023) montre que lors de la stimulation du précuneus antérieur, des modifications dans la localisation du soi (sensation de flotter ou de tomber) étaient rapportées chez 7 patients. Un patient rapporte également une dissociation entre le soi et le corps, semblable à un sentiment de dépersonnalisation (« mon corps m'a quittée ») (Figure 17.C). Au total, 14 cas de patients pourraient être ajoutés à notre revue.

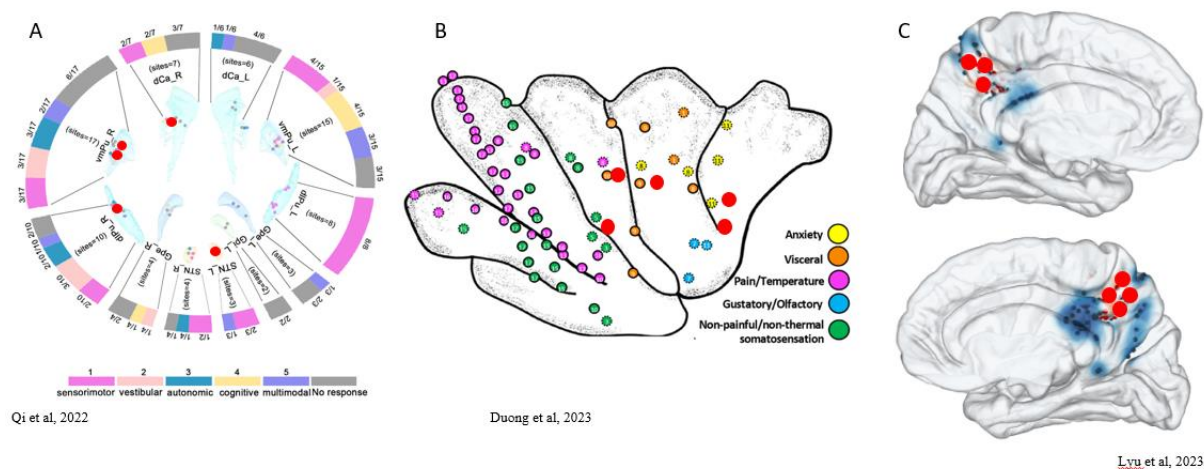


Figure 17 : Localisation des stimulations ayant induit une modification d'un ou plusieurs composants du soi corporel. Les points rouges représentent la localisation des sites stimulés ayant induit une modification du soi corporel. A) Patients rapportant une modification de la localisation du soi, de l'image du corps et du sentiment d'appartenance à la suite de stimulations des ganglions de la base. Image adaptée de l'étude Qi et al. (2022). B) Patients rapportant une modification dans la localisation du soi et dans l'agentivité à la suite de stimulation de l'insula. Image adaptée de Duong et al. (2023). C) Patients rapportant des modifications de la localisation du soi et de dépersonnalisation à la suite de stimulation du précuneus antérieur. Image adaptée de Lyu et al. (2023).

REVIEW ARTICLE

Neural bases of the bodily self as revealed by electrical brain stimulation: A systematic review

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Abstract

An increasing amount of recent research has focused on the multisensory and neural bases of the bodily self. This pre-reflective form of self is considered as multifaceted, incorporating phenomenal components, such as self location, body ownership, first-person perspective, agency, and the perceptual body image. Direct electrical brain stimulation (EBS) during presurgical evaluation of epilepsy and brain tumor resection is a unique method to causally relate specific brain areas to the various phenomenal components of the bodily self. We conducted a systematic review of the literature describing altered phenomenal experience of the bodily self evoked by EBS. We included 42 articles and analyzed self reports from 221 patients. Three-dimensional density maps of EBS revealed that stimulation in the middle cingulum, inferior parietal lobule, supplementary motor area, posterior insula, hippocampal complex/amygdala, and precuneus most consistently altered one or several components of the bodily self. In addition, we found that only EBS in the parietal cortex induced disturbances of all five components of the bodily self considered in this review article. These findings inform current neuroscientific models of the bodily self.

KEYWORDS

self consciousness, bodily self, electrical brain stimulation, epilepsy, parietal cortex

1 | INTRODUCTION

The functionality, morphology, and state of our body have shown to play a major role in many cognitive, affective, and social processes and crucially define our self consciousness. Such bodily self is considered to result from a constant multisensory integration and fine-tuning of bottom-up signals (visual, somatosensory, interoceptive, and vestibular signals) and top-down expectancy (Blanke, 2012; Lenggenhager & Lopez, 2015; Park & Blanke, 2019; Tsakiris, 2010). Various phenomenal components of the bodily self have been described in the literature, of which five main components will be

differentiated in the present review article: self location, body ownership, the first-person perspective, the sense of agency, and the perceptual body image (Table 1). Self location refers to the experience of occupying a volume of space, typically localized within one's own physical body boundaries (Blanke & Metzinger, 2009). Body ownership is the experience of owning a physical body (Tsakiris et al., 2007). The first-person perspective refers to “the experience from where I perceive the world” (Blanke, 2012). The first-person perspective is usually centered on the body and corresponds to an egocentric perspective/viewpoint (Vogeley & Fink, 2003). Agency is the sense of being in control of one's own actions (Jeannerod, 2006). The

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TABLE 1 Five core phenomenal experiences underlying the bodily self

Bodily experiences	Definition	Exemplary experimental paradigm in healthy participants	Exemplary cases in neurology and psychiatry
Self location	A volume of space, normally localized within the physical boundaries of one's body	Rubber-hand illusion (Botvinick & Cohen, 1998), full-body illusion (Lenggenhager et al., 2007)	Out-of-body experience, heautoscopy
Body ownership	The feeling that our body and its parts belong to us	Rubber hand illusion, full-body illusion (Petkova et al., 2011), real hand illusion (Kannape et al., 2019)	Somatoparaphrenia, hemiasomatognosia, body integrity dysphoria
First-person perspective	The experience from where I perceive the world	Mental imagery perspective-taking tasks (Vogeley et al., 2004), full-body illusion (Ehrsson, 2007)	Heautoscopy, out-of-body experience
Agency	The feeling of being at the origin of our actions	Rubber hand illusion, full body illusion, arm agency illusions (Farrer et al., 2003), full-body agency illusions (Kannape & Blanke, 2013)	Schizophrenia, alien hand syndrome
Perceptual body image	Own body perceptions that can be verbalized: size, weight, body shape, etc.	Body shape distortions in the full-body illusion (Piryankova et al., 2014), rubber hand illusion (Linkenauger et al., 2013), Pinocchio illusion (Lackner, 1988)	Macro/microsomatognosia, supernumerary phantom limb, depersonalization, body integrity dysphoria, anorexia, Alice in Wonderland syndrome

Note: Definition of the bodily experiences, examples of experimental paradigms used to alter and study the respective component in healthy participants, and examples of neurological and psychiatric conditions leading to alterations in these bodily experiences.

perceptual body image refers to the perceptual experience of one's own body, such as the perceived size and shape of one's own body (Gallagher, 2005).

An increasing amount of research has investigated the neural mechanisms underlying the bodily self and its different phenomenal aspects (Blanke, 2012; Blanke et al., 2015). Such research includes investigations in neurological and psychiatric patients with specific alterations in the bodily self, as well as functional and structural neuroimaging in healthy participants (reviewed in Berlucchi & Aglioti, 2010; Blanke, 2012; Park & Blanke, 2019; see Table 1 for a summary). Results point to a widely distributed cerebral network, encompassing particularly the temporo-parietal, premotor, posterior parietal, and extrastriate cortices, underlying the stable sense of a bodily self. In neurological patients, for example, it has been proposed that lesion to the posterior insula and parietal operculum can lead to a sense of loss of ownership for one's own hand or arm (e.g., somatoparaphrenia; Gandola et al., 2012). Disembodied self location, on the other hand, has been linked to lesion or seizure involving the temporo-parietal junction (Blanke et al., 2004), or the posterior insula (Heydrich & Blanke, 2013). Lesions to the posterior parietal and the prefrontal cortex have been shown to distort own-body representations, for example the sense that the body is split in two (Heydrich et al., 2010), or the experience of having an additional limb (Hari et al., 1998).

Most studies in healthy participants combined functional neuroimaging with experimental manipulations of the bodily self through synchronous, but mismatching, multisensory stimulation, altering specific components of the bodily self (reviewed in Blanke, 2012; Dieguez & Lopez, 2017). Illusory ownership of a fake hand

(Botvinick & Cohen, 1998; Ehrsson et al., 2004), self identification with a virtual body and altered self location (Ionta et al., 2011; Lenggenhager et al., 2007; Nakul, Orlando-Dessaints, et al., 2020), altered sense of agency (Farrer et al., 2003), or distortions in the structure and size of the felt body (de Vignemont et al., 2005; Ehrsson, Kito, Sadato, Passingham & Naito, 2005) have been induced using such techniques in healthy participants (see Table 1 for a summary). Functional neuroimaging studies revealed an involvement of the premotor cortex, primary somatosensory cortex, extrastriate body area, insula, the putamen, and intraparietal sulcus in illusory self identification with a rubber hand or with a virtual body (Chancel et al., 2022; Ehrsson et al., 2004; Ehrsson, Holmes, & Passingham, 2005; Gentile et al., 2015; Guterstam, Björnsdotter, Bergouignan, et al., 2015; Ionta et al., 2011; Limanowski et al., 2014; Limanowski & Blankenburg, 2015; Petkova et al., 2011). Other studies found that the temporo-parietal junction, primary somatosensory cortex, premotor cortex, cingulate cortex, and the posterior superior temporal gyrus are related to illusory changes in the self location (Guterstam, Björnsdotter, Gentile, & Ehrsson, 2015; Ionta et al., 2011). The sense of agency on the other hand, has been related to the insula and inferior parietal cortex (Chambon et al., 2013; Farrer et al., 2003; Farrer, Frey, et al., 2008; Farrer, Bouchereau, et al., 2008; Farrer & Frith, 2002), whereas experimentally-induced changes in the perceptual body image (perceived shape and size or posture of the body) have been related to the postcentral sulcus, intraparietal sulcus, insula, and inferior parietal lobule (Ehrsson et al., 2005; Kavounoudias et al., 2008; Naito et al., 2017). While the neural networks revealed by these neuroimaging studies are typically based on a correlative approach, a more causal link has been suggested by non-invasive transcranial

direct current stimulation (de Boer et al., 2020; Lira et al., 2018; van Elk et al., 2017), or even more directly by invasive, intracranial electrical brain stimulation (EBS) (Arzy et al., 2006; Blanke et al., 2002; Bos et al., 2016; Desmurget et al., 2009; Schaller et al., 2021).

EBS is typically used during presurgical evaluation of focal intractable epilepsy to define as accurately as possible the seizure onset zone and perform functional brain mapping (Trebuchon et al., 2020; Trébuchon & Chauvel, 2016), or in awake patients during brain tumor resection (Duffau, 2015). During EBS an electrical current of several mA is directly delivered to the brain through intracerebrally implanted electrodes (stereoelectroencephalography, SEEG) or through subdural grids and strips of electrodes placed at the surface of the cerebral cortex (electrocorticography, ECoG; Grande et al., 2020; Isnard et al., 2018; Lesser et al., 2010). SEEG electrodes are implanted either unilaterally or bilaterally, and each electrode has multiple contacts to record activity from several brain regions and/or to apply EBS (Isnard et al., 2018). The electrodes allow to stimulate and record activity in deep brain regions such as the insular, cingulate, and orbitofrontal cortex, or the amygdala. During EBS, clinicians record the patients' phenomenal experience (including perceived disturbances of the bodily self), behavioral responses (e.g., muscle contraction), and electroencephalographic activity (i.e., SEEG and ECoG). During brain tumor resection, electrical current is applied through electrodes directly on the cortex or on subcortical fibers. Under local anesthesia, patients perform various cognitive and motor tasks to identify the resection boundaries, while largely preserving functionally significant areas and pathways. Since the pioneering work from neurosurgeon Wilder Penfield (e.g., Penfield & Rasmussen, 1950), clinicians have increasingly used EBS, providing functional maps (Duffau et al., 2003; Salanova et al., 1995a, 1995b) and connectivity maps (Duffau, 2015) of the human cerebral cortex. Given these advantages, EBS during awake surgery might be a particularly interesting perspective to assess the sense of self (Schaller et al., 2021).

EBS offers some advantages for mapping brain functions (reviewed in Mercier et al., 2022). EBS enables three-dimensional recordings of epileptic discharges, changes in cortical excitability and in brain connectivity evoked by EBS with a high temporal resolution (Isnard et al., 2018). Furthermore, EBS is usually considered to provide *causal* rather than just *correlative* evidence for a link between neural structures and phenomenal experience, such as somatosensory, visual, auditory, vestibular, emotional, and autonomic perceptions (reviewed in Selimbeyoglu & Parvizi, 2010), or more complex sensations, like reminiscence of past experience, déjà-vu, dreamy state and memory illusions (Curot et al., 2017; Penfield, 1955).

While in his seminal investigations Penfield did not investigate specifically disturbances of the bodily self, he reviewed 190 cases of surgery for focal epilepsy in awake patients under local anesthesia carried out during a nine-year period and described "psychical responses," during which the patient is conscious and usually capable of introspection (Penfield, 1947, 1955). Psychical responses include experiential responses, defined as psychical hallucinations of past experience (e.g., flash back, dream), and interpretive responses, defined as psychical illusion about the present experience (e.g., déjà-

vu, fear, disembodiment). Interestingly, both experiential and interpretive responses encompass distortions of the bodily self as defined in the present study, as they refer to illusions about the experienced state of the body (posture, weight, size, shape) and self (location, connection to the body). Penfield (1955) identified 10 relevant cases and concluded that psychical responses "result from the stimulation principally of the lateral and superior surfaces of either temporal lobe. The superior surface is that portion of the temporal lobe that is hidden within the Sylvian fissure and in the circular sulcus that surrounds the insula beneath it" (see areas highlighted in pink in Figure 1). In line with earlier work by Penfield, more recent EBS studies confirmed the role of the superior temporal cortex and temporo-parietal junction in self location and embodiment. For example, an especially spectacular phenomenon reported during EBS in the temporo-parietal junction is an out-of-body experience (OBE), during which the self is perceived as located outside of the physical body, resulting in alterations of several components of the bodily self, especially self location and first-person perspective (Blanke et al., 2002; Bos et al., 2016; De Ridder et al., 2007; reviewed in Nakul & Lopez, 2017). However, full-blown OBEs seem very rare in the context of EBS, and investigations of the neural bases of other components of the bodily self have been poorly described in earlier EBS studies, have attracted less attention, and have not been systematically reviewed.

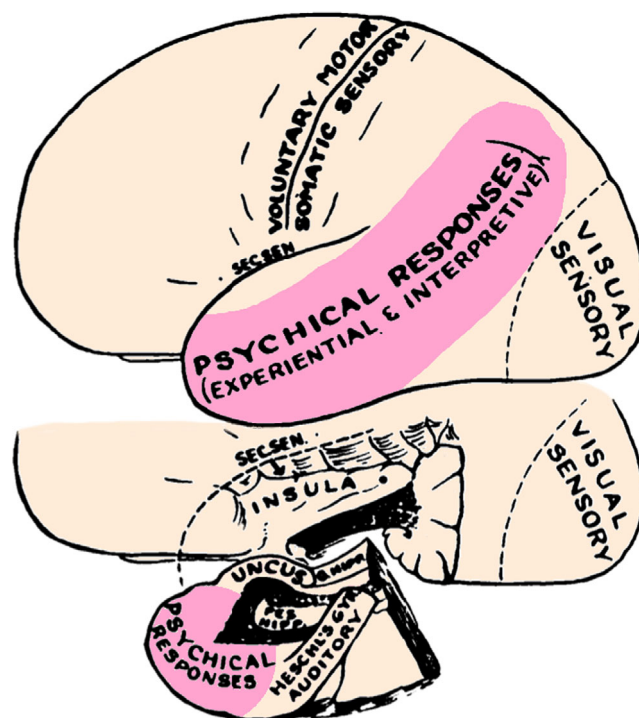


FIGURE 1 Brain areas responsible for psychical responses identified by Penfield. In this anatomical description of the left cerebral hemisphere, Penfield has represented the temporal lobe cut and turned down in order to show the superior and mesial surface of the temporal lobe. Modified from Penfield (1955) "The Twenty-Ninth Maudsley Lecture: The Role of the Temporal Cortex in Certain Psychical Phenomena" with the permission from Cambridge University Press

Here, we provide a systematic review of the literature on the neural bases of the bodily self as revealed by EBS in neurological patients, following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Page et al., 2021). We focus on disturbances in the five core phenomenal components of the bodily self described above—self location, body ownership, first-person perspective, agency and perceptual body image—and aim at identifying the underlying brain areas.

2 | MATERIALS AND METHODS

2.1 | Search strategy

This systematic literature review is reported in accordance with the PRISMA guidelines (Page et al., 2021; Tables S1 and S2). We searched articles published in English in PubMed up to March 23, 2022 without date restriction using keywords in all available fields (title, abstract, keywords). The full search strategy is detailed in Table S3. Keywords searched included several synonyms for the stimulation and recording methods: “SEEG,” “stereo-EEG,” “electrical cortical stimulation,” “stereoencephalography,” “electrical stimulation,” “direct electrical stimulation,” “direct stimulation,” “stereo EEG,” “intracranial electroencephalography,” “stereo-electro-encephalography,” “epilepsy,” “awake,” “craniotomy,” “glioma.” For the bodily self disturbances, keywords included various disorders of self and own body perception: “embodiment,” “disembodiment,” “doppelgänger,” “feeling of a presence,” “heautoscopy,” “depersonalisation,” “self location,” “derealisation,” “autoscopy,” “bodily self,” “out of body experience,” “self consciousness,” “out-of-body illusion,” “body schema,” “body image,” “ownership,” “agency,” “vestibular,” “posture,” “proprioception.”

2.2 | Study selection

We included only primary articles (original research articles, case reports, prospective and retrospective case series) but not review articles. Inclusion criteria were studies reporting patients who received EBS with implanted depth electrodes (SEEG), subdural grids and strips of electrodes (EcoG), or during awake brain surgery. Studies were included in our review only if they reported a disturbance of one or several phenomenal components of the bodily self that could be related to the direct effect of EBS. Inclusion criteria were defined as follows:

- *Disturbances of self location* include (1) *OBE*, that is, full-blown illusory perception of being disembodied; (2) *vestibular sensations*, that is, illusory self motion without disembodiment, including illusory translations of the entire body, sensation of falling, floating in the air, rocking, and being tilted; and (3) *proprioceptive sensations*, that is, illusory motion of a body part without disembodiment, such as illusory elevation of an arm.

- *Disturbances of body ownership* correspond to the inability to recognize a body part as one's own, or to sensation of disownership, estrangement or disembodiment of a body part or of the whole body.
- *Disturbances of first-person perspective* correspond to a change in the multisensory perspective, or viewpoint on the world, which may be allocentric instead of egocentric, distanced and elevated.
- *Disturbances of agency* correspond to the sensations of not being at the origin of the bodily actions, of not controlling and generating them, or when one feels the urge to execute actions, or when one experiences a resistance to planned actions.
- *Disturbances of the perceptual body image* correspond to own body perceptions that can be verbalized, including sensations of lightness or heaviness of a body part (without illusory or real motion of this body part), sensations that a body part is absent or lost, or a perceived body size distortion.
- *Other disturbances of the bodily self*, which did not clearly fit into the above categories were also considered. This category encompasses the sense of depersonalization, that is, a dissociative experience combining sensations of being detached from the body, of losing control over the body, actions, or thoughts (Simeon & Abugel, 2006). This category also includes the feeling of a presence, the vivid sensation that somebody is present nearby (Fénelon et al., 2011), as it has been proposed that a sensed presence is a sensorimotor double of the patient's own body (Arzy et al., 2006; Bernasconi et al., 2021).

2.3 | Data extraction

The characteristics of the publications were extracted (authors, year of publication, region in the world), as well as information about the clinical population (sample size, number of patients reported, disease), methods of the applied EBS (brain areas explored, stimulation parameters). For each EBS-evoked bodily self disturbance, we identified the category of bodily self disturbance and the location of the stimulation (cerebral hemisphere, lobe, brain area, and coordinates of electrode location). Only four publications reported coordinates in a standardized atlas (14 cases from 2 studies in Talairach coordinates; 14 cases from 2 studies in MNI coordinates). Authors from recent studies were contacted by email to require coordinates of activation if they were not reported in their original publication. Six authors provided additional electrode coordinates (71 cases from 6 studies in MNI coordinates). All data are summarized in Table S4.

2.4 | Analysis of the neuroanatomical localization of EBS

The localizations of the EBS evoking different types of bodily self disturbances were summarized on a 3D rendering of the right cerebral hemisphere on the MNI brain template from FreeSurfer (Fischl et al., 2004). We used 3Dviewer tool for the visual

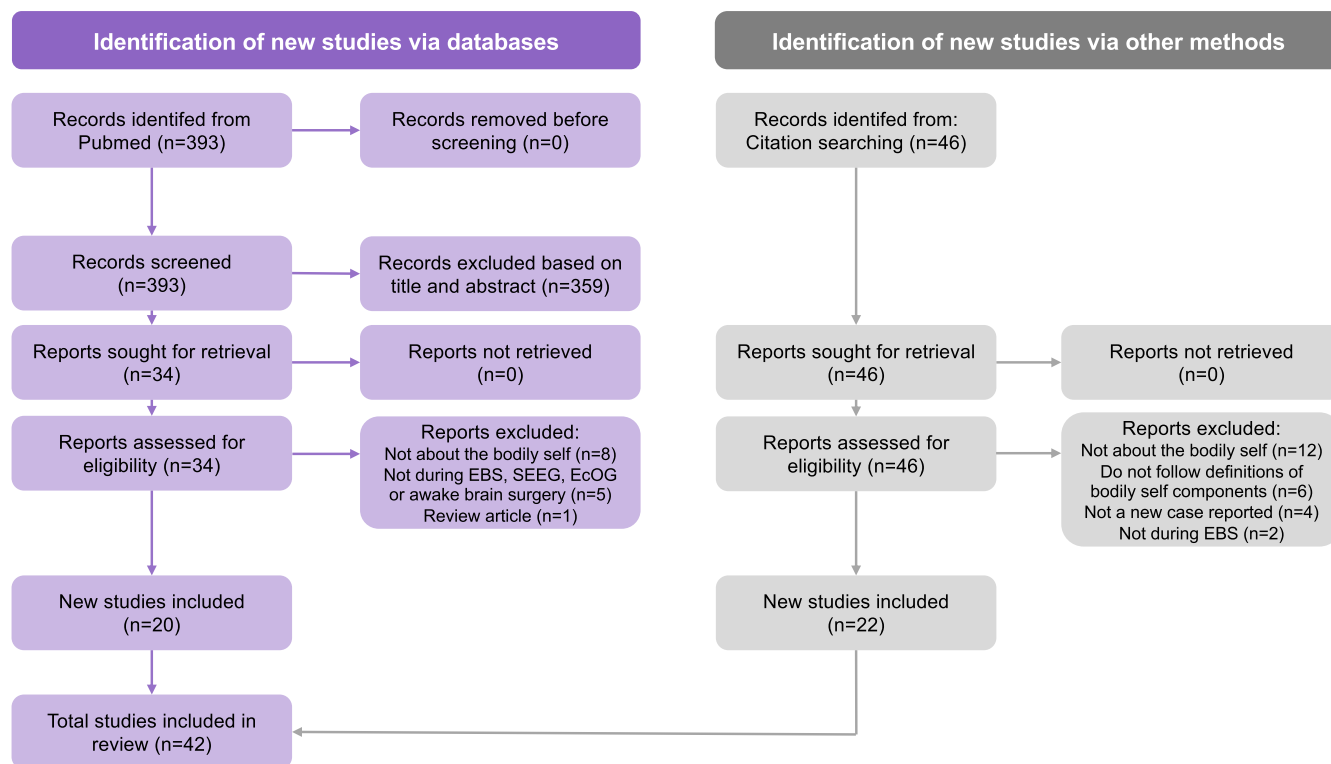


FIGURE 2 Flow diagram for the preferred reporting items for systematic reviews and meta-analyses (PRISMA)

representation (Medina Villalon et al., 2018) available at <https://meg.univ-amu.fr/wiki/3DViewer>. We converted the coordinates from Talairach to MNI coordinates when necessary, using custom-based scripts in MATLAB 2020 (The MathWorks, Inc., USA). When possible, we reported the other EBS localizations with the best approximation possible on the MNI template, considering the published MRI or implantation schema, and considering the original description of EBS localizations in terms of gyrus, sulcus, and Brodmann area. Sites of EBS were plotted on a single right cerebral hemisphere surface, by projecting coordinates on its closest mesial or lateral parts. Each point was projected on the surface, except for the amygdala, hippocampus, and insula, for which we created a mesh on which points were projected.

2.5 | Statistical analysis

To identify the core areas underpinning the bodily self, we calculated 3D spatial density of electrode contacts evoking disturbances of the bodily self using custom-based scripts in MATLAB 2020 and projected the spatial density maps on a 3D rendering of the right cerebral hemisphere on the MNI template. We also analyzed the proportion of evoked responses per brain region, as well as the hemispheric dominance of EBS for each component of the bodily self, using the Fisher's Exact test and z-tests (SPSS 26, IBM, USA).

3 | RESULTS

3.1 | Literature review

We identified 393 articles in the database, of which 20 were eligible to be included in the systematic review. We also searched for relevant studies in the references provided in each of these publications and included 22 other articles on the effects of EBS on the bodily self. In total, 42 articles were included in the systematic review. Figure 2 presents the PRISMA flow diagram of the study selection.

3.2 | Characteristics of the studies

The 42 articles included in the systematic review were published between 1937 and 2022. More than half of the studies were from Europe (52.3%; $n = 22$), 33.3% ($n = 14$) were conducted in North America, and 14.3% ($n = 6$) in Asia. Twenty-three articles were retrospective studies (sample size: 33–1132 patients; mean $\pm$ SD: 196 ± 231 patients), 7 articles were case series (13–47 patients; 21 ± 16 patients), and 12 studies were single case reports. Table 2 summarizes the study characteristics, as well as clinical population, stimulation parameters, location of electrodes, and phenomenal experience.

TABLE 2 Summary of the publications included in the systematic review reporting bodily self disturbances evoked by electrical brain stimulation

Publication	Region	Clinical population and EBS procedure	Type of study: Sample size	Number of patients included in the review	Prevalence of bodily self disturbances (%)	Category of bodily self disturbance reported	Brain areas explored by EBS
Penfield and Boldrey (1937)	N. America	Epilepsy (ABS)	RS: 163	3	1.8	SL (vest), Ag.	Frontal, parietal, temporal
Penfield (1947)	N. America	Epilepsy (ABS)	RS: 190	1	0.5	SL (vest), Other	Temporal
Penfield (1955)	N. America	Epilepsy (ABS)	RS: 190	1	0.5	SL (OBE)	Temporal
Penfield (1957)	N. America	Brain tumor and epilepsy (ABS)	RS: 108	1	0.9	SL (vest)	Temporal, central
Mullan and Penfield (1959)	N. America	Epilepsy (ABS)	RS: 217	4	1.8	Other	Temporal
Penfield and Perot (1963)	N. America	Epilepsy (ABS)	RS: 1132	1	0.1	SL (vest)	Whole brain
Halgren et al. (1978)	N. America	Epilepsy (ABS)	CS: 36	15	—	SL (prop), Ag., SL (vest)	Temporal
Fried et al. (1991)	N. America	Epilepsy (subdural grid)	CS: 13	7	—	Ag., SL (prop)	Fronto-parietal
Richer et al. (1993)	N. America	Epilepsy (SEEG)	RS: 40	3	7.5	SL (prop), SL (vest)	Rolandic, parietal
Salanova et al. (1995a)	N. America	Epilepsy (ABS)	RS: 82	6	7.3	SL (vest), BI, Other	Parietal
Salanova et al. (1995b)	N. America	Epilepsy and brain tumor (ABS, subdural grid)	RS: 34	1	2.9	BI	Parietal
Blanke et al. (2000)	Europe	Epilepsy (subdural grid)	CR: 1	1	—	SL (vest)	Frontal, temporal, parietal
Kremer et al. (2001)	Europe	Epilepsy (SEEG)	CR: 1	1	—	Ag.	Cingulate
Blanke et al. (2002)	Europe	Epilepsy (subdural grid)	CR: 1	1	—	SL (vest), BI, 1PP, SL (OBE)	Frontal, temporal, parietal
Ostrowsky et al. (2002)	Europe	Epilepsy (SEEG)	CS: 30	2	—	BI	Temporal
Kahane et al. (2003)	Europe	Epilepsy (SEEG)	RS: 260	13	5	SL (vest)	Whole brain
Wiest et al. (2004)	Europe	Epilepsy (subdural grid)	CR: 1	1	—	SL (vest)	Parietal
So and Schaüble (2004)	N. America	Epilepsy (subdural grid)	CR: 1	1	—	Own.	Fronto-central
Isnard et al. (2004)	Europe	Epilepsy (SEEG)	RS: 50	12	24	SL (vest), Other	Temporal, insular
Arzy et al. (2006)	Europe	Epilepsy (subdural grid)	CR: 1	1	—	Other	Frontal, temporal, parietal
Vignal et al. (2007)	Europe	Epilepsy (SEEG)	RS: 180	3	1.7	Other, SL (OBE)	Temporal
De Ridder et al. (2007)	Europe	Tinnitus (paddle electrode)	CR: 1	1	—	SL (OBE)	Temporo-parietal
Mulak et al. (2008)	Europe	Epilepsy (SEEG)	RS: 339	5	1.5	Other	Whole brain
Desmurget et al. (2009)	Europe	Brain tumor (ABS)	CS: 7	3	—	Ag., SL (prop)	Parietal, premotor

TABLE 2 (Continued)

Publication	Region	Clinical population and EBS procedure	Type of study: Sample size	Number of patients included in the review	Prevalence of bodily self disturbances (%)	Category of bodily self disturbance reported	Brain areas explored by EBS
Mazzola et al. (2014)	Europe	Epilepsy (SEEG)	RS: 219	13	5.9	SL (vest)	Insula
Blanke et al. (2014)	Europe	Epilepsy, brain tumor (subdural grid)	CS: 5	3	—	Other	Insular, temporal, fronto-parietal
Balestrini et al. (2015)	Europe	Epilepsy (SEEG)	RS: 274	16	5.8	BI, Other, SL (vest)	Parietal
Bos et al. (2016)	Europe	Brain tumor (ABS)	CR: 1	1	—	SL (prop), SL (OBE), 1PP	Parietal, temporal, Sylvian fissure
Caruana et al. (2018)	Europe	Epilepsy (SEEG)	RS: 329	25	7.6	SL (vest)	Cingulate
Yu, Liu, et al. (2018)	Asia	Epilepsy (SEEG)	CR: 1	1	—	SL (OBE), 1PP	Frontal, temporal, parietal
Yu, Yu, et al. (2018)	Asia	Epilepsy (SEEG)	RS: 43	3	7	BI, SL (vest)	Operculo-insular
Popa et al. (2019)	Europe	Epilepsy (SEEG)	RS: 110	11	10	BI, SL (vest), SL (prop), 1PP	Cingulate
Mandonnet et al. (2020)	Europe	Brain tumor (ABS)	CR: 1	1	—	BI	Superior parietal
Fornia et al. (2020)	Europe	Brain tumor (ABS)	CS: 12	8	—	Ag.	Premotor and S1
Andelman-Gur et al. (2020)	Asia	Epilepsy (subdural grid)	RS: 62	23*	—	Ag., SL (vest), SL (OBE)	Frontal, parietal, occipital, temporal
Oane et al. (2020)	Europe	Epilepsy (SEEG)	CS: 47	6	—	SL (vest)	Whole brain
Fox et al. (2020)	N. America	Epilepsy (SEEG, subdural grid, strip of electrodes)	RS: 67	7	10.4	SL (vest)	Frontal, temporal, parietal, cingulate
Sun, Zhang, Ren, et al. (2021)	Asia	Epilepsy (SEEG)	RS: 20	1	—	BI	Parietal (S1)
Sun, Zhang, Yu, et al. (2021)	Asia	Epilepsy (SEEG)	RS: 33	9	27.3	Ag.	Parietal (S1)
Parvizi et al. (2021)	N. America	Epilepsy (SEEG)	CR: 1	1	—	Other	Frontal, temporal, parietal
Bratu et al. (2021)	Europe	Epilepsy (SEEG)	CR: 1	1	—	SL (OBE)	Whole brain
Hao et al. (2022)	Asia	Epilepsy (SEEG)	RS: 376	3	0.8	BI	Whole brain

Note: Publications are sorted by year of publication. Region of the sample: North America (N. America). Procedures for electrical brain stimulation (EBS): stimulation during awake brain surgery (ABS) for resection of brain tumor or epileptic zone, and stimulation during presurgical evaluation of epilepsy (stereoelectroencephalography [SEEG] or subdural electrodes), or implantation to treat tinnitus. Type of study: retrospective study (RS), case report (CR), and case series (CS). To avoid bias, the prevalence of bodily self disturbance (in % of the patients sample) is reported only when sample size is above 30. Categories of bodily self disturbance: SL (vest): self location (vestibular); SL (OBE): self location (out-of-body experience); SL (prop): self location (proprioceptive); Ag: agency; BI: body image; 1PP: first-person perspective; Own: ownership; Other (feeling of a presence, depersonalization, derealization). S1: primary somatosensory cortex. *Individual EBS evoking bodily self disturbances were reported as different cases as the number of patients was not indicated.

3.3 | Characteristics of clinical populations

Together, the studies included in this systematic review analyzed the EBS responses of a total of 4680 patients, of which 51.7% ($n = 2421$) received EBS during the presurgical evaluation of intractable epilepsy, 48.2% ($n = 2258$) received EBS during awake brain surgery for epilepsy or brain tumor, and 0.02% ($n = 1$) received EBS for intractable tinnitus. Out of these, we identified 221 patients (4.7% of all reported patients) who experienced a disturbance of one or several components of the bodily self during EBS. Eighty percent of the patients who reported a disturbance of their bodily self ($n = 176$) received EBS through SEEG, ECoG or strips of electrodes, whereas 20% ($n = 45$) received EBS during awake brain surgery.

3.4 | Prevalence of bodily self disturbances during EBS

When considering only the retrospective studies with a sample above 30 patients in order to avoid bias related to small samples (for similar procedures, see Dai et al., 2022), we observed that the prevalence of bodily self disturbances ranged from 0.1% to 27.3% (mean $\pm$ SD: 6.2% $\pm$ 7.3%; Table 2).

3.5 | Categories of bodily self disturbances evoked by EBS

Figure 3 compares the number of EBS-evoked disturbances of the different components of the bodily self and Table S4 summarizes the individual phenomenal reports.

The by far most commonly reported disturbance of the bodily self was a change in the perceived self location (163 responses representing 55.8% of all responses). Disturbances in the perceived self location were evoked significantly more often than any other component of the bodily self (all $z > 9.05$, and all p -values $< .0001$). The most common responses within this category included a perceived change in self location with vestibular sensations ($n = 131$; 44.9% of all responses; all $z > 6.55$ and $p < .0001$) characterized by illusory translation of the entire body (reported by 43 patients, e.g., Case 43 in Table S4: "Sliding towards the lower end of the bed"; Blanke et al., 2000), sensation of falling (in 39 patients, e.g., Case 45: "The patient reported that she was 'sinking into the bed' or 'falling from a height'"; Blanke et al., 2002), or feeling of floating in the air (in 31 patients, e.g., Case 34: "Feeling their whole body floating just above the bed"; Richer et al., 1993), without the sense of disembodiment.

The second most frequent EBS-evoked disturbance of the bodily self affected the sense of agency ($n = 57$; 19.5% of all responses). Disturbance in the sense of agency was also significantly more frequently evoked than other components of the bodily self, excluding self location (all $z > 2.13$ and all p -values $< .05$). Disorders of agency included the sensation an external agent moving (parts of) the body (reported by 17 patients, e.g., Cases 11–19: "The patients perceived all the above movements as being induced by an agent outside themselves"; Halgren et al., 1978), an "urge to move" for 8 patients (Andelman-Gur et al., 2020; Sun, Zhang, Yu, et al., 2021), an intention to move (5 patients, e.g., Case 85: "A pure intention, that is, a felt desire to move without any overt movement being produced"; Desmurget et al., 2009), or a resistance to perform an action (10 patients, e.g., Cases 171–180: "I feel resistance to anything I am told to do [...] the possibility of continuing in any action is blocked"; Andelman-Gur et al., 2020).

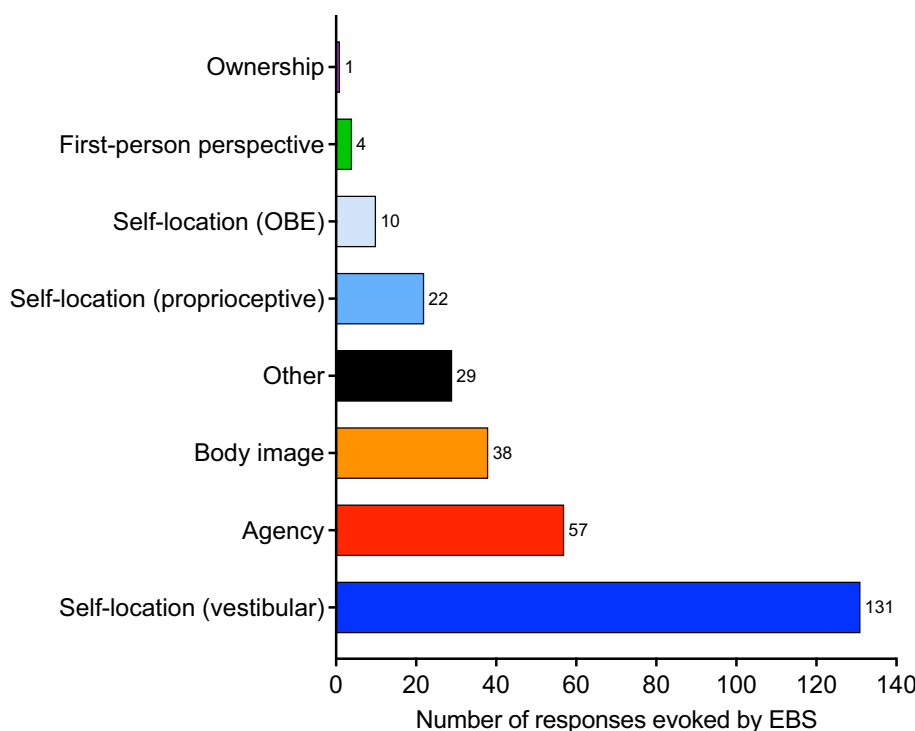


FIGURE 3 Distribution of the EBS-evoked disturbances in the different components of the bodily self. Disturbances of self location are plotted separately for vestibular illusions, proprioceptive illusions, and out-of-body experiences (OBE). Note that the number of responses reported exceeds the number of patients: when patients reported disturbances in several components of the bodily self for a given EBS, all components were counted separately

Disturbances of the perceptual body image represented 13% ($n = 38$) of the bodily self related responses. The cases included sensations that a body part was larger (in 15 patients, e.g., Cases 104–117: “He feels his right hand larger and swollen”; Balestrini et al., 2015), sensations that a body part was smaller (only in Case 45: “She reported seeing her legs ‘becoming shorter’.”; Blanke et al., 2002), or heavier (in 6 patients, e.g., Case 151: “Sensation that the upper right limb is heavier”; Popa et al., 2019), that a body part was missing (in 11 patients, e.g., Case 146: “The patient reported that he could not feel the existence of his right hand”; Yu, Yu, et al., 2018; Case 40: “Feeling that the leg is absent” (Salanova et al., 1995b), or the sensation that a body part was distorted (in 4 patients, e.g., Case 42: “My hand feels as if it is going around like a screwdriver”; Salanova et al., 1995a). There was no reported case of a supernumerary limb.

Other disturbances represented 9.9% ($n = 29$) of all bodily self related responses after EBS, a proportion of responses that did not differ from that of the perceptual body image ($z = 1.17$, $p = .24$). They included the sense of depersonalization (in 22 patients, e.g., Case 217: “This feeling of being disconnected from something. [...] It's like being weightless in your own mind as a personality”; Parvizi et al., 2021) and the feeling of a presence (in 5 patients, e.g., Case 75: “He is behind me, almost at my body, but I do not feel it”; Arzy et al., 2006).

There were 22 cases of disturbances of self location with proprioceptive illusion, which represented 7.5% of all responses (e.g., Case 45: “The patient felt her right leg being drawn towards the opposite wall of the operating theatre”; Blanke et al., 2002); Case 159: “Sensation that the upper part of the body moves upwards” (Popa et al., 2019).

We found only very rare cases of full-blown OBEs, which include changes in the first-person perspective and body ownership during EBS. We identified 10 cases of illusory self location during OBEs, representing 3.4% of all responses. OBE included the perception that the self was disembodied with autoscopia (e.g., Case 120: “She felt as if she floated just below the ceiling and saw her own body lying on the operating table”; Bos et al., 2016) or disembodiment without autoscopia (e.g., Case 5: “Oh God! I am leaving my body, an altered relationship to his own person as though he were outside of his body”; Penfield, 1955). We identified three responses of changes in the first-person perspective, associated with OBE, which represented 1% of all responses (e.g., Case 45: “I see myself lying in bed, from above, but I only see my legs and lower trunk”; Blanke et al., 2002). However, we found only one case of altered sense of body ownership during EBS in a patient with epilepsy (Case 62: “Sudden estrangement of the left lower extremity from the rest of his body”; So & Schaüble, 2004).

3.6 | Localization of EBS evoking disturbances of the different components of the bodily self

3.6.1 | Effect of EBS in the different lobes

Figure 4a summarizes the localization of EBS evoking disturbances of the bodily self and Figure 4b quantifies the different categories of

bodily self disturbances separately for each lobe and the cingulum. Disturbances of the bodily self were evoked by EBS in the parietal lobe ($n = 90$ responses evoked by EBS, representing 32.1% of all evoked responses in all brain regions stimulated), cingulum ($n = 60$, 21.4%), temporal lobe ($n = 54$, 19.3%), frontal lobe ($n = 39$, 13.9%) and insular lobe ($n = 32$, 11.4%). EBS in the occipital lobe only rarely evoked disturbances of the bodily self ($n = 5$, 1.8%). Statistical analyses indicated a significantly higher proportion of responses in the parietal lobe (32.1%) than in all other regions stimulated (all $z > 2.86$ and all p -values $< .01$). The proportion of responses did not differ between the cingulate and temporal cortex ($z = 0.63$, $p = .53$), but was higher in the cingulate than in the frontal cortex ($z = 2.32$, $p < .05$).

Figure 4b shows that only EBS in the parietal lobe evoked disturbances of all five phenomenal components underlying the ordinary and healthy sense of the bodily self that were considered in the present systematic review (including all three subcategories of self location, agency, perceptual body image, first-person perspective, body ownership).

3.6.2 | Localization of EBS changing the perceived self location

Vestibular sensations were evoked by EBS in the cingulate (36% of self location responses), parietal (27%), insular (16%) and temporal (15%) cortex (Figure 4b). Although the proportion of vestibular sensations did not differ significantly between the cingulate and parietal cortex ($z = 1.51$, $p = .12$), the proportion of vestibular responses in each of these areas was significantly higher than in the insular cortex (all $z = 2.01$ and $p < .05$) and temporal cortex (all $z = 2.36$ and $p < .05$). Stimulation in the anterior, middle and posterior cingulate cortex induced an illusory displacement of entire body. Similar sensations were evoked by insula stimulation, especially during EBS in the posterior insula. Illusory whole-body displacements were also evoked by temporal cortex stimulation, mostly in the hippocampal/amygdala complex (e.g., Cases 20–25), superior temporal gyrus, as well as less frequently by EBS in the middle and inferior temporal gyri. In the parietal cortex, EBS in the parietal operculum, angular gyrus or precuneus predominately evoked feelings of body elevation and illusions that the body moved toward one side (e.g., Case 54).

Proprioceptive sensations were evoked by EBS in the parietal (36% of the proprioceptive responses), temporal (32%), and cingulate (18%) cortex (statistical tests on proportions were not conducted due to the low number of responses). Responses including illusory translation of a body part (e.g., Case 159) occurred after stimulation of the right angular and supramarginal gyri, subcortical white matter in the temporo-parietal junction or middle cingulate cortex.

Ten OBEs were evoked during EBS in the temporal (50% of all OBE responses), parietal (20%), occipital (10%), frontal (10%) and insular (10%) cortex (statistical tests on proportions were not conducted due to the low number of responses). More precisely, OBE was evoked by EBS in the angular gyrus, the posterior part of the superior

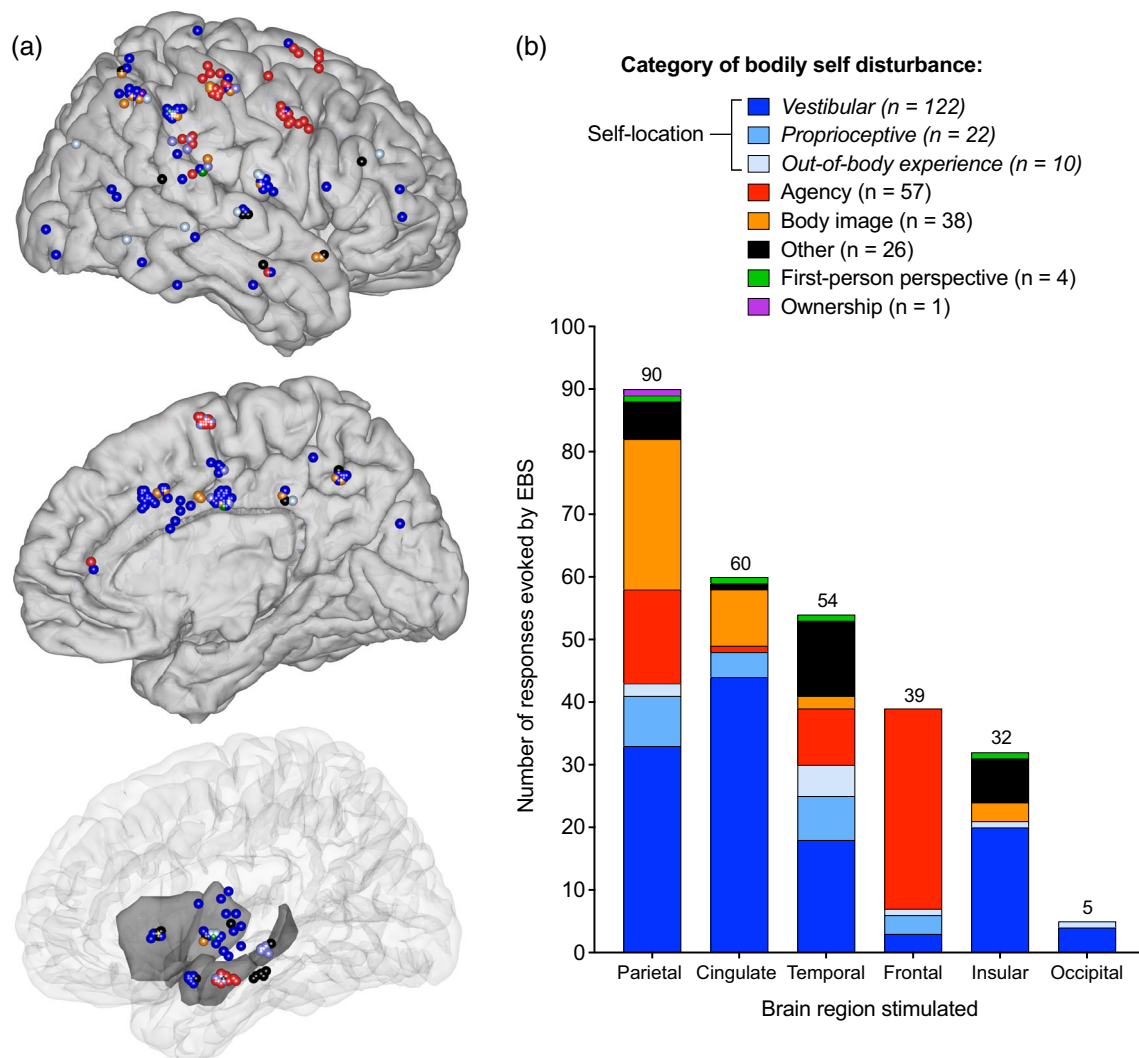


FIGURE 4 Localization of EBS evoking bodily self disturbances. (a) EBS sites are summarized on 3D views of the right cerebral hemisphere, with a color code indicating the category of bodily self disturbances. The lower part shows EBS in the insula and mesio-temporal region. (b) Number of disturbances in the different components of the bodily self according to the brain region stimulated. 292 EBS could be located based on the anatomical data available in the articles considered in the review. Changes in the experience of self location are plotted separately for vestibular illusions, proprioceptive illusions and out-of-body experiences (OBE). Note that patients may report disturbances of several components of the bodily self for a given stimulation, which was coded in several categories

temporal gyrus at the junction with the angular gyrus, the subcortical white matter in the temporo-parietal junction, the anterior insula and in middle frontal gyrus and middle occipital gyrus.

3.6.3 | Localization of EBS changing the sense of agency

Fifty-six percent of the sensations to urge movements or sensations of a resistance to move were reported after EBS in the frontal cortex, whereas 26% of the responses were reported after parietal lobe stimulation, such as in the angular gyrus or somatosensory cortex. There was a significantly higher proportion of responses in the frontal cortex than in all other regions stimulated (all $z > 3.23$ all p -values $< .01$). Disturbances in the sense of agency were especially evoked by EBS in

the superior frontal gyrus (mesial and lateral parts) and precentral gyrus, including the supplementary motor area and the premotor cortex (e.g., Cases 171 and 172; “feeling a strong resistance to performing the task”). Stimulation in the mesial temporal lobe (hippocampus; 16% of the response) induced, for example, the sensation that the patient’s movements were “induced by an agent outside themselves” (e.g., Cases 11–19).

3.6.4 | Localization of EBS changing the perceptual body image

Disturbance of the perceptual body image was reported after EBS in the parietal (63% of all body image responses), cingulate (24%) and insular (8%) cortex. There was a significantly higher proportion of

responses in the parietal cortex than in all other regions stimulated (all $z > 3.47$ and p -values $< .001$). Sensation that a body part becomes heavier or lighter was induced, for example, after EBS in the angular gyrus or middle cingulate cortex (e.g., case 151). Illusory distortions of the body size (e.g., Case 45) occurred after EBS in the precuneus, postcentral gyrus, posterior cingulum, and superior parietal lobule. Finally, sensations that a body part is absent (e.g., Case 161) was reported when the superior part of the anterior insular long gyrus, middle cingulate cortex, superior parietal lobule and postcentral gyrus were stimulated.

3.6.5 | Localization of EBS changing the first-person perspective

Patients reported observing their environment from a viewpoint outside their body (together with a feeling of disembodiment, OBE) after stimulation in the parietal (25% of the responses), temporal (25%), cingulate (25%), and insular (25%) cortex (e.g., Cases 45, 120, 149, 153; statistical tests on proportions were not conducted due to the low number of responses). More precisely, changes in the first-person perspective were found after EBS in the angular gyrus, subcortical white matter in the temporo-parietal junction, anterior insula, and middle cingulate cortex. EBS at similar location evoked an OBE and a change in the first-person perspective, but OBE could also be evoked without a change in the first-person perspective.

3.6.6 | Localization of EBS changing the sense of body ownership

One case was identified during which EBS in the superior parietal lobule evoked an estrangement of the left lower extremity from the rest of the patient's body (Case 61).

3.6.7 | Localization of EBS evoking other disorders of the bodily self

Cases of depersonalization-derealization were reported during EBS in the superior temporal gyrus (12%), posterior cingulate cortex (4%), parahippocampal gyrus (19%), hippocampus (8%), insula (27%), and amygdala (4%; statistical tests on proportions were not conducted due to the low number of responses). The feeling of a presence was for example evoked by EBS in the left temporo-parietal junction (Case 75: "The patient had the impression that somebody was behind her").

3.7 | Identification of the main areas underpinning the bodily self

Two quantifications helped determine the main areas underpinning the bodily self. First, we plotted the histograms showing the number

of bodily self disturbances as a function of the main gyri and areas reported in the articles considered in our review. 280 EBS could be localized using this method (Figure 5). We found that disturbances of the bodily self were consistently evoked by EBS in the middle cingulum ($n = 50$, 18% of all responses evoked in all brain regions), inferior parietal lobule (angular and supramarginal gyrus, $n = 34$, 12%), mesial and lateral parts of the superior frontal gyrus (supplementary motor area and premotor cortex, $n = 23$, 8%), posterior insula ($n = 21$, 7.5%) and hippocampus ($n = 19$, 6.8%). EBS in these regions induced disturbances in one or more phenomenal components of the bodily self.

Second, we calculated 3D density maps of EBS for which coordinates were available, irrespective of the category of bodily self disturbance. Figure 6 revealed that six brain areas seem crucially involved in the bodily self as their stimulation most consistently altered the bodily self across the different studies. This approach revealed the predominant implication of the inferior parietal lobule, middle cingulum, supplementary motor area, posterior insula, hippocampal complex/amygdala, and the precuneus.

3.8 | Hemispheric laterality of EBS and category of bodily self disturbances

As not all information about the lateralization was available, we only listed the EBS where the lateralization was clearly indicated (203 responses; Figure 7). The statistical analysis of the effect of the stimulation side could only be carried out for self location, agency, body image and other sensations, for which there were enough cases reported. When considering these four experiences, we found a significant association between the hemisphere stimulated and the evoked responses ($\chi^2(3) = 55.84$, $p < .001$). The Bayes factor strongly supports the hypothesis for this association ($BF_3 = 1.23 \times 10^{11}$). Results of the z -tests indicated that for self location, the proportion of response after EBS in the right hemisphere was significantly higher than the proportion of response after EBS in the left hemisphere (77.6% of all responses evoked by EBS of the right hemisphere vs. 33.3% of all responses evoked by EBS of the left hemisphere, respectively). By contrast, for agency we found that the proportion of response in the left hemisphere was significantly higher than the proportion of response in the right hemisphere (32.1% vs. 0.8%, respectively). There was no statistically significant difference for the body image and other sensations.

4 | DISCUSSION

This systematic review of the literature presents the largest series of EBS in awake patients reporting disturbances of the bodily self. We describe below the nature of the phenomenal experience reported by the patients and the role of the stimulated brain areas in generating the sense of a bodily self.

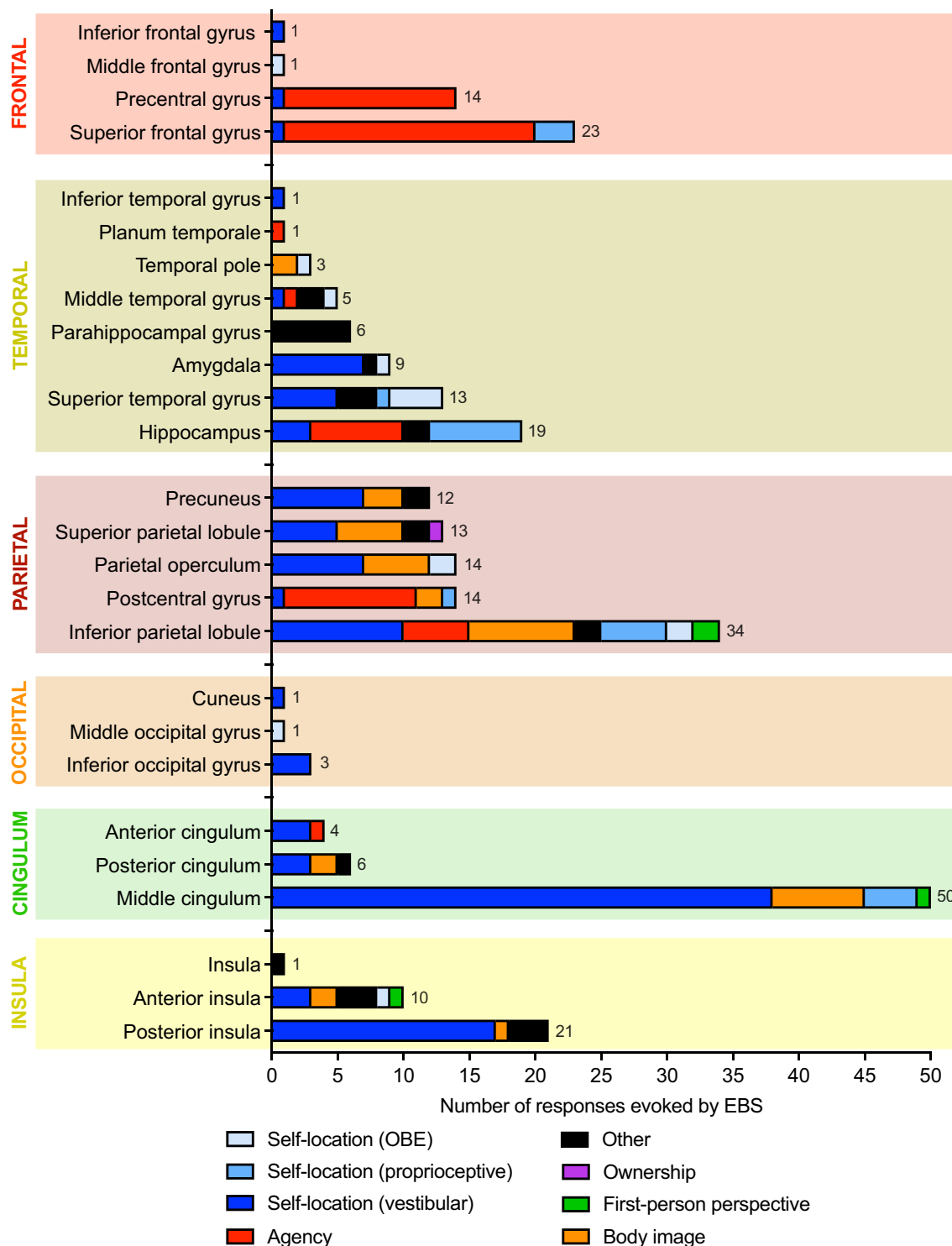


FIGURE 5 Number of disturbances of the different components of the bodily self as a function of EBS location. 280 EBS could be localized according to the main gyri for each lobe and the cingulum

4.1 | Nature and frequency of distorted components of the bodily self during EBS

The present systematic review of the literature shows that not all components of the bodily self were equally altered by EBS in awake patients.

The high prevalence of illusory self location in space (vestibular illusions of floating, levitation or translation and proprioceptive illusions such as illusory movement of a body part) that do not involve the sense of disembodiment is likely related to the relatively simple and unisensory nature of these illusions. They are also commonly experienced during hypnagogic and hypnopompic states in

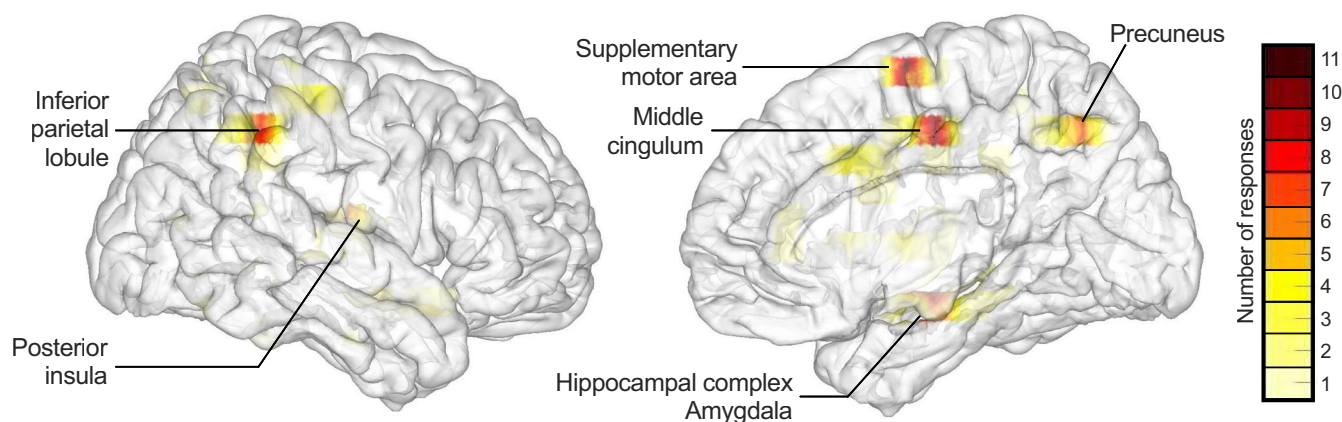


FIGURE 6 Color-coded density maps showing the number of EBS evoking disturbances of the bodily self. This analysis, conducted irrespective of the category of bodily self disturbances, revealed 6 main areas underlying the bodily self

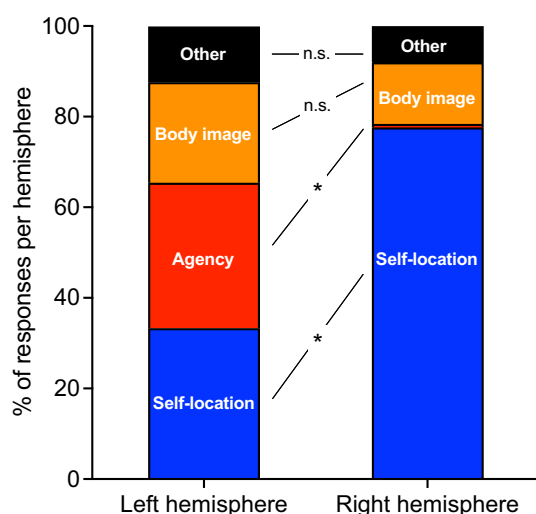


FIGURE 7 Percentage of all reported responses according to the stimulation side. * Statistically significant differences ($p < .05$) for the z-tests comparing the number of responses evoked by the stimulation of the right vs. left cerebral hemisphere

neurotypical populations (reviewed in Windt, 2015). A high prevalence of illusory self location can also be accounted by the widespread cortical vestibular network, encompassing a large number of multisensory areas in the parietal, temporal, insular, and cingulate cortex (Dieterich et al., 2003; Kahane et al., 2003; Lopez, Blanke, & Mast, 2012; Zu Eulenburg et al., 2012), which are strongly and reciprocally interconnected (Raiser et al., 2020). Similarly, illusory self location with proprioceptive illusions are in line with a large fronto-parietal network processing signals from muscle spindle afferents (Cignetti et al., 2014; Kavounoudias et al., 2008; Naito et al., 2017). In addition, there is evidence that the intrinsic cortical network architecture can predict the frequency of responses elicited by EBS in patients with epilepsy (Fox et al., 2020; McGonigal et al., 2021). EBS in “unimodal brain networks at the base of the cortical hierarchy elicited frequent and simple effects,” such as EBS in somatomotor and visual networks (Fox et al., 2020).

Abnormal sense of agency was the second most frequent type of EBS-evoked disturbances of the bodily self, whereas distortions of the perceptual body image and other disturbances were the third most frequent disturbances of the bodily self. One should note that this is in part related to the high prevalence of the reported “urge” to perform an action (Fried et al., 1991), which we included as disturbance of agency, defined in a non-restrictive way. Full-blown disturbance of agency, such as the feeling that someone else is controlling the action, an experience sometimes reported by patients with schizophrenia or depersonalization disorders, was however rarely found. Disturbances of the body image were mostly experiences that the body shape was distorted, usually involving the sense of a larger body part or a loss of a body part. Although we report of few cases of asomatognosia (missing limb, estrangement of body part) during EBS, the feeling of an additional body part seems to be rarely evoked by EBS. We found only one case of supernumerary phantom limb due to EBS of the motor cortex for treating central pain (Canavero et al., 1999), which did not follow our inclusion criteria. The patient reported once every 1–2 weeks the presence of a painful supernumerary left arm. However, this illusion was reported about 6 weeks after the stimulator implantation, and could not be causally related to the direct effect of EBS, when compared to the immediate effects of EBS in patients with epilepsy or during awake brain surgery. Consistent with our observations on the effects of EBS, supernumerary phantom limbs are also rare during seizures (Hari et al., 1998) or stroke (Khateb et al., 2009; Miyazawa et al., 2004). Other types of disturbances of the bodily self reported here were mainly related to depersonalization, which combines various sensations of being detached from the body, or losing control over the body, actions, or thoughts, or a feeling of a presence.

It is interesting to note that in our analysis OBE including changes in the first-person perspective and body ownership were very rarely found. While the rare cases have revealed important insights on the fundamentals of the bodily self (Blanke & Metzinger, 2009) and have been widely discussed in the scientific and general literature, there is no clear answer as to why these phenomena are so rare during EBS.

The low prevalence of OBE, changes in the first-person perspective and body ownership does not seem to be related to different excitability of the underlying intrinsic brain network (Fox et al., 2020), as these illusions were mostly triggered by EBS in the network where the most frequent disorders of the bodily self were also triggered. All these three disturbances of the bodily self are much more complex illusions than simple illusory elevation of the body, or illusory flexion of a body part, as they involve interpreting the experience from several senses together, and/or require a breakdown of a larger brain network. At a first glance, this low prevalence seems in contrast with the fact that 5%–10% of individuals from the general population have had at least an OBE in their lifetime, sometimes including changes in the visuospatial perspective (Blanke & Dieguez, 2009; Lopez & Elzière, 2018). On the other hand, experimentally-induced conflicts between senses in healthy participants have to date never evoked full-blown OBEs, but rather illusory self location toward an avatar and self identification with an avatar, without overt disembodiment (Ionta et al., 2011; Lenggenhager et al., 2007; Nakul, Orlando-Dessaints, et al., 2020). Alternatively, EBS may be effective only in populations prone to these illusory changes in embodiment, first-person perspective, and body ownership. Indeed, disturbances of self location and the perceptual body image, together with mental imagery abilities about the own body and spatial perspective, have been related to several factors and personality traits, including anxiety, migraine, depersonalization (Braithwaite et al., 2017; Lopez & Elzière, 2018), and schizotypy (Arzy et al., 2007; Mohr et al., 2006), or to different reliance on interoceptive and visual signals (Nakul, Dabard, et al., 2020; Pfeiffer et al., 2013; Tsakiris et al., 2011). It is therefore speculated that illusory disembodiment and changes in ownership were evoked mostly or only in these subpopulations of participants. Finally, it is also possible that the conditions to evoke such illusions require a particular involvement of the synchrony of the underlying neural systems (Hsu et al., 2022), as it is the case for complex phenomena such as memory reminiscence (Barbeau et al., 2005; Bartolomei et al., 2017).

4.2 | Prevalence of bodily self disturbances among experiential phenomena during EBS

Despite the increasing use of SEEG in clinical practice for presurgical evaluation of epilepsy (Parvizi & Kastner, 2018), there are only few retrospective studies in large samples of patients, and no prospective studies available, to correctly estimate the prevalence of EBS-evoked bodily self disturbances. A previous review article summarized the effects of EBS reported in the literature up 2010 (Selimbeyoglu & Parvizi, 2010). Based on their data, we calculated that out the 566 responses evoked after EBS, 9% were disturbances of the bodily self as defined in our present review article.

In the sample of patients included in our systematic review of the literature, we estimated that the prevalence of bodily self disturbances averaged 6.2% (of the patients receiving EBS) based on retrospective studies with a sample size above 30 patients. However, there was a very large variability in the prevalence across

studies, ranging from 0.1% to 27.3%, depending on the stimulated brain regions. The highest prevalence was found in the parietal cortex (primary somatosensory cortex: 27.3%; Sun, Zhang, Yu, et al., 2021) and temporo-insular cortex (24%; Isnard et al., 2004), whereas the lowest prevalence was found for early whole-brain or temporal cortex mapping by Penfield and colleagues (0.1%–1.8%; Penfield & Perot, 1963; Penfield, 1947, 1955, 1957).

The generally comparatively low occurrence of bodily self responses during EBS might have several causes. It has been argued that EBS is not ideal to investigate complex cognitive functions and perceptions due to the nature of the brain networks involved and because of methodological limitations pertaining to EBS procedures during SEEG and awake brain surgery (Herbet, 2021; Mandonnet, 2021). While low-level sensorimotor perceptions rely on rather local and unimodal neural networks, with limited spatial variability between brains, high-level cognitive and perceptual functions are based on more distributed networks of multisensory cortical and subcortical brain areas, which present with larger variability between individuals. There is recent evidence to suggest that EBS in network that are heteromodal and higher in the cortical hierarchy evoke rare and more variable perceptions (such as stimulation of the limbic and default mode network; Fox et al., 2020), which may render particularly difficult the study of higher cognitive functions. This may also account for the intra-individual and inter-individual variability of the responses during EBS in a same network (e.g., Halgren et al., 1978), sometimes given as a limitation of EBS procedures (Borchers et al., 2011). In addition to the nature of the networks involved, EBS procedures may limit the investigation of high-level cognitive functions and perceptions, such as distortions of the bodily self. Indeed, EBS is often applied during cognitive tasks such as reading, picture naming, memory tasks or motor tasks. Accordingly, the self reports and clinical responses collected are oriented toward the performance of these tasks, rather than toward detailed introspective analysis from the patients about their sense of self.

4.3 | Neural network underpinning the bodily self

The disturbances in the bodily self reported in the present review of the literature fall into the category of interpretive responses and psychical illusions defined by Penfield (1955), as they are illusions about the current state of the body and self. In contrast to Penfield's description of a core area for psychical responses in the temporal cortex (Figure 1), we identified a much larger network involved in the sense of self, encompassing mainly the inferior parietal lobule, middle cingulum, supplementary motor area, posterior insula, precuneus, and hippocampus (Figure 6). As reviewed in details elsewhere, all these areas belong to brain networks related to the sense of self in functional neuroimaging in healthy participants or in brain lesion studies (Berlucchi & Aglioti, 2010; Blanke, 2012; Blanke & Metzinger, 2009; Lenggenhager & Lopez, 2015; Park & Blanke, 2019; Serino et al., 2013; Seth, 2013; Tsakiris, 2010; Vogeley & Fink, 2003). These areas have also been related to phantom perceptions in general

(De Ridder et al., 2011). This might explain why EBS within areas belonging to this network can trigger various illusory contents about the self and body, either in relation to the perceptual and emotional state of the body (through cingulate, prefrontal, parietal, and precuneus activation), or to memories through activation of the hippocampus, parahippocampal area, and amygdala (De Ridder et al., 2011). Interestingly, the areas reported here as underpinning the bodily self overlap to a great degree with the posterior brain networks underlying conscious experience in general (Koch, 2018; Raccach et al., 2021). However, the bodily self, as a minimal and immediate form of self (Blanke & Metzinger, 2009; Gallagher, 2000), does not seem to involve the prefrontal cortex, which is more implicated in higher cognitive functions and reflective aspects of consciousness (Boly et al., 2017; Dehaene & Changeux, 2011; Odegaard et al., 2017) and is in general less likely to evoke responses and perceptions during EBS (Fox et al., 2020).

4.3.1 | Inferior parietal lobule

The present review revealed that only stimulation of the parietal cortex induced a modification of all components of bodily self and that the proportion of responses evoked by EBS in the parietal cortex was higher than in any other brain area stimulated. Except for disturbance of body ownership, which was only evoked once by EBS in the superior parietal lobule, EBS applied in the inferior parietal lobule resulted in a change in all other core components of the bodily self. Moreover, the analysis of EBS spatial density indicates a strong overlap of stimulation sites in the inferior parietal lobule (angular gyrus and supramarginal gyrus). This result from EBS studies showing causal implication of the inferior parietal lobule in the bodily self is in line with results from previous functional neuroimaging studies in healthy participants and brain lesion studies. Studies found that all areas within the inferior parietal lobule were strongly connected to the inferior frontal, insular and posterior temporal cortex, as well as to a broad network of other posterior brain regions, such as the somatosensory cortex and superior parietal areas, as well as with the auditory and visual cortex (Caspers et al., 2011). Results from diffusion tensor imaging and tractography studies (reviewed in Seghier, 2013) showed that the angular gyrus is especially strongly connected to areas that we identified as underpinning the bodily self, such as the precuneus, supramarginal gyrus, the hippocampus and parahippocampal gyrus, the middle temporal gyrus, the superior frontal gyrus, and the inferior frontal gyrus (Catani et al., 2005; Makris et al., 2007; Rushworth et al., 2006; Uddin et al., 2010). Because of this extensive pattern of connection, the inferior parietal lobule belongs to and interact with fronto-temporal systems, or the default mode network.

4.3.2 | Middle cingulate cortex

We found that EBS in the middle cingulate cortex evoked mostly sensations of illusory self location (vestibular illusions) and distortions of

the body image. The middle cingulate cortex has been involved in a very large range of functions, including “feedback processing, pain, salience, action-reward association, premotor functions, and conflict monitoring” in humans and in non-human primates (reviewed in Procyk et al., 2016; p. 467). More posterior stimulation during awake brain surgery have been related to altered states of consciousness (Herbet et al., 2016). A large retrospective analysis of the effects of EBS in the cingulate cortex indicates that the majority of vestibular responses—in relation to illusory self location in the present review article—were evoked by stimulation of the caudal part of the middle cingulate cortex (Caruana et al., 2018). In general, EBS in the posterior regions of the cingulate cortex (caudal part of the middle cingulate cortex and posterior cingulate cortex) were characterized by sensory illusions concerning the vestibular, interoceptive, somatosensory, and visual systems (Caruana et al., 2018). The role of the middle and posterior cingulate cortex in self location is also confirmed by their activation in fMRI studies that have used optokinetic stimulation or galvanic vestibular stimulation, evoking illusory self motion perception (Cardin & Smith, 2010; Smith et al., 2011), or experimentally-induced illusions of self location and body ownership (Guterstam, Björnsdotter, Gentile, & Ehrsson, 2015). Given the importance of these senses for the experienced bodily self, the posterior regions of the cingulate cortex may play an important role in the bodily self.

4.3.3 | Supplementary motor area

The supplementary motor area was mostly involved in changes in the sense of agency, as broadly defined in the present review article, although a few EBS also evoked illusory self location. The medial frontal cortex has consistently been involved in action monitoring in various fMRI studies (Yomogida et al., 2010), studies using transcranial magnetic stimulation and transcranial direct current stimulation (Cavazzana et al., 2015; Moore et al., 2010) and using SEEG recordings (Bonini et al., 2014). Here, we provide further causal evidence of the role of the mesial frontal cortex in the sense of agency.

4.3.4 | Insula

The insula has attracted a lot of attention recently in neuroscience. Functional MRI and PET studies have linked the insula to a large range of sensory, emotional and cognitive functions (Craig, 2002, 2009; Kurth, Zilles, et al., 2010; Kurth, Eickhoff, et al., 2010). The posterior insula has more specifically been involved in the processing of somatosensory, thermosensory, nociceptive, and vestibular information (Bottini et al., 1994, 2001; Dieterich et al., 2003; Mazzola et al., 2019; Ostrowsky et al., 2002). Recent meta-analyses of functional neuroimaging data revealed that the posterior insula is more particularly involved in sensorimotor processing, whereas the anterior insula is more involved in cognitive and socio-emotional functions (Kurth, Zilles, et al., 2010). Of note, the posterior insula contains

neurons responding to somatosensory stimuli to various body parts, and also to the entire body, making it a crucial area for whole-body integration and perception (Coq et al., 2004; Evrard, 2019; Schneider et al., 1993). The posterior insula also overlaps with the human equivalent of the monkey parieto-insular vestibular cortex, as revealed by functional neuroimaging and electrophysiological data (Bense et al., 2001; Bottini et al., 2001; Dieterich et al., 2003; Frank et al., 2014; Frank & Greenlee, 2018; Guldin & Grüsser, 1998; Lopez, Blanke, & Mast, 2012; Nakul et al., 2021). This area, which is considered the core of the vestibular cortical network, is involved in processing signals about self motion, and should therefore be important for the bodily self, given the recognized role of vestibular information for the neural underpinning of the bodily self (Lenggenhager & Lopez, 2015; Lopez, 2013, 2016; Lopez & Elzière, 2018; Lopez, Schreyer, et al., 2012). The fact that EBS evoked mostly changes in the bodily self during stimulation of the posterior rather than the anterior insula, is in line with the sensorimotor foundations of the bodily self, a minimal and immediate form of self (Blanke & Metzinger, 2009; Gallagher, 2000).

4.3.5 | Hippocampal complex

Stimulation of the hippocampus and parahippocampal gyrus evoked illusory self location (proprioceptive and vestibular), depersonalization, and distorted sense of agency. There is a large body of neurophysiological and neuroimaging evidence demonstrating that the hippocampus is crucially involved in self location and spatial memory, as it contains place cells coding the specific location of an animal (Barry & Burgess, 2014; Burgess & O'Keefe, 2003; O'Keefe & Conway, 1978; Poucet et al., 2003; Wiener et al., 2002) or a human (Ekstrom et al., 2003; Miller et al., 2013) within a real or virtual space. A seminal intracranial EEG study in patients with epilepsy identified place selectivity in the hippocampus in patients immersed in a virtual environment (Ekstrom et al., 2003). In addition, an MRI study during experimentally-induced OBE-like illusion teleporting the participants in another location of the room showed that activity in the hippocampus predicted the perceived location of the bodily self in the room (Guterstam, Björnsdotter, Gentile, & Ehrsson, 2015). Accordingly, EBS in the hippocampus may disturb the neural underpinnings of self location and/or disturb the encoding of sensory afferents to the hippocampus. There is indeed evidence that the hippocampus processes vestibular signals, which are crucial for self location (Hitier et al., 2021; Horii et al., 2004; O'Mara et al., 1994; Smith, 1997; Suzuki et al., 2001; Vitte et al., 1996). Moreover, the hippocampus is well-known for its role in episodic memory. EBS in the hippocampus has been shown to evoke various psychical experiences (Halgren et al., 1978; Penfield, 1958; Penfield & Perot, 1963), including episodic memories, personal semantics, familiarity and reminiscences of a dream (reviewed in Curot et al., 2017). This could explain the feelings of unreality reported by some patients during stimulation of the hippocampus.

4.3.6 | Precuneus

We found that stimulation of the precuneus also evoked disturbances of the body image, self location, and depersonalization. There is a large body of evidence indicating that the precuneus is involved in self processing, self awareness and consciousness (Cavanna & Trimble, 2006). Functional MRI and PET studies showed precuneus activations during numerous self related tasks, such as during visuo-spatial tasks conducted from a first- versus a third-person perspective, when participants attribute seen actions to self versus others, or judgment of personality traits pertaining to self versus others (David et al., 2006; Farrer & Frith, 2002; Kircher et al., 2000; Lambrey et al., 2012; Ruby & Decety, 2001; Vogeley et al., 2004). Interestingly, a PET study in a patient receiving EBS at the temporo-parietal junction, which triggered an OBE, revealed that the disembodied experience was related to activation of a brain network encompassing the right precuneus (De Ridder et al., 2007). The precuneus also receives vestibular information (Dieterich et al., 2003), which may explain the illusory self location reported during EBS. Tracer studies in animals indicate that the precuneus is interconnected with most of the brain areas that we found involved in the bodily self, including the supplementary motor area, the cingulate cortex, the inferior parietal lobule, and more generally the temporo-parieto-occipital cortex (Cavanna & Trimble, 2006). Accordingly, EBS in the precuneus may activate a large parieto-temporo-frontal network underlying self experience.

4.4 | Hemispheric dominance for the neural bases of the bodily self

Here, we found a right hemisphere dominance for self location and a left hemisphere dominance for the sense of agency, and no significant dominance for the perceptual body image and the other types of bodily self disturbances. The right dominance for self location is congruent with the dominance in the right cerebral hemisphere of vestibular information processing, which is crucial for the sense of self location, and represents the majority of the distortions of the bodily self collected in our systematic review. This right hemispheric dominance of the vestibular cortex has consistently been shown in right-handed individuals by a series of functional neuroimaging, anatomical and clinical studies (Dieterich et al., 2003; Dieterich et al., 2017; Janzen et al., 2008; Kirsch et al., 2016, 2018), as well as by a meta-analysis of functional neuroimaging data (Lopez, Blanke, & Mast, 2012). The right hemispheric dominance for self location is also in line with the right dominance of the proprioceptive networks (e.g., Naito et al., 2017). Overall, self awareness in a broad sense has long been associated with a right hemispheric dominance (Devinsky, 2000; Feinberg & Keenan, 2005; Keenan et al., 2005). Previous studies showed that the right hemisphere is specialized in own-body recognition and motor awareness (Antonello & Gottesman, 2017; Martinaud et al., 2017), as well as in first-person perspective (Vogeley et al., 2004) and the experience of an embodied self location (Ionta et al., 2011).

We found that the sense of agency was mostly disturbed when EBS was applied on the left side. While this result is in line with the large number of feeling of the “urge” to move and execute an action and the dominance of the motor areas in the left cerebral hemisphere of right-handed participants, it is not congruent with the implication of the mostly right insula and angular gyrus in the conscious sense of agency. However, these areas are more likely involved in the conscious sense of agency for ongoing actions (i.e., “monitoring intentional fluency” and “the subjective sense of control”; Haggard & Chambon, 2012) manipulated experimentally in fMRI studies, rather than in the feeling of urge to move evoked by EBS in otherwise immobile individuals.

4.5 | Limitations of EBS studies for neuroscientific investigations of the bodily self

Despite the recognized clinical advantages of EBS (George et al., 2020; Grande et al., 2020; Mandonnet et al., 2010), functional brain mapping using EBS has several limitations related to procedures and clinical constraints, which have been discussed in details elsewhere (Borchers et al., 2011; Parvizi & Kastner, 2018; Ritaccio et al., 2018).

First, EBS is limited by the unequal implantation of electrodes in the different cortices, which could be a bias for the results reported here. Most of focal epilepsies originate from the temporal and frontal lobes, which explains that the majority of electrodes was implanted in the temporal and frontal lobes (Parvizi & Kastner, 2018). In addition, there is an overrepresentation of some regions which have intensively been mapped and reported during the last years in retrospective studies, such as the effects of EBS in the insula (Mazzola et al., 2009, 2014, 2019; Ostrowsky et al., 2002; Yu, Yu, et al., 2018), cingulate cortex (Balestrini et al., 2015; Herbet et al., 2016; Oane et al., 2020; Popa et al., 2019), and frontal cortex (Fornia et al., 2020; Fox et al., 2018). We also note that because subcortical structures are only rarely implanted (with the exception of the hippocampus and amygdala) when compared to the cortex, we currently lack descriptions of the cerebellar and subcortical (brainstem, basal ganglia, thalamus) contributions to the bodily self, a spatial sampling bias which has been referred to as “cortico-centric myopia” (Parvizi, 2009).

Second, EBS allows to investigate functions in various areas of the brain and create a causal link between neural activity and behavior (Borchers et al., 2011; Parvizi & Kastner, 2018) and is considered “the gold standard” for brain mapping (Mandonnet et al., 2010). However, distant and indirect effects of EBS have also been described and the causal effect of EBS is deemed controversial (Borchers et al., 2011; Desmurget et al., 2013). The effects of EBS are the result of inhibition and excitation of population of neurons at local and/or distant sites (Borchers et al., 2011; Ritaccio et al., 2018). Accordingly, locations of electrodes reported here may represent the effect of EBS on a larger brain network rather than the action on the neural populations close to the stimulation electrode only. There is indeed evidence that local stimulation, evoking for example ecstatic sensations, autobiographical

memories and own-body perceptions, were associated with increased or decreased pattern of functional connectivity within larger cerebral networks (Bartolomei et al., 2012, 2017, 2019; Popa et al., 2019).

Third, EBS is by definition applied to the brain of patients who have abnormal brain tissue functioning and/or tumors, which may hamper the generalization of findings to non-neurological individuals. Patients with long-lasting epilepsy exhibit changes in functional connectivity in epileptogenic networks (Besson et al., 2017; Bettus et al., 2008, 2009; Lagarde et al., 2022; Wirsich et al., 2016). We note that recent EBS studies report only the effects of stimulation in non-epileptic tissue and/or the effects of stimulation not followed by epileptic discharges. In the case of low-grade glioma, brain reorganization before EBS may have modified the structure and function of the brain networks investigated (Duffau, 2015). Of note, only 20% of the patients reported in the present review underwent awake brain surgery. The advantage of a systematic review like ours is to identify the brain areas and phenomenal responses that are consistent across studies and patients, despite differences in the stimulation methods and paradigms (frequency, duration, intensity...).

With respect to the study of the sense of self, another limitation is related to the way clinical assessments are done during EBS. Neuropsychological and sensorimotor assessments performed during EBS in patients with epilepsy or during awake brain surgery typically focus on language, memory and visuo-spatial abilities, whereas self and own-body perceptions may not be spontaneously reported by the patients and not recorded. Patients may also have difficulty expressing what they are feeling or be afraid to say what is happening to them, resulting in a reporting bias. Regarding spontaneous self reports, the lack of structured questionnaires or interview, rarely compatible with clinical routine during EBS, limits the detailed description that would be needed to fully describe the often complex phenomenal experience associated with changes in the sense of self. For example, structured questionnaires and scales have shown to be helpful for screening emotional responses during EBS in the amygdala (Lanteaume et al., 2007).

Finally, a limitation of systematic reviews of the literature is the efficiency of online search and citation searching in published articles to identify all published cases related to the sense of self. We note that our online search was not able to identify articles published before 1993, including the work by Penfield and colleagues, probably due to the lack of keywords and referenced abstract. The large number of keywords used to define the various facets of the bodily self in our review should have allowed a comprehensive identification of the cases of bodily self disturbances published until 2022.

5 | CONCLUSIONS AND PERSPECTIVES

This systematic review of the literature reveals that EBS can evoke a large variety of phenomenal content related to the bodily self, including a disturbed sense of self location (regarding the whole-body, body parts, or disembodiment) and agency, change in the first-person perspective, altered body ownership, distorted body image, or symptoms

of depersonalization. While these different phenomenal components of the bodily self are relatively rare and were not equally altered by EBS, they were all evoked by the stimulation of the parietal cortex. We also identified a network of six main areas that were most consistently involved in disturbances of the bodily self, including the inferior parietal lobule, middle cingulum, supplementary motor area, posterior insula, precuneus, and hippocampus. This seems in contrast with earlier work by Penfield (1955, 1947), who found that “psychical responses” (i.e., experiential and interpretive responses) were mostly evoked by EBS in the lateral and superior surfaces of the temporal lobes. Future electrophysiological studies should endeavor to determine how changes in neural network electrophysiology, such as dynamics of functional connectivity between distant brain areas, underpin the bodily self. The possibility to use sensory and cognitive tasks during EBS and SEEG recordings open interesting avenues, such as the simultaneous experimental manipulation of the bodily self (e.g., using the rubber hand illusion or the full-body illusion) and recordings of intracranial EEG signals (Guterstam et al., 2019).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data used in this article are available in Table S4.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Supplementary Table 4. Cases of bodily self disturbances evoked by electrical brain stimulation sorted by year of publication. Components of bodily self disturbances evoked by electrical brain stimulation (EBS): SL (vest): self-location (vestibular); SL (OBE): self-location (out-of-body experience); SL (prop): self-location (proprioceptive); Ag.: agency; BI: body image; 1PP: first-person perspective; Own.: ownership; Other (feeling of a presence, depersonalization, derealization). Stimulation parameters: F: frequency, I: intensity (or voltage), D: duration. S1: primary somatosensory cortex. BA: Brodmann area. ¹All coordinates are reported in the MNI space, unless otherwise specified. ²Coordinates in the Talairach space. ³Additional information provided by the authors who were contacted personally. ⁴Individual EBS evoking bodily self disturbances were reported as different cases when the number of patients was not indicated in the article.

Publication	Sample size	Patients population	EBS procedure	Category of bodily self disturbances	Brain area explored	Cases included in our review and phenomenological description	Stimulation parameters	Site of EBS evoking a response and EBS coordinates ¹		
								x	y	z
Penfield and Boldrey (1937)	163	Epilepsy	Awake brain surgery	SL (prop)	Frontal and parietal cortex	Case 1: “The patient realized he had not moved but observed that it felt as though his finger, arm, foot, etc., had moved”.		Fissure of Rolando		
				Ag.	Frontal, parietal, and temporal cortex	Case 2: “Desire to move”. “The patient said the tongue did not actually move, but as the mouth was closed this could not be verified objectively”.		Postcentral gyrus		
				Ag.	Frontal, parietal, and temporal cortex	Case 3: “Desire to move”. “She wanted to move her opposite hand up and down”.		Middle temporal gyrus		
Penfield (1947)	190	Epilepsy	Awake brain surgery	SL (vest), Other	Temporal cortex	Case 4: “I feel queer, as though I were floating away.” “I have a queer sensation as if I am not here”. “As though I were half and half here.” (Patient GA)		Right superior temporal gyrus		
Penfield (1955)	190	Epilepsy	Awake brain surgery	SL (OBE)	Temporal cortex	Case 5: ““Oh God! I am leaving my body”, an altered relationship to his own person as though he were outside of his body”. (Patient VF)		Right temporal region near the insula		
Penfield (1957)	108	Brain tumour, epilepsy	Awake brain surgery	SL (vest)	Temporal and central areas	Case 6: “Sinking feeling and sensation of full head” (Patient 5).		Right superior temporal gyrus		
Mullan and Penfield (1959)	217	Epilepsy	Awake brain surgery	Other	Temporal cortex	Case 7: “Queer feeling, as though everything were out of this world—the world is unreal; there is a strange feeling as though you weren’t the same person you were before—there are waves of peculiarity in things”. (Patient PB)		Left temporal cortex		
						Case 8: “As if I were not here.” (Patient HD)		Left middle temporal gyrus		
						Case 9: “Out of this world” (Patient DA)		Right Insula		
						Case 10: “There was a feeling as though I were somewhere else, as though you were all waiting here for me to come back. I have had that feeling before.” (Patient MM)		Right superior temporal gyrus		
Penfield and Perot (1963)	1132	Epilepsy	Awake brain surgery	SL (vest)	Temporal cortex	Case 10: “My whole body seemed to be moving back and forth, particularly my head” (Patient MM)		Right temporo-occipital junction		
Halgren et al. (1978)	36	Epilepsy	SEEG	SL (prop), Ag.	Temporal lobe	Cases 11–19: “Patient reports a movement of his body. Most commonly, this movement was a localized twitch, tremor, or small displacement”. “The patients perceived all the above movements as being induced by an agent outside themselves.” (14 stimulation)	F: 30 Hz I: 5–10 mA	Right and left anterior, middle, and posterior hippocampus, anterior and middle hippocampal gyrus		

					Cases 20–25: “Spatial illusions: this included three types of responses: (i) an illusional translation of the entire body with respect to the environment; (ii) an illusional movement of the environment; and (iii) dizziness.” (9 stimulation)		Right and left amygdala, anterior and middle hippocampus
					Case 26: “Urge to move”	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)
					Case 27: “Urge to move”	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)
					Case 28: “Urge to move”	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)
					Case 29: “Urge to move right leg inward.” (Patient 12) (A3-B3)	F: 50 Hz I: 4 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to move right arm, slight extension right elbow.” (A4-B4) (Patient 12)	F: 50 Hz I: 5 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to move right arm” (A5-6) (Patient 12)	F: 50 Hz I: 4 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to move right arm away from midline”. (A5-6) (Patient 12)	F: 50 Hz I: 5 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to lift right elbow”. (A6-B6) (Patient 12)	F: 50 Hz I: 6 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to pronate right forearm, slight elbow flexion.” (A6-B6) (Patient 12)	F: 50 Hz I: 7 mA D: 5 s	Left supplementary motor area
					Case 29: “Sensation of tension at right wrist “urge” to move right hand and forearm”. (A6-B6) (Patient 12)	F: 50 Hz I: 8 mA D: 5 s	Left supplementary motor area
					Case 29: “Urge to move right arm” (A6-B6) (Patient 12)	F: 50 Hz I: 9 and 10 mA D: 5 s	Left supplementary motor area
					Case 29: “Strong urge to raise right elbow.” (A6-A7) (Patient 12)	F: 50 Hz I: 5 mA D: 5 s	Left supplementary motor area
					Case 30: “Subjective experience of movement in the absence of overt motor activity. (e.g. one patient reported “I felt my arm is moving”)”.	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)
					Case 31: “Subjective experience of movement in the absence of overt motor activity.	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)
					Case 32: “Subjective experience of movement in the absence of overt motor activity.	F: 50 Hz D: 5 s	Supplementary motor area (side unknown)

Fried et al.
(1991)

13

Epilepsy

Subdural
grid

Ag.

Fronto-parietal
region

SL (vest)

SL (prop)

Richer et al. (1993)	40	Epilepsy	SEEG	SL (prop)	Rolandic and parietal regions	Case 33: “Feeling his legs and seat floating above the bed”.	F: 50 Hz I: 1–10 mA D: 5 s	Sub-parietal sulcus: next to the horizontal portion of the sulcus, adjoining the cingulate sulcus (side unknown) Sub-parietal sulcus: next to the vertical portion of the sulcus, adjoining the cingulate sulcus (side unknown) Sub-parietal sulcus: next to the horizontal portion of the sulcus, adjoining the cingulate sulcus (side unknown)
				SL (vest)		Case 34: “Feeling their whole body floating just above the bed”.		
				SL (vest) BI		Case 35: “Feeling their whole body floating just above the bed”.		
Salanova et al. (1995a)	82	Epilepsy	Awake brain surgery	BI	Parietal lobe	Case 36: “Sensation of ‘rolling’ off the table”.	F: 60 Hz I: 4 V	Left superior parietal gyrus
				Other		Case 37: Patient “felt a twisting sensation in the contralateral extremity”.		Left superior parietal, behind the postcentral gyrus
				Other		Case 38: “A man behind”.		Left superior parietal lobule
				Other		Case 39: “A patient described by Penfield (1938) reported a ‘far away sensation’, and ‘things seem distant and small’.		Left superior parietal, just behind the sensory area
				BI		Case 40: “Feeling that the leg is absent”.		Right parietal operculum and superior parietal behind the postcentral gyrus
Salanova et al. (1995b)	34	Epilepsy	Subdural grid, awake brain surgery	BI	Parietal lobe	Case 41: “Limpness of right hand”.	F: 60 Hz I: 4V	Left parietal operculum behind the cyst
				BI		Case 42: “Oh, I feel as though I were going to have an attack, because my hand feels as if it is going around like a screwdriver.”		Right inferior parietal lobe
Blanke et al. (2000)	1	Epilepsy	Subdural grid	SL (vest)	Frontal, temporal, and parietal cortex around the central sulcus	Case 43: “Sliding towards the lower end of the bed”. “I’m rolling to the right and falling out of the bed”.	I: 4.5–5.5 mA D: 2 s	Left inferior parietal lobule at the anterior part of the intraparietal sulcus
				SL (vest)		Case 43: “I feel the urge to hold on to something in order to prevent myself from falling out of the bed”.		–62 –46 –21 ²
				BI		Case 43: “My whole body moves”. “He felt as if he were lying in a swinging hammock”.		–62 –59 23 ²
Kremer et al. (2001)	1	Epilepsy	SEEG	Ag.	Cingulate cortex	Case 43: “My whole body moves”. “He felt as if he were lying in a swinging hammock”.	I: 8 mA	–57 –45 21 ² –57 –60 23 ²
				Ag.		Case 44: “Urge to grasp”.	F: 50 Hz I: 1.2 mA D: 5 s	Right ventral bank of the anterior cingulate sulcus
Blanke et al. (2002)	1	Epilepsy	Subdural grid	SL (vest)	Frontal, temporal, and parietal cortex around the lateral sulcus	Case 45: “The patient reported that she was “sinking into the bed” or “falling from a height”.	F: 50 Hz I: 2–3 mA D: 2 s 3 stim.	Right angular gyrus
				BI		Case 45: “The patient was then asked to watch her (real) legs during the electrical stimulation. As before, she was lying down (upper body supported at an angle of 45°, legs outstretched). This time, she reported seeing her legs “becoming shorter”.	F: 50 Hz I: 4.0, 4.5 mA D: 2 s 2 stim.	

						Case 54: “Sensation to be attracted (head → body) toward the right”. Case 55: “Falling backward”. Case 56: “Falling backward (head and trunk)”. Case 57: “Sensation of falling flat”. Case 58: “Sensation to be pushed (head) from the left toward the right”. Case 58: “Sensation of rocking motion (head → trunk), backward”. Case 59: “Body oscillations toward the right and left.” Case 60: “Sensation of falling flat”.	F: 50 Hz I: 1.5 mA D: 5 s F: 50 Hz I: 3 mA D: 5 s F: 50 Hz I: 3 mA D: 5 s F: 50 Hz I: 2 mA D: 5 s F: 50 Hz I: 1.6 mA D: 5 s F: 50 Hz I: 1.2 mA D: 5 s F: 50 Hz I: 3 mA D: 5 s F: 50 Hz I: 1 mA D: 5 s I: 1 mA I: 10–11 mA I: 10 mA 3 stim. I: 11 mA 1 stim. F: 50 Hz I: 3 mA D: 5 s	Right parietal operculum 41 –31 25 ² Right parietal operculum 47 –37 29 ² Right parietal operculum 44 –45 28 ² Right precuneus 3 –38 48 ² Right precuneus 6 –44 54 ² Right anterior cingulate gyrus 9 3 31 ² Right 3 rd frontal gyrus 56 24 15 ² Right deepness of cingulate sulcus (BA 7/5) 15 –36 50 ² Right paramedian precuneus Right posterior parietal region (superior parietal lobule) Insula Insula Left temporo-parietal junction –57.15 42.08 15.63 ³ –57.15 31.96 23.00 ³ Right hippocampus
Wiest et al. (2004)	1	Epilepsy	Subdural grid	SL (vest)	Parietal cortex			
So and Schaible (2004)	1	Epilepsy	Subdural grid	Own.	Frontocentral region			
Isnard et al. (2004)	50	Epilepsy	SEEG	Other SL (vest)	Temporal lobe and insula			
Arzy et al. (2006)	1	Epilepsy	Subdural grid	Other	Frontal, temporal, and parietal cortex around the lateral sulcus			
Vignal et al. (2007)	180	Epilepsy	SEEG	Other	Temporal lobe			

Blanken et al. (2014)	5	Epilepsy, brain tumour, brain lesion and abnormality	Subdural grid	Other	Insula, fronto-parietal cortex Temporal et parietal cortex Temporal lobe	Case 93: “Feeling of body rising”. Case 94: “Feeling of body rising (like a bubble)”. Case 95: “Feeling of falling laterally on right side of bed”. Case 96: “Feeling of limb rising (as if she were flying away); associated with electrical sensation in both hands”. Case 97: “Feeling of being projected, of falling backward; associated with electrical sensation moving from left hand to head”. Case 98: “Feeling of falling to right side associated with auditory illusion (whistling in right ear)”. Case 99: “Feeling of falling backward”. Case 100: “Feeling of falling backward; associated with paraesthesia in left hand”. Case 101: “Presence of a man, behind to her right, in peripersonal space, fear and anxiety”. (Patient d) Case 102: “Presence of a male shadow, behind to the right, same position, echopraxia”. (Patient i) Case 103: “Presence behind to the right, strictly unilateral, unpleasant, no echopraxia”. (Patient k)	F: 50 Hz I: 0.5–11 mA D: 2 s	Right insula 40 -15 1 Left insula -36 -9 -2 Right insula 40 -12 8 Right insula 33 -10 14 Right insula 36 -13 17 Right insula 34 -8 -4 Right insula 36 -1 12 Right insula 35 -16 8 Unknown location
						Cases 104–117: “Body image alteration: including altered subjective perception of body image or movement” (e.g., “Patient reports that he feels his right hand larger and swollen”, “Patient feels his body moving towards the left side”)	F: 1–50 Hz D: 5–30 mA	Right precuneus Right inferior parietal lobule Right post-central gyrus Right precuneus Right inferior parietal lobule Right posterior cingulum Right inferior parietal lobule Right inferior parietal lobule Right inferior parietal lobule Right precuneus Right superior parietal lobule Right inferior parietal lobule Right superior parietal lobule Right superior parietal lobule Right precuneus
						Case 118–119: “Psychic phenomena (e.g., “Patient describes to feel “like a doll”, “Patient reports the feeling of “being as in a parallel word”, Patient describes to feel a sensation of strangeness, unfamiliarity”).		Left posterior cingulum

Bos et al. (2016)	1	Low grade glioma	Awake brain surgery	SL (prop)	Parietal lobe, temporal lobe, and the sylvian fissure	Case 120: “The patient felt her right leg being drawn towards the opposite wall of the operating theatre”. Case 120: “She experienced a complete OBE with autoscopic, in which she felt as if she floated just below the ceiling and saw her own body lying on the operating table”.	I: 8–12 mA	Left subcortical white matter in the temporo-parietal junction
				SL (OBE), 1PP				
Caruana et al. (2018)	329	Epilepsy	SEEG	SL (vest)	Cingulate cortex	Case 121–145: e.g., “Feeling of falling into a void” (and dizziness, vertigo)”. (19 patients stimulated on the right side and 6 patients on the left side)	F: 50 Hz I: 0.4–5 mA D: 5 s	Left ventral posterior middle cingulate cortex
								–3.3 23.7 41.1 ³
								Right ventral posterior middle cingulate cortex
								3.9 –20.8 41.2 ³
Yu et al. (2018a)	43	Epilepsy	SEEG	BI	Operculo-insular cortex	Case 146: “The patient reported that he could not feel the existence of his right hand when we stimulated the contralateral contacts”. Case 147: “Changes in the perception of the body’s location, such as the feeling of body elevation or movement to one side”. Case 148: “Sensations of deficiency of the contralateral limb or trunk”.	F: 50 Hz I: 1.0 mA D: 3 s	Left ventral anterior middle cingulate cortex
								–3 0.1 35.3 ³
								Left superior part of the anterior insular long gyrus
								Parietal operculum (side unknown)
Yu et al. (2018b)	1	Epilepsy	SEEG	SL (OBE), 1PP	Frontal, temporal, and parietal areas	Case 149: “She saw herself elevating to the left upper side 2 m high under the ceiling without any vestibular sensations like floating, flying, rotation and vertigo. She felt the virtual body was real herself and saw her own body entirely lying in bed being electrode stimulated by the doctor and nurses walking around in the sickroom”.	F: 50 Hz I: 0.5 mA D: 3 s	Parietal operculum (side unknown)
								Left anterior insula
Popa et al. (2019)	110	Epilepsy	SEEG	BI	Cingulate cortex	Case 150: “Sensation that the lower limb detaches from the body, loses it”. (Patient 2) Case 151: “Right upper limb feels lighter”. (Patient 5) Case 151: “Sensation that the upper right limb is heavier”. (Patient 5) Case 152: “Sensation of floating of the left hemibody”. (Patient 1) Case 153: “Sensation that the head turns to the right side, that the head will explode, will detach from the neck, sees himself from outside” (i.e., autoscopia). (Patient 7) Case 154: “Sensation that the left upper limb becomes heavier”. (Patient 8)	F: 50 Hz I: 0.75 mA D: 5 s	Right middle cingulate cortex
				BI				Left middle cingulate cortex
				BI				Left middle cingulate cortex
				SL (prop)				Right middle cingulate cortex
				BI, 1PP				Left middle cingulate cortex
				BI				Right middle cingulate cortex

						Case 155: “Sensation that the upper right limb becomes heavier associated to pain”. (Patient 11)	F: 50 Hz I: 1 mA D: 5 s	Left middle cingulate cortex
				BI		Case 156: “Sensation that the right hemibody and all the head become heavier”. (Patient 10)	F: 50 Hz I: 1 mA D: 5 s	Left middle cingulate cortex
				SL (vest)		Case 157: “Sensation that the body is being pushed to the left”. (Patient 3)	F: 50 Hz I: 1 mA D: 5 s	Left middle cingulate cortex
				SL (prop)		Case 158: “Feels that the right hand is pulled from behind”. (Patient 6)	F: 50 Hz I: 0.75 mA D: 5 s	Right middle cingulate cortex
				SL (prop)		Case 159: “Sensation that the upper part of the body moves upwards”. (Patient 9)	F: 50 Hz I: 2 mA D: 5 s	Right middle cingulate cortex
				SL (prop)		Case 160: “Sensation that upper right limb moves to the left side”. (Patient 12)	F: 50 Hz I: 1 mA D: 5 s	Right middle cingulate cortex
Sun et al. (2020)	20	Epilepsy	SEEG	BI	Anterior parietal lobe involving S1	Case 161: “An illusion that the hand was absent”.	F: 50 Hz I: 0.1–6 mA D: 3 s	Right superior parietal lobule and post central gyrus 41.05 ± 6.26 -29.46 ± 8.66 52.3 ± 7.29
Mandonnet et al. (2020)	1	Glioblastoma	Awake brain surgery	BI	Superior parietal lobule	Case 162: “Feeling that there was a discrepancy between the visual and proprioceptive perceptions of her right hand: “I do not feel my (right) hand where I see it”.”	F: 60 Hz I: 3 mA D: 3 s	Left superior parietal lobule
Fornia et al. (2020)	12	Low grade glioma	Awake brain surgery	Ag.	Premotor cortex and somatosensory cortex (S1)	Cases 163–170: EBS “was effective in interfering with motor execution when applied to both premotor cortex and S1, but, crucially, it dramatically altered the patients’ motor awareness only when applied to the premotor cortex.”	F: 60 Hz I: 2–4.5 mA	Left premotor cortex -60 9.2 35.6 ³ -58.4 8 38.8 ³ -60.6 5.8 38 ³ -61.1 3.3 38.9 ³ -61.7 1.9 38.6 ³ -61 -0.4 40.7 ³ -60.1 -1.5 42.1 ³ -55.3 1.7 42.5 ³ -57.3 -0.1 43.1 ³ -58.3 -0.7 45.4 ³ -47.3 -6.2 56.9 ³
Andelman-Gur et al. (2020)	62	Epilepsy	Subdural grid	Ag.	Frontal, parietal, temporal, occipital lobes	Cases 171–180: Change in will/urge, e.g., “Feeling a strong resistance to performing the task said despite his conscious will to continue with the task something blocks him”. See : case report (Andelman-Gur et al., 2019) ³ “I feel resistance to anything I am told to do [...] the possibility of continuing in any action is blocked”.	F: 50 Hz I: 1–10 mA for subdural electrodes I: 1–4 mA for depth electrodes D: 5 s	Left precentral gyrus -2 -22 56 ³ -2 -32 56 ³ Left superior frontal gyrus -14 14 66 ³ -18 14 66 ³ -20 14 64 ³ -22 14 60 ³ -22 14 60 ³ -20 6 66 ³ -16 4 68 ³

Fox et al. (2020)	67	Epilepsy	SEEG or/and subdural strip of electrodes	SL (vest)	Frontal, temporal, parietal and cingulate cortices	Case 201: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 4 mA	- 62.792	- 35.335	- 6.726 ³
						Case 202: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 3 mA	- 45.859	- 65.760	8.723 ³
						Cases 203: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 10 mA	- 37.649	- 65.592	49.965 ³
							F: 50 Hz I: 10 mA	- 24.163	- 60.957	52.125 ³
						Case 204: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 4 mA	- 53.879	0.564	43.596 ³
						Case 205: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 6 mA	- 2.452	- 39.961	44.367 ³
Sun et al. (2021b)	33	Epilepsy	SEEG	Ag.	Primary somatosensory cortex	Case 206: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 8 mA	- 16.193	- 34.338	75.675 ³
						Cases 207: “Vestibular effects, such as feelings of rotation, flotation and acceleration”.	F: 50 Hz I: 8 mA	- 8.598	46.356	11.650 ³
							F: 50 Hz I: 8 mA	- 10.517	46.903	0.683 ³
							F: 50 Hz I: 0.1–5.0 mA	BA 3 (side unknown) BA 1 (side unknown) BA 2 (side unknown)		
						Cases 208–210: “Urge to move”. ⁴				
						Case 211: “Urge to move”. ⁴				
Parvizi et al. (2021)	1	Epilepsy	SEEG	Other	Posteromedial cortex, medial frontal cortex, lateral posterior parietal cortex, mesial and lateral temporal lobes and anterior and left posterior insula	Cases 212–216: “Urge to move”. ⁴				
						Case 217: “Okay, I know. Maybe my depersonalization? This feeling of being disconnected from something. (...) I don't want to say weightlessness, or.... It's like being weightless in your own mind as a personality”.	F: 50 Hz (electrodes LJ3–LJ4) I: 6 mA			
						Case 217: “My personality was more attached to my body. That was less like floating in myself as a personality. That was less like who I am was cut off from the other parts of my body. That was more like, it was more like imagine if 40% of who you are becomes what you are and 60% becomes diffuse. So, the dissociation you become 40% of. You know how people will describe consciousness as difficult to describe. You ever hear that, I don't know how to put it.”	F: 50 Hz (electrode LJ4) I: 8 mA			
						Case 217: “Absolutely, so spatial coordinates are just geometry right. So, you have the plane and that theta angle, and you have 3D space. My sense of self does not associate with 3D space at all. Even day to day I would be pretty impressed either of your three selves did. Your sense of self is associated more with, my sense of self is associated more with the characteristics and qualities of who I am and the way I think, right? And the way I process information. So, my sense of self can be removed from 3D space. This could be because of epilepsy, this could easily be because of that. But if I can't move my right leg that does not make me different. Um, I would almost describe this as an ongoing thing maybe because I've had so many episodes of my epilepsy, sorry seizures. But I no longer, for a very long time I would				

Left posteromedial cortex (precuneus)

						say, those were two separate things. So, what you just kind of put me, <i>what you created was that separation. But not of my control over my body. Maybe in the same way a pilot can lose control over a plane. They can be forced out of the cockpit but still, or forced to not control it, but still see what is happening to the whole plane. That's kind of what just happened. I got pulled out of the cockpit, but, or I got pulled out of the chair, the pilot's chair, but I could still see all the gauges, and all the....</i> You know how I always try to. (...) No, not passive.... This is what I mean by a lot of the things I've told you guys is that there are ways to make whoever is in control of the plane snap back, snap everything back into place or for the plane to realize I can sit in this chair again. What you did was maybe move me out of that chair a little bit. But I'm very used to being out of that chair. (...) No, <i>I was floating more in myself</i> ".		
						Case 217: "My confidence in my ability to hold on to my body and my sensors really for lack of a better phrase. I'm losing confidence in it and I know where it's going so I can still reach a chair. I guess I can wrestle control, I can still push myself into a chair and into a position where I won't fall".	F: 50 Hz (electrodes LJ4-5) I: 8 mA	
Bratu et al. (2021)	1	Epilepsy	SEEG	SL (OBE), 1PP	Temporal, occipital, frontal, cingulate, parietal, insular cortex	Case 218: "The patient mentioned seeing his face, mouth from outside his body, from above like in a mirror with no additional sensation, no other visual symptoms."	F: 43.3 Hz I: 6 mA	Right anterior part of the periventricular nodular heterotopia
Hao et al. (2022)	376	Epilepsy	SEEG	BI	Temporal, occipital, frontal, cingulate, parietal, insular cortex	Case 219: "Loss of the right hand". (Patient 1)	F: 50 Hz I: 3 mA D: 3 s	Left posterior short gyrus of the insula
						Case 220: "Loss of the right hand". (Patient 2)	F: 50 Hz I: 4 mA D: 3 s	Left posterior dorsal cingulate
						Case 221: "Loss of the right hand". (Patient 3)	F: 50 Hz I: 1 mA D: 3 s	Left posterior part of the anterior long gyrus of the insula
						Case 221: "Loss of the right upper limb". (Patient 3)	F: 50 Hz I: 2 mA D: 3 s	Left parietal operculum
						Case 221: "Sensation of loss of the right side of the body". (Patient 3)	F: 50 Hz I: 2 mA D: 3 s	Left parietal operculum

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Article 3 : Bases neurales du soi corporel révélées par des approches de stimulations électriques intracérébrales chez des patients épileptiques

Avant-propos

Un point central de cette thèse repose sur la volonté de mettre en évidence le réseau cérébral du soi corporel de façon causale. Dans notre introduction, nous avons proposé d'évaluer la force de la causalité selon un continuum. Deux approches méthodologiques obtiennent un score élevé dans la force de leur inférence causale : l'étude des lésions et les stimulations électriques intracérébrales. Dans le cadre de notre thèse, et dans le cadre de notre collaboration avec le service d'Épileptologie et Rythmologie Cérébrale, de la Timone à Marseille, nous avons décidé d'aborder l'approche de la causalité dans la cartographie du soi corporel par l'intermédiaire des stimulations électriques intracérébrales.

Dans un premier temps, nous avons répertorié, avec Christophe Lopez et Jacques Léonard, l'ensemble des stimulations électriques intracérébrales appliquées lors des évaluations pré-chirurgicales de l'épilepsie entre août 2000 et décembre 2021 ayant induit une réponse de tout type, excepté les changements de performances liées à la lecture. Chez 354 patients stimulés plus de 19 700 stimulations (dont 11 000 à 50 Hz et 8 700 à 1 Hz), nous avons répertorié plus de 2 200 réponses ([Figure 18](#)). Chaque réponse a été classifiée en 18 catégories. Les réponses somatosensorielles (sensations de picotements, fourmillement, de courant électriques dans le corps une partie du corps) sont les réponses les plus fréquemment évoquées (18% de toutes les réponses). Les réponses visuelles simples (12%) (apparition de points lumineux, flash, etc.), les réponses autonomiques (10%) (sensations épigastriques, nausée, rubéfaction, etc.) et les réponses motrices (10%) (clonies, contraction musculaire, mouvement, etc.) sont rapportées à la fois par des stimulations par chocs et par trains. Les réponses plus complexes telles que les réponses émotionnelles (angoisse, peur, anxiété), douloureuses ou de déjà-vu sont davantage rapportées lors de stimulation à haute fréquence (50 Hz).

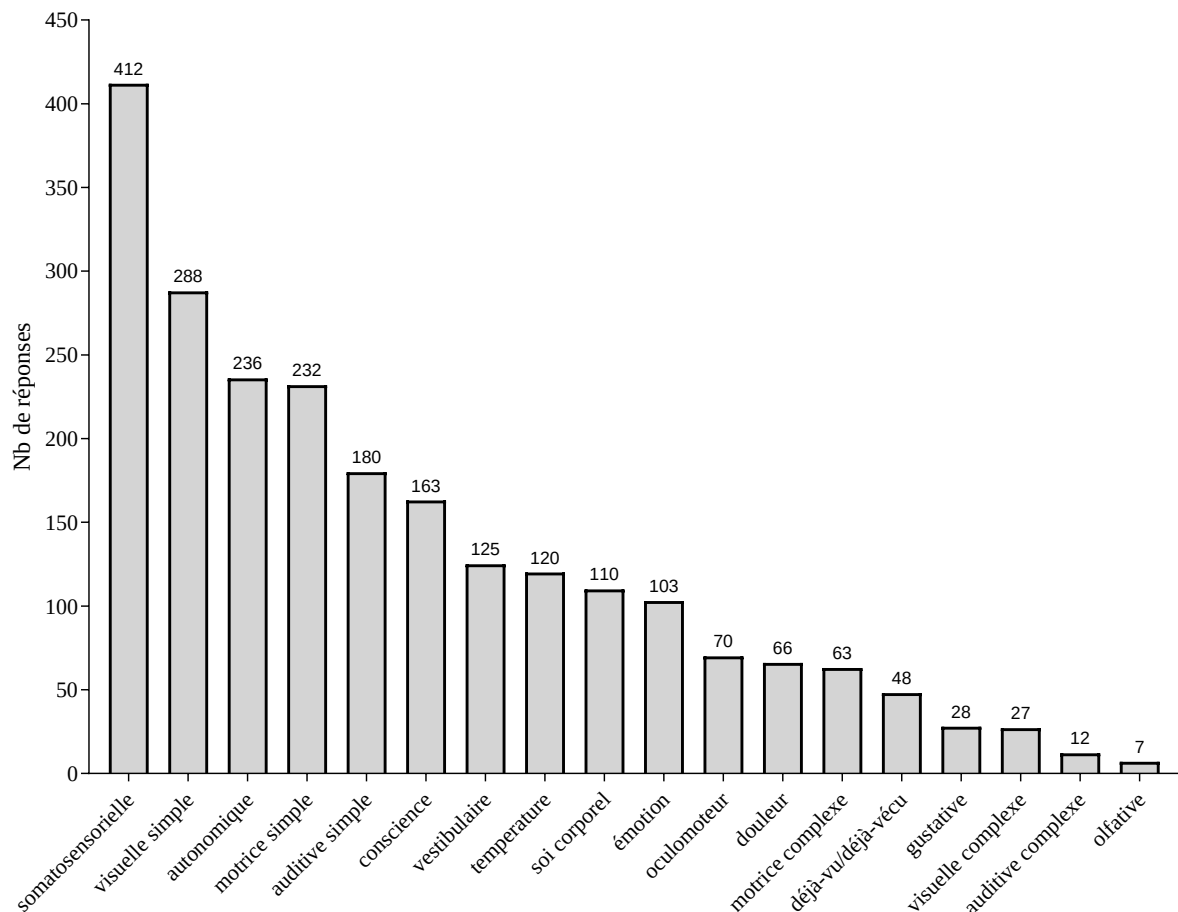


Figure 18 : Réponses évoquées à la suite de stimulation électriques intracrâniennes chez 354 patients épileptiques.

La base de données contient également le sexe et l'âge du patient, le nombre d'électrodes implantées à gauche et à droite, le nombre total de stimulation à haute et basse fréquence, ainsi que le nom du contact bipolaire de l'électrode stimulée ayant induit une réponse, la transcription de la réponse énoncée par le patient et la présence ou non de décharge après la stimulation. Grâce à ce jeu de données 4 études sont en cours ou ont été réalisées.

Une première étude figure dans le corps de cette thèse : elle traite des réponses en relation avec le soi corporel. Une deuxième étude, portant sur les sensations vestibulaires, est en cours de réalisation. Comme cette thèse se focalise sur les bases neurales du soi corporel, et donc dans un souci de cohérence, cette étude en préparation ne sera pas détaillée dans le corps de ce travail. Pour chacune des deux études, nous avons suivi la même méthodologie (Figure 19).

Une troisième étude (Annexe) a déjà été publiée dans le journal *Cortex* et se focalise les bases neurales des émotions positives et les sensations agréables (Villard et al. 2023). Dans cet article, en plus de l'utilisation de notre base de données, j'ai également contribué à la réalisation des figures et à la correction du manuscrit. Les résultats de cet article montrent que seulement 13 stimulations électriques ont induit des émotions positives (0,6 % de toutes les réponses) chez seulement 9 patients. A l'inverse, 5,3% (n = 111) des stimulations évoquées sont des réponses émotionnelles à valence négatives. La majorité des réponses émotionnelles positives étaient évoquées par la stimulation de l'insula antérieure et de l'amygdale.

Enfin, nous collaborons également avec une équipe du Brenigham & Women's Hospital à Boston qui s'intéresse aux réponses visuelles et auditives complexes. Dans cette collaboration, je suis chargée de déterminer la localisation précise des stimulations ayant induit des réponses visuelles (hallucination d'une scène réelle, etc.) et auditives complexes (illusion d'entendre un texte, d'entendre quelqu'un chanter, etc.). Nous avons identifié 12 patients sur les 354 répertoriés.

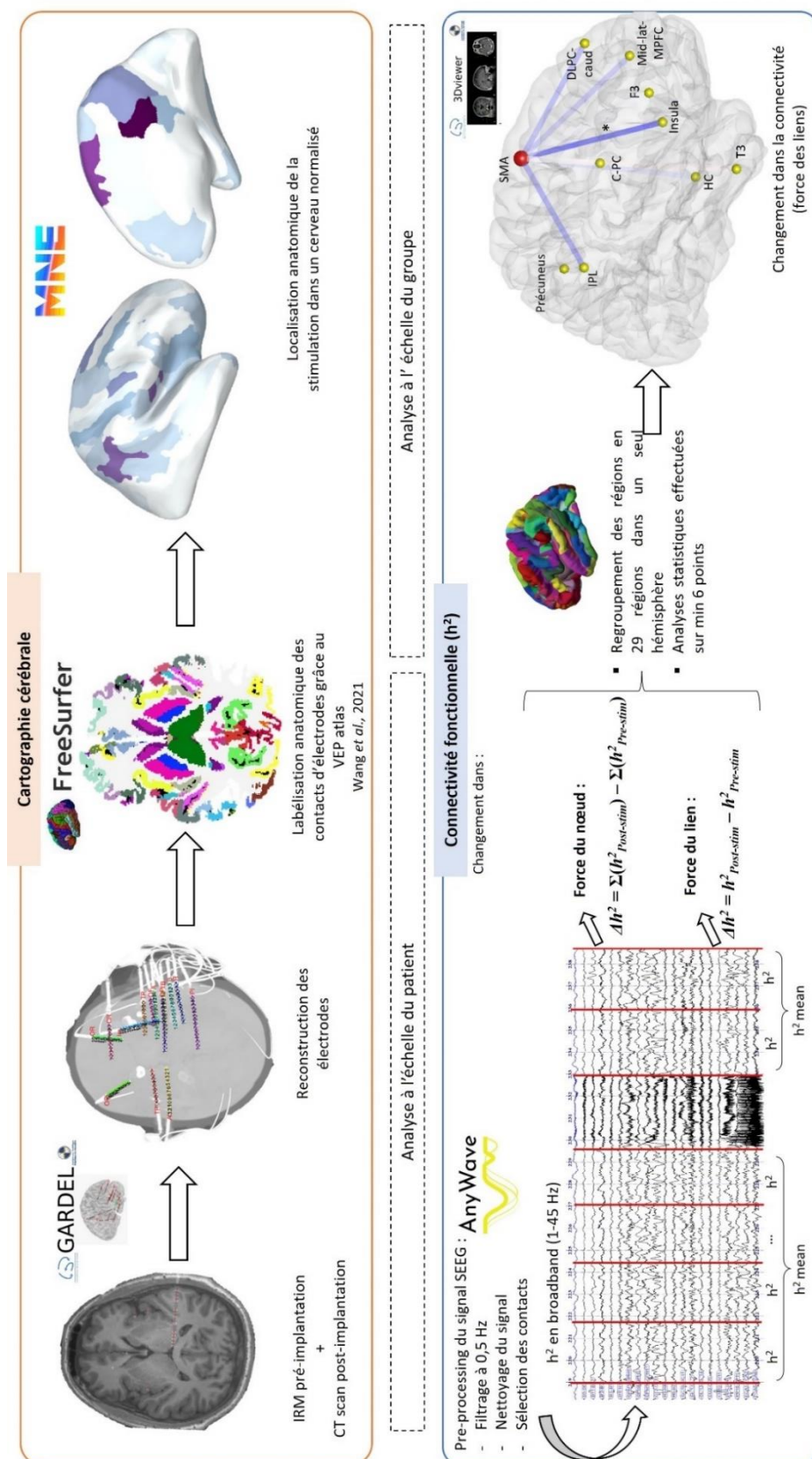


Figure 19 : Méthodologie conduite pour les études sur les réponses évoquant des modifications du soi corporel ou des sensations vestibulaires.

Unravelling the Neural Networks of the Bodily Self: Insights from Intracranial Electrical Stimulation in Epileptic Patients.

La majorité des études qui rapportent des modifications du soi corporel à la suite de stimulations électriques intracérébrales se focalisent sur la stimulation de régions spécifiques (insula, cortex cingulaire moyen, précuneus, etc.) ou sur une composante particulière du soi corporel. Aucune étude sur les bases neurales du soi corporel n'a, à ce jour, montré la disparité des régions impliquées dans le soi corporel dans une seule et même étude⁴. Il s'agit donc du premier objectif de ce travail. Nous souhaitons, par des approches causales, mettre en évidence l'ensemble des régions impliquées dans le soi corporel. Pour cela, nous avons réalisé une analyse rétrospective chez 354 patients avec une épilepsie pharmaco-résistante implantés en SEEG. Le second objectif est de décrire le réseau fonctionnel du soi corporel. Pour cela, nous analyserons l'activité électrophysiologique intracrânienne lorsque les patients rapportent une modification du soi corporel. A notre connaissance, seulement deux études ont eu une telle approche, dont une décrit un unique cas clinique (Bratu et al. 2021) et l'autre se focalise sur des modifications de l'image du corps (Popa et al. 2019). Ainsi, notre étude tend à montrer, pour la première fois, le réseau cérébral du soi corporel en établissant des liens de causalité.

Nous avons analysé les données de 50 patients qui ont rapporté des modifications du soi corporel à la suite de stimulations électriques intracrâniennes. Cela représente 78 stimulations soit 3,3% de toutes les réponses répertoriées chez les 354 patients. Nous avons seulement trouvé 4 expériences corporelles perturbées à la suite de stimulation : des modifications de l'image du corps (n = 29 réponses), des sensations de dépersonnalisation (n = 23), des modifications de la localisation du soi (n = 17) et de l'agentivité (n = 15).

Nos résultats sur la localisation des réponses relatives au soi corporel suggèrent l'implication du cortex cingulaire antérieur et postérieur, de l'insula, de l'aire motrice supplémentaire (SMA), du précuneus et de l'opercule pariétal. L'identification des réseaux par expériences corporelles montre une prédominance du gyrus central, du cortex cingulaire antérieur et de l'insula pour l'image corporelle. La dépersonnalisation est évoquée à la suite de stimulations dans le cortex cingulaire antérieur et postérieur, le précuneus ou encore l'amygdale. Le complexe amygdalo-hippocampique est d'ailleurs prédominant dans le réseau de la localisation du soi. Enfin, des modifications de

⁴ L'étude d'Andelman-Gur (2020) amorce un travail de la sorte. Il rapporte des réponses à des stimulations relatives à des modification de l'agentivité et la localisation du soi. Cependant, l'objectif de son étude n'est pas de mettre en évidence les bases neurales du soi corporel ; il se focalise sur les hallucinations visuelles complexes. De ce fait, nous ne considérons pas qu'il s'agisse d'une étude sur les bases neurales du soi corporel.

l'agentivité sont rapportées au niveau des régions frontales (aires précentrales, SMA) et pariétales (aires somatosensorielles primaires).

Notre analyse de connectivité fonctionnelle montre l'existence de sous-réseaux fonctionnels pour chaque expérience corporelle. Cependant, il semblerait que ces derniers se recouvrent et partagent des nœuds communs tels que l'insula. Les résultats de la connectivité fonctionnelle, toute expérience confondue, montrent une diminution de la force du lobule pariétal inférieur et du gyrus temporal inférieur, suggérant une déconnexion de ces nœuds dans le réseau du soi corporel. L'analyse de la force des liens établit une diminution de la connectivité fonctionnelle entre le lobule pariétal inférieur et le gyrus temporal médian. De même, on observe une diminution de la connectivité fonctionnelle entre le gyrus temporal inférieur et le complexe hippocampique ainsi que le sulcus temporal supérieur. Ensemble ces résultats mettent en évidence l'existence d'un réseau temporo-limbique qui sous-tendrait le soi corporel.

Unraveling the Neural Networks of the Bodily Self: Insights from Intracranial Electrical Stimulation in Epileptic Patients

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Abstract

Understanding the neural mechanisms underlying the bodily self, an immediate and pre-reflective form of self, is fundamental for elucidating human self-consciousness. Here, we retrospectively analysed the perceptual and neurophysiological effects of intracerebral electrical brain stimulation (EBS) in 354 patients who underwent stereoelectroencephalography (SEEG) for presurgical evaluation of pharmacoresistant epilepsy. We investigated different facets of bodily self disturbances induced by direct cortical and subcortical EBS (changes in self-location, body ownership, body image, first-person perspective, agency, depersonalization) and analysed EBS-evoked changes in functional connectivity using local field potentials recorded when patients reported disturbances of the bodily self. Disruptions of the bodily self represented 3.4% of all EBS-evoked responses (78 responses in 50 patients). They were evoked primarily when EBS were applied in the anterior and posterior cingulate cortex, insula, hippocampus, SMA, parietal operculum, and precuneus. Functional connectivity analyses revealed an overall decreased connectivity of the inferior parietal lobule during disturbances of the bodily self. Our study also identified subnetworks for different components of the bodily self, with the insula as a central hub. Connectivity analysis of edges revealed a decrease in functional connectivity within both lateral and medial temporal regions. These findings provide causal evidence of a widespread neural network underpinning the bodily self, with disturbances in the bodily self associated with changes in connectivity between the sensorimotor networks and that underlying mesial temporal structures related to narrative, emotional and autobiographical aspects of the self.

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Introduction

The nature of the interactions between the body and the self has long been a central study focus in philosophy and neuroscience. For many years, scientific research has been shaped by Cartesian dualism, which posits a disembodied thinking self, or by materialistic monism, which reduces consciousness to a singular substance—the brain—thus embracing reductionism. In contrast, a line of thought in neuroscience, influenced by phenomenology (Merleau-Ponty, 1945) and represented by figures such as Damasio, asserts that the self is rooted in the experience of being a body in the world (Damasio, 1994). Thus, neuroscientists must not overlook the body to understand the self and cognition.

Recent studies have explored the minimal self, or proto-self, defined as the immediate and prereflective experience of self (Blanke and Metzinger, 2009; Damasio, 1999), proposing that it relies on the internal states of the body and sensorimotor signals (Christoff et al., 2011). This form of self, primarily mediated through the body, has also been termed the bodily self (Blanke, 2012). Traditionally, the bodily self encompasses the sense of being the agent of an action or a thought (agency), of being embodied (self-location), of perceiving the body and the world from an egocentric viewpoint (first-person perspective), and of ownership or identification over a body (Blanke, 2012). The perceived unity of the self and the body thus depends on integrating coherent sensory signals from outside and inside the body (i.e., exteroceptive or interoceptive signals) (Park and Blanke, 2019). Indeed, experimental manipulations inducing sensory and perceptual incoherence (Ehrsson, 2007; Lenggenhager et al., 2007), as well as cases of patients with impaired sensory systems (Lopez and Elzière, 2018) or brain structures involved in multisensory integration (Blanke et al., 2004), are examples of transient or long-term alterations of the bodily self.

Given the prevalence of self and identity disturbances in many neurological and psychiatric conditions (Hewett and Bartolomei, 2013; Heydrich et al., 2019; Invernizzi et al., 2013; Salomon et al., 2022), identifying the brain networks underlying the bodily self and their functions appears pivotal in developing novel interventional therapies (e.g., invasive or non-invasive neuromodulation) for individuals with bodily self disturbances.

Various approaches have tried deciphering the brain networks involved in the bodily self. Early clinical investigations focused on the effects of brain lesions or focal epileptic seizure, characterized by disturbances in one or multiple components of the bodily self, yielding classic clinical cases in neurology, such as out-of-body experiences, somatoparaphrenia, or alien hand illusions, which respectively manifest deficits in self-location, body ownership, and agency (Feinberg et al., 1990; Gandola et al., 2012; Heydrich et al., 2011). Another approach involved studying disruptions of the bodily self during invasive electrical stimulation in specific brain regions, notably self-location (Blanke et al., 2002; Penfield, 1955), agency (Desmurget et al., 2009), and depersonalization (Lyu et al., 2023). Finally, the advent of non-invasive functional neuroimaging since the 1990s has enabled the delineation of some of the neural correlates of the bodily self in neurotypical individuals, suggesting the involvement of numerous sensorimotor areas (Farrer et al., 2008; Ionta et al., 2014).

However, despite the wealth of data from neurology and functional neuroimaging, knowledge about the brain networks supporting the bodily self remains uncertain. Notably, alterations in experiences underlying the bodily self can be elicited by electrical stimulations applied to vastly different brain locations (Andelman-Gur et al., 2020; Desmurget et al., 2009; Fornia et al., 2020; Fried et al., 1991; Penfield and Boldrey, 1937), and lesions in different brain lobes also result in alterations of the experiences underpinning the bodily self (Adolphs, 2016; Joutsa et al., 2022). Our own systematic review of the literature and meta-analysis of intracerebral electrical stimulation data reveal contributions to the bodily self from at least seven brain regions distributed across various brain lobes (Dary et al., 2023). Collectively, these findings lead us to propose that the experience of a minimal bodily self emerges from neural activity within richly interconnected brain regions (Thiebaut de Schotten and Forkel, 2022), and that invasive brain stimulations, along with focal brain lesions, disrupt the bodily self network by altering functional connectivity within this network.

This study aims to delineate the extent of the cerebral network underpinning the bodily self, using data from intracerebral electrical brain stimulation (EBS) in patients with epilepsy, a method regarded as the gold standard for analyzing brain network function and providing causal evidence of a brain region's involvement in a mental state or cognitive mechanism (Desmurget et al., 2013; Siddiqi et

al., 2022). Firstly, we localized the bodily self network by mapping the regions causally involved in bodily self disturbances during EBS in a large cohort of patients with epilepsy performed outside any brain lesion or tissue altered by epilepsy. Subsequently, we analyzed local field potentials at the level of depth electrodes' contacts to reveal changes in functional connectivity within this network. For this purpose, we employed mathematical indices derived from graph theory applied to the analysis of correlations of electrophysiological signals recorded exactly when patients underwent EBS-evoked bodily self disturbances.

Methods

Participants

We retrospectively reviewed responses evoked by EBS in 354 adult and pediatric patients with medication refractory focal epilepsy (176 females; age range: 2–70 years; mean age $\pm$ SD: 25.5 ± 14 years) who underwent invasive stereoelectroencephalography (SEEG) in our center between August 2000 and December 2021. Each patient underwent a comprehensive assessment, including detailed medical history, neurological examination, neuropsychological evaluation, brain magnetic resonance imaging (MRI), and surface electroencephalography (EEG), before undergoing invasive SEEG with depth electrodes. SEEG was carried out within the usual clinical pathway to precisely delineate the epileptogenic zone and its relation with eloquent cortices (Isnard et al., 2018). EBS was performed to trigger usual seizures (Trébuchon et al., 2020) and for functional mapping purposes [Trébuchon et al., 2020; Trébuchon and Chauvel, 2016]. Inclusion criteria for the study encompassed patients meeting the following conditions: (1) Patients being at least 8 years old. This criterion aligns with the age at which global functional brain architecture is considered mature (Menon, 2013), and children of this age can provide reliable self-reports regarding their bodily self (Cowie et al., 2018); (2) Patients reported a disruption in one or more components of the bodily self during EBS; (3) EBS-evoked bodily self disturbances were localized outside of lesion or epileptogenic zones and did not trigger usual auras or seizures. Under these conditions, findings from anatomical and functional investigations in this population may, to some extent, be generalized to neurotypical individuals (Parvizi and Kastner, 2018).

Ethical approval

This retrospective study was approved by our Institutional Review Board (n° PADS24-22_dgr). All patients, parents or guardians provided a written consent to the SEEG investigations and further analyses of the data for clinical and research purposes.

Electrodes placement and SEEG recording

The choice of SEEG implantation sites was made for clinical diagnosis only, and thus, no additional electrode was implanted for research purposes. The implantation schema was decided during a multidisciplinary meeting involving epileptology specialists and neurosurgeons to target the hypothesized epileptic zone from non-invasive evaluation (*see above*), respecting anatomical and vascular limitations.

SEEG exploration was performed using multi-contact electrodes (Dixi Medical or Alcis) consisting of 10–15 contacts, 2 mm long, 0.8 mm in diameter, and 1.5 mm apart. In the patient's cohort ($n = 354$), 49 had electrodes implanted only in the left cerebral hemisphere, 40 had electrodes implanted only in the right cerebral hemisphere, and 265 had bilateral electrode implantations. Both cerebral hemispheres were equally sampled in our cohort, as the number of electrodes implanted in the left (range: 1–17; *Mdn*: 5; Mean $\pm$ SD: 6 ± 5) and right (range: 1–17; *Mdn*: 6; Mean $\pm$ SD: 6 ± 5) hemispheres did not differ significantly ($t = 0.96$, $p = 0.338$). SEEG signals were recorded on a 128- or 256-channel Natus system, sampled at 256, 512, or 1024 Hz; depending on the year of recording, saved directly on a hard drive (with 16 bits/sample resolution) without digital filtering. During data acquisition, two hardware filters were used: a high-pass filter (set at a cut-off frequency of 1 Hz at 3 dB) and an antialiasing low-pass filter (set at a cut-off frequency of 97 Hz for a 256 Hz sampling rate, 170 Hz for a 512 Hz sampling rate, and 340 Hz for a 1024 Hz sampling rate). The reference electrode was placed in the white matter on adjacent contacts of electrodes.

Intracranial EBS

EBS were conducted with patients tested in a sitting or supine position, and instructed to maintain their eyes open and to relax. Patients were occasionally asked to read a text, repeat words, count, or maintain their arms stretched and lifted frontwards while EBS were delivered, as classically done for functional brain mapping during EBS (Mercier et al., 2022). EBS were administered using a current-regulated neurostimulator specifically designed for diagnostic purposes (Inomed, Colmar, France), following standard procedures established in our department and French guidelines on SEEG (Isnard et al., 2018).

Square current pulses were administered between adjacent contacts of an electrode (1) at high frequency (50 Hz), with a pulse width of 0.5-1 ms, and train duration of 3–8 s; or (2) at low frequency (1 Hz), with single pulse width of 1–2 ms, and train duration of 20–60s (Isnard et al., 2018). These parameters were selected to moderate risks of tissue damage, maintaining the charge density per square pulse below 50 $\mu\text{C}/\text{cm}^2$ (Ritaccio et al., 2018). The stimulation intensity was incrementally increased from 0.2 mA in steps of 0.2 mA, until either a sensation or an after-discharge was elicited, with a maximum intensity of 5 mA. However, EBS at an intensity above 3 mA was very rarely applied. Each patient received in total from 1 to 175 high-frequency EBS (*Mdn*: 27; Mean $\pm$ SD: 31 $\pm$ 25 EBS), and between 1 and 185 low-frequency EBS (*Mdn*: 12; Mean $\pm$ SD: 25 $\pm$ 33 EBS).

After each EBS, patients were asked to provide detailed reports on any sensations or symptoms elicited by the stimulation. Both the SEEG responses, including any after-discharges, and the clinical effects were meticulously documented in specialized notebooks and/or directly on SEEG recordings using markers and text. Video and SEEG recordings of instances where responses were evoked were archived for further analysis.

Retrospective analysis of responses evoked by EBS

We retrospectively analyzed records of patients' subjective reports (e.g., changes in the bodily self), behavioral responses (e.g., muscle contraction) and change in SEEG (e.g., after-discharge) evoked by EBS and collected evoked responses into an Excel file (version 16.79.2, Microsoft), together with stimulation parameters (frequency, intensity) and name of bipolar electrode contacts. We identified 2197 responses evoked by high-frequency EBS delivered at an average intensity of 1.4 $\pm$ 0.6 mA (range: 0.2–5 mA; *Mdn*: 1.5 mA), with 91% of the stimulation delivered at 0.5, 1, 1.5, 2 and 2.5 mA. In addition, we identified 819 responses evoked by low-frequency EBS delivered at an average intensity of 1.8 $\pm$ 0.7 mA (range: 0.2–5 mA; *Mdn*: 2 mA), with 88% of the stimulation delivered at 1, 1.5, 2, and 3 mA.

For the purpose of this study, we collected among the responses evoked by high- and low-frequency EBS, cases of patients reporting a disturbance of one or several phenomenal components of the bodily self, as defined in Dary et al. (2023):

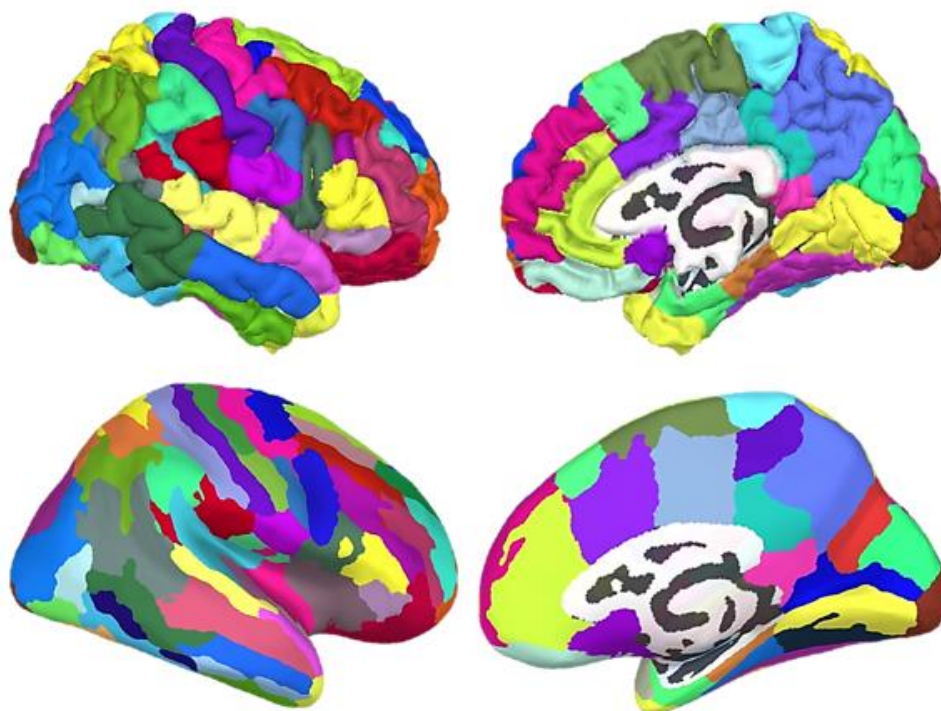
- *Body ownership* was considered altered when patients failed to self-identify with their own body parts, or when they reported sensation of disownership or disembodiment of a body part.
- *Self-location* was considered altered when patients reported full-blown sensations of being disembodied, or illusory motion of the entire body or self, including feeling of floating in the air and sensation of falling, without disembodiment. Of note, these sensations did not include unspecific sensations of vertigo, dizziness or unsteadiness.
- *First-person perspective* was considered altered when patients reported a different perspective or viewpoint on the world, which may be allocentric instead of egocentric, distanced, and elevated.
- *Agency* was considered altered when patients reported the sensations of not being at the origin of the bodily actions, of not controlling and generating them, the feeling of an urge to execute actions, or of a resistance to planned actions.
- *Body image* was considered altered when patients experienced sensations of lightness or heaviness of a body part, illusory motion of a body part, sensations that a body part was absent or lost, or perceived body size distortion (i.e., Alice in Wonderland syndrome, micro/macrosomatognosia).
- *Depersonalization* encompassed disturbances of the bodily self that do not belong to the above categories.

We did not include in the analysis electrodes contacts located in an epileptogenic zone, or within a lesion, neither EBS that evoked auras or seizures. Responses were verified on video-SEEG by a neurologist (SL) and a neuroscientist (ZD).

Localization of EBS and data representation

Electrode contacts localization and anatomical labelling. Electrode contacts where EBS elicited disturbances of the bodily self were localized with two levels of spatial granularity, depending on the period of electrode implantation (**Figure 1**).

For patients implanted after 2010, we performed automatic localization and labeling of each electrode contact using the open-source graphical user interface GARDEL (<https://meg.univ-amu.fr/wiki/GARDEL:presentation>) (Medina Villalon et al., 2018). The process involved co-registering of the pre-implantation MRI and the post-implantation CT scans, followed by automatic recognition of each electrode contact and precise anatomical localization, resulting in patient-specific 3D maps of electrode contacts. GARDEL automatically assigned each electrode contact to its corresponding anatomical region by projecting the FreeSurfer Virtual Epileptic Patient (VEP) atlas (Wang et al., 2021) onto the patient's MRI. The VEP atlas comprises 162 brain regions (**Supplementary Table 1** and **Supplementary Figure 1**) based on grey matter segmentation and cortex parcellation from Destrieux Atlas (Destrieux et al., 2010), following anatomical nomenclature by Duvernoy (1999). The resulting data included contact coordinates, their placement within cerebral gray or white matter, and anatomical labelling, which can be utilized for visualizing SEEG signal processing outcomes for each electrode contact. The anatomical labelling of all electrode contacts was carefully verified on the MRI by an expert neurologist (SL). For group analyses, electrode coordinates in the patient's brain were converted to the MNI coordinates using custom-based scripts in Matlab 2020 (The MathWorks, Inc., USA) implanted in GARDEL using SPM 12 (Ashburner et al., 2016). Through this method, we successfully mapped 48 EBS sites in 29 patients (13 in the left hemisphere; 35 in the right hemisphere) in MNI brain template using the 3D viewer. For patients before 2009, post-implantation CT and/or MRI scans were no longer available. As precise electrode contact coordinates could not be extracted for these patients, we reported EBS localization from the SEEG reports (assessed by clinicians from post-implantation MRI scans) according to the brain parcellation in 162 regions from VEP atlas (**Supplementary Table 1** and **Supplementary Figure 1**) and used these anatomical labelling for quantitative group analyses only. Through this method, we mapped 30 EBS sites in 21 patients (15 in the left hemisphere; 16 in the right hemisphere).



Supplementary Figure 1. Parcellation of the right hemispheric surface according to the VEP atlas. Top: pial view. Bottom: inflated view.

Supplementary Table 1. List of the 162 cortical and subcortical regions from the VEP atlas. Reproduced from (Wang et al., 2021).

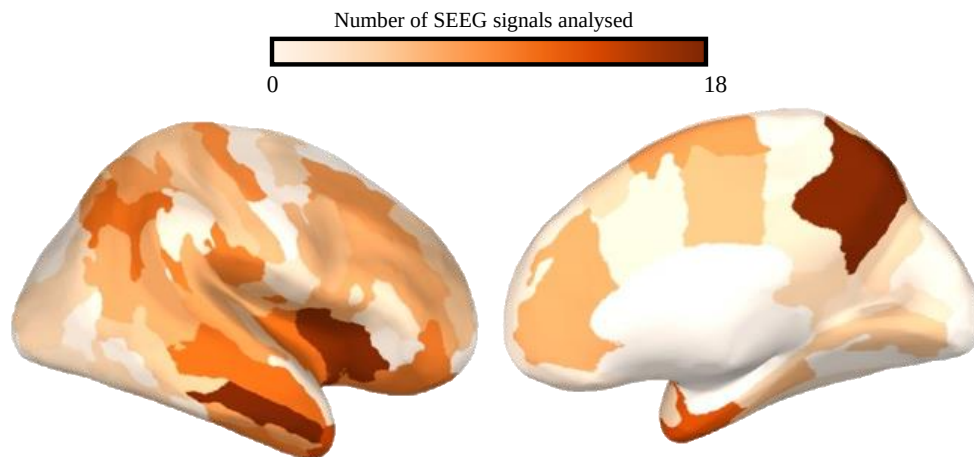
Cortical structures	Cortical structures	Subcortical structures
1 Frontal-pole	37 Gyrus-of-Heschl	73 Hippocampus-anterior
2 Orbito-frontal-cortex	38 T1-planum-temporale	74 Hippocampus-posterior
3 Gyrus-rectus	39 T1-lateral-anterior	75 Amygdala
4 F3-Pars-Orbitalis	40 T1-lateral-posterior	76 Thalamus
5 F3-Pars-triangularis	41 STS-anterior	77 Caudate-nucleus
6 F3-pars-opercularis	42 STS-posterior	78 Putamen
7 Inferior-frontal-sulcus	43 ITS-anterior	79 Pallidum
8 F2-rostral	44 ITS-posterior	80 Nucleus-accumbens
9 F2-caudal	45 T2-anterior	81 Cerebellar-cortex
10 Middle-frontal-sulcus	46 T2-posterior	
11 SFS-rostral	47 T3-anterior	
12 SFS-caudal	48 T3-posterior	
13 F1-mesial-prefrontal	49 Fusiform-gyrus	
14 PreSMA	50 Occipito-temporal-sulcus	
15 SMA	51 Collateral-sulcus	
16 F1-lateral-prefrontal	52 Lingual-sulcus	
17 F1-lateral-premotor	53 Parahippocampal-cortex	
18 Subcallosal-area	54 Rhinal-cortex	
19 Precentral-sulcus-inferior-part	55 Postcentral-gyrus	
20 Precentral-sulcus-superior-part	56 Postcentral-sulcus	
21 Precentral-gyrus-head-face	57 Superior-parietal-lobule-P1	
22 Precentral-gyrus-upper-limb	58 Supramarginal-anterior	
23 Central-sulcus-head-face	59 Supramarginal-posterior	
24 Central-sulcus-upper-limb	60 Angular-gyrus	
25 Paracentral-lobule	61 Intraparietal-sulcus	
26 Central-operculum	62 Precuneus	
27 Parietal-operculum	63 Marginal-branch-of-the-cingulate-sulcus	
28 Anterior-cingulate-cortex	64 Parieto-occipital-sulcus	
29 Middle-cingulate-cortex-anterior-part	65 Anterior-occipital-sulcus-and-preoccipital- notch	
30 Middle-cingulate-cortex-posterior-part	66 O3	
31 Posterior-cingulate-cortex-dorsal	67 O2	
32 Posterior-cingulate-cortex-retrosplenial-gyrus	68 O1	
33 Insula-gyri-brevi	69 Occipital-pole	
34 Insula-gyri-longi	70 Lingual-gyrus	
35 Temporal-pole	71 Calcarine-sulcus	
36 T1-planum-polare	72 Cuneus	

Group level visualization and response rate analyses. For each region delineated in the VEP atlas, we extracted the number of EBS applied and the total count of EBS-evoked disturbances to the bodily self. Rather than directly analyzing response counts, we computed response rates (defined as the ratio of responses to the number of EBS administered) for each region, as the number of EBS varied across regions. We used MNE-Python (version 1.6.1) (Gramfort et al., 2013) to plot response rates for each cortical surface area, and Freeview, a visualization tool from FreeSurfer, to plot response rates in the thalamus, putamen, hippocampus, and amygdala. Subsequently, for regions where at least four EBS were administered, we conducted statistical analyses to determine whether the response rate significantly deviated from zero, employing a bootstrap procedure on proportions (Çetinkaya-Rundel and Hardin, 2022) implemented through a MATLAB custom-script. This bootstrap method involved randomly selecting i data points from a stimulation series of i values (with replacement), calculating the corresponding response rate, and repeating this process 20,000 times to generate a distribution of bootstrapped response rates. Subsequently, we computed the 95% confidence interval (CI) of this distribution. A response rate was deemed significantly different from zero if zero fell outside the 2.5% lowest percentile of the bootstrapped distribution.

Functional connectivity analysis from SEEG signals

We conducted functional connectivity analysis from SEEG signals recorded in patients experiencing disturbances of the bodily self during high-frequency (50 Hz) EBS, for which electrode contacts were accurately localized, and SEEG recordings were of sufficient quality for analysis. Functional connectivity was assessed in a cohort of 21 patients (9 females, 25 ± 12 years old) (**Table 2**).

Pre-processing. SEEG pre-processing involved selecting a *pre-stimulation* time window, comprising the 8 s preceding high-frequency EBS, and a *post-stimulation* time window comprising the 6 s after stimulation offset. As EBS were administered with a minimum 40-s interval between them, this ensured that the *pre-stimulation* time window captured a form of baseline state of functional connectivity corresponding to unaltered bodily self. We used a 0.5 Hz high-pass filter and a bipolar re-referencing, obtained by subtracting monopolar signals recorded from two adjacent electrode contacts within the same brain structure, rather than monopolar signals. This was done to minimize the influence of potential residual activity recorded by the common electrode reference located in the white matter, and to mitigate volume conduction effects (Lagarde et al., 2018). For each patient and each EBS evoking a change in the bodily self, bipolar channels situated within the gray matter devoid of artifact and, when multiple channels were located in the same anatomical area, exhibiting the highest signal amplitude was selected for analysis (Lagarde et al., 2018). We did not include electrode contacts located in the white matter and electrode contacts associated with EBS-induced after-discharges. This resulted in analyzing SEEG signals from 425 bipolar channels related to changes in the perceptual body image ($n = 165$), depersonalization ($n = 119$), self-location ($n = 82$), and agency ($n = 70$) (**Supplementary Figure 2**).



Supplementary Figure 2. Spatial sampling for the functional connectivity analysis. The number of bipolar channels (i.e., pairs of adjacent electrode contacts, here referred to as *nodes*) used for the functional connectivity analyses is shown on the VEP atlas.

Functional connectivity estimation. We employed non-linear correlation coefficient h^2 , which quantifies the relation between time-series on all selected bipolar channels, regardless of their specific relationship, by assessing the relation of signal i with respect to signal j and estimating the variance of this relationship (Wendling et al., 2001). h^2 values are bounded between 0 (no correlation) and 1 (perfect correlation). In a first step, we calculated the h^2 correlation coefficient on broadband signals (1–45 Hz), independently for the *pre-stimulation* ($h^2_{Pre-EBS}$) and the *post-stimulation* periods ($h^2_{Post-EBS}$), for each EBS, and each pair of nodes (where a node represents adjacent bipolar SEEG channels), using a sliding window of 2 s, with steps of 500 ms, using the AnyWave open-source software (<http://meg.univ-amu.fr/wiki/AnyWave>) (Colombet et al., 2015). h^2 values are also estimated at each sliding windows across various time shifts (from 0 to 100 ms) between SEEG signals and we retained the maximal value across these explored time shift. Non-linear regression was chosen because of the non-linear dynamics exhibited by neural networks (Jirsa et al., 2014). The h^2 correlation coefficient was shown an efficient marker in analyzing SEEG signals for clinical research (Bartolomei et al., 2017; Wendling et al., 2001), as well as to decipher brain networks underpinning perception (Oane et al., 2020; Popa et al., 2019). We averaged connectivity matrices across the pre-EBS and post-EBS periods.

Graph-theory analyses. These connectivity matrices were subsequently analyzed using graph theory metrics (Fornito et al., 2016). Brain networks were described in terms of *nodes* and *edges*, where each bipolar SEEG channels serves as a node, and edges represent direct connections between nodes. We computed the *node strength* as the sum of the undirected weights of the edges connected to each node (Fornito et al., 2016). Thus, node strength represents the cumulative connectivity of a node with all other nodes. For instance, in a given patient and EBS scenario, the node strength of an electrode in the insula before EBS is determined by the sum of the $h^2_{Pre-EBS}$ values between those bipolar channels and all other selected bipolar channels within the same patient. Changes in node strength induced by EBS were assessed by computing the difference: $\Sigma(h^2_{Post-EBS}) - \Sigma(h^2_{Pre-EBS})$, where positive and negative values signify increased and decreased node strength, respectively. When analyses revealed a significant change in the node strength, we evaluated the changes in strength of all edges connected to this node, evoked by EBS.

Group-level statistical analysis. Group analysis was conducted by aggregating differences in node strength and edge strength for all bipolar channels within brain structures derived from the VEP atlas. Due to variable spatial sampling across patients, we reduced the dataset (1) by grouping sampling points in a single cerebral hemisphere; and (2) aggregating nodes into 29 larger anatomical regions based on the VEP atlas (Wang et al., 2021) and based on Raccah et al. (2021) for frontal regions (**Supplementary Table 2**). Statistical analyses were only conducted for regions with at least 5 studied EBS from distinct patients. Following confirmation of the normality of the distribution of the differences in node and edge strengths for each brain structure (Shapiro–Wilk test), we performed two-tailed Student's *t*-tests to determine whether changes in functional connectivity differed significantly from zero. The analyses were carried out in R studio (4.3.1) (RStudio Team., 2015) and are reported with an uncorrected *p*-value of 0.05, as well as with FDR-corrected *p*-values.

Supplementary Table 2. Grouping of areas from the VEP atlas into larger anatomo-functional regions for functional connectivity analyses.

New label	Regions from the VEP atlas
Frontal pole	Frontal-pole
Lateral and medial orbito frontal cortex (Lat.med OF)	Orbito-frontal-cortex, Gyrus-rectus, Subcallosal-area
Inferior frontal gyrus (F3)	Inferior-frontal-sulcus
Middle lateral and mesial dorso lateral prefrontal cortex (MLM-DPC)	F2-rostral, F1-lateral-prefrontal, Middle-frontal-sulcus, SFS-rostral, F1-mesial-prefrontal
Caudal dorso lateral prefrontal cortex (C.DLPC)	F2-caudal, SFS-caudal, F1-lateral-premotor
Supplementary motor area (SMA)	Pre-SMA, SMA
Central and Precentral areas (C-PC)	Precentral-sulcus-inferior-part, Precentral-sulcus-superior-part, Precentral-gyrus-head-face, Precentral-gyrus-upper-limb, Central-sulcus-head-face, Central-sulcus-upper-limb, Paracentral-lobule, Central-operculum
Parietal operculum	Parietal-operculum
Anterior cingulate cortex (ACC)	Anterior-cingulate-cortex
Middle cingulate cortex (MCC)	Middle-cingulate-cortex-anterior-part, Middle-cingulate-cortex-posterior-part
Posterior cingulate cortex (PCC)	Posterior-cingulate-cortex-dorsal, Posterior-cingulate-cortex-retrosplenial-gyrus
Insula	Insula-gyri-brevi, Insula-gyri-longi
Temporal pole (TP)	Temporal-pole, T1-planum-polare
Superior temporal gyrus posterior part	Gyrus-of-Heschl, T1-planum-temporale, T1-lateral-posterior
Superior temporal gyrus anterior	T1-lateral-anterior
Superior temporal sulcus (STS)	STS-anterior, STS-posterior
Inferior temporal sulcus (ITS)	ITS-anterior, ITS-posterior
Middle temporal gyrus (T2)	T2-anterior, T2-posterior
Inferior temporal gyrus (T3)	T3-anterior, T3-posterior
Fusiform	Fusiform-gyrus, Occipito-temporal-sulcus
Hippocampal complex (HC)	Collateral-sulcus, Parahippocampal-cortex, Rhinal-cortex, Anterior hippocampus, posterior hippocampus
Somatosensory area (S1)	Postcentral-gyrus, Postcentral-sulcus
Superior parietal lobule (SPL)	Superior-parietal-lobule-P1
Inferior parietal lobule (IPL)	Supramarginal-anterior, Supramarginal-posterior, Angular-gyrus
Intraparietal sulcus	Intraparietal-sulcus
Precuneus	Precuneus, Parieto-occipital-sulcus, Marginal-branch-of-the-cingulate-sulcus
Occipital lateral	Anterior-occipital-sulcus-and-preoccipital- notch, O3, O2, O1, Occipital-pole
Lingual	Lingual-gyrus, Lingual-sulcus
Cuneus	Calcarine-sulcus, Cuneus
Thalamus	Thalamus
Basal ganglia	Putamen, Caudate nucleus, Pallidum, Nucleus accumbens

Results

The retrospective analysis identified 65 patients (37 females, mean age $\pm$ SD: 24 ± 11 years) exhibiting disturbances in one or more phenomenal components of the bodily self during EBS, representing a total of 110 responses pertaining to the bodily self. As only EBS outside the lesion and epileptogenic zone were included (**Figure 1**), we ultimately analyzed 78 responses evoked by EBS in a subsample of 50 patients (26 females, mean age $\pm$ SD: 24 ± 12 years). Demographic and clinical data for this subsample is summarized in **Table 1**.

Categories of bodily self disturbances evoked by EBS

Bodily self disturbances represented 3.4 % ($n = 78$) of all EBS-evoked responses in 354 patients. High-frequency EBS (50 Hz) evoked 66 bodily self responses (intensity, mean $\pm$ SD: 1.4 ± 0.5 mA) while EBS at low frequency (1 Hz) evoked 12 responses (1.9 ± 0.6 mA). Phenomenal components of bodily self were unequally altered by EBS. Individual self-reports are summarized in **Supplementary Table 3** and **Supplementary Figure 3**.

The most frequently reported disturbance of bodily self was a change in perceptual body image ($n = 29$, 35% of all bodily self responses¹). Cases included sensations such as a feeling of heaviness or lightness of a body part (5 patients and 8 EBS; e.g., Patient 37: “*Sensation of heaviness of the right upper limb*”), sensation of absence of a body part (2 patients and 2 EBS; e.g., Patient 2: “*I can't feel my left foot*”), sensation of distortion of a body part (6 patients and 7 EBS; e.g., Patient 25: “*As if her arm were moving like a snake, it swells*”), and proprioceptive illusion (10 patients and 12 EBS; e.g., Patient 18: “*Sensation of the right hand rising*”).

The second most frequent disturbance evoked by EBS were depersonalization disorders ($n = 23$, 27% of all bodily self responses). Patients reported feelings of disembodiment and detachment from their bodies (12 patients and 17 EBS; e.g., Patient 27: “*I had the impression that my mind was projected elsewhere*”), feelings of presence (Patient 16: “*Sensation in the head. Presence.*”), or feelings of unreality or strangeness (5 patients and 5 EBS; e.g., Patient 43: “*A feeling of strangeness, of unreality*”, Patient 50: “*Impression of seeing things differently*”).

Disturbances of the sense of self-location represented 20% ($n = 17$, 20% of all bodily self responses) of the bodily self responses. These included a perceived change in self-location characterized by illusory translation of the entire body (4 patient and 8 EBS, e.g., Patient 18: “*She feels strange, like if she were duplicated, and as if she were moving upwards*”), sensation of falling or feeling of floating in the air without the sense of disembodiment (9 patient and 9 EBS; e.g., Patient 4: “*feeling of floating*”).

Finally, disturbances of the sense of agency ($n = 15$) accounted for 17% of bodily self responses. These included sensations of an external agent moving or controlling (parts of) the body (6 patients and 8 EBS; e.g., Patient 28: “*My arms move against my will*”, Patient 33: “*It forced me to lower my arm*”), an “urge to move” (3 patients and 4 EBS, e.g., Patient 29: “*Tingling in the left arm and urge to move it*”), an intention to move, or a resistance to perform an action (3 patients and 3 EBS; e.g., Patient 10: “*Feeling that it is impossible to move the left upper limb*”).

Stimulation intensity did not significantly modulate the type of bodily self disturbance ($\chi^2 = 1.5$, $p = 0.7$) (**Supplementary Figure 4**). For high-frequency EBS, the mean intensity that elicited changes in agency was 1.5 mA, 1.4 mA for body image, 1.5 mA for self-location, and 1.4 mA for depersonalization.

¹ Note that when patients reported disturbances in several components of bodily self for a given instance of EBS, all components were counted separately, thus explaining why the number of responses reported here exceeds the number of instances of EBS previously reported.

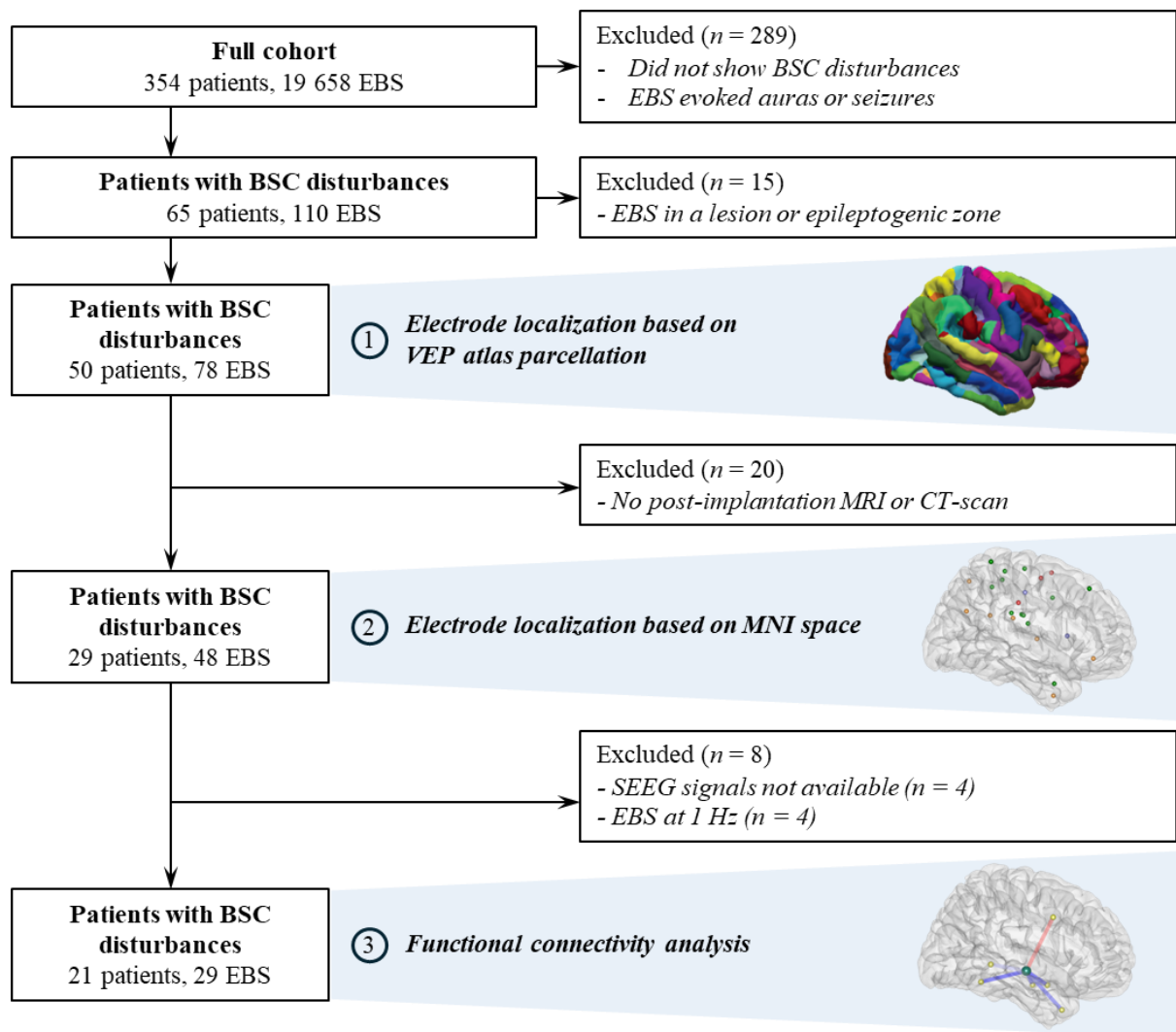


Figure 1. Flow chart of patients inclusion and selection for the different analyses.

Table 1: Demographic and clinical data. M: male; F: female; R: right; L: left; B: bilateral; FCD: focal cortical dysplasia; DNET: dysembryoplastic neuroepithelial tumor.

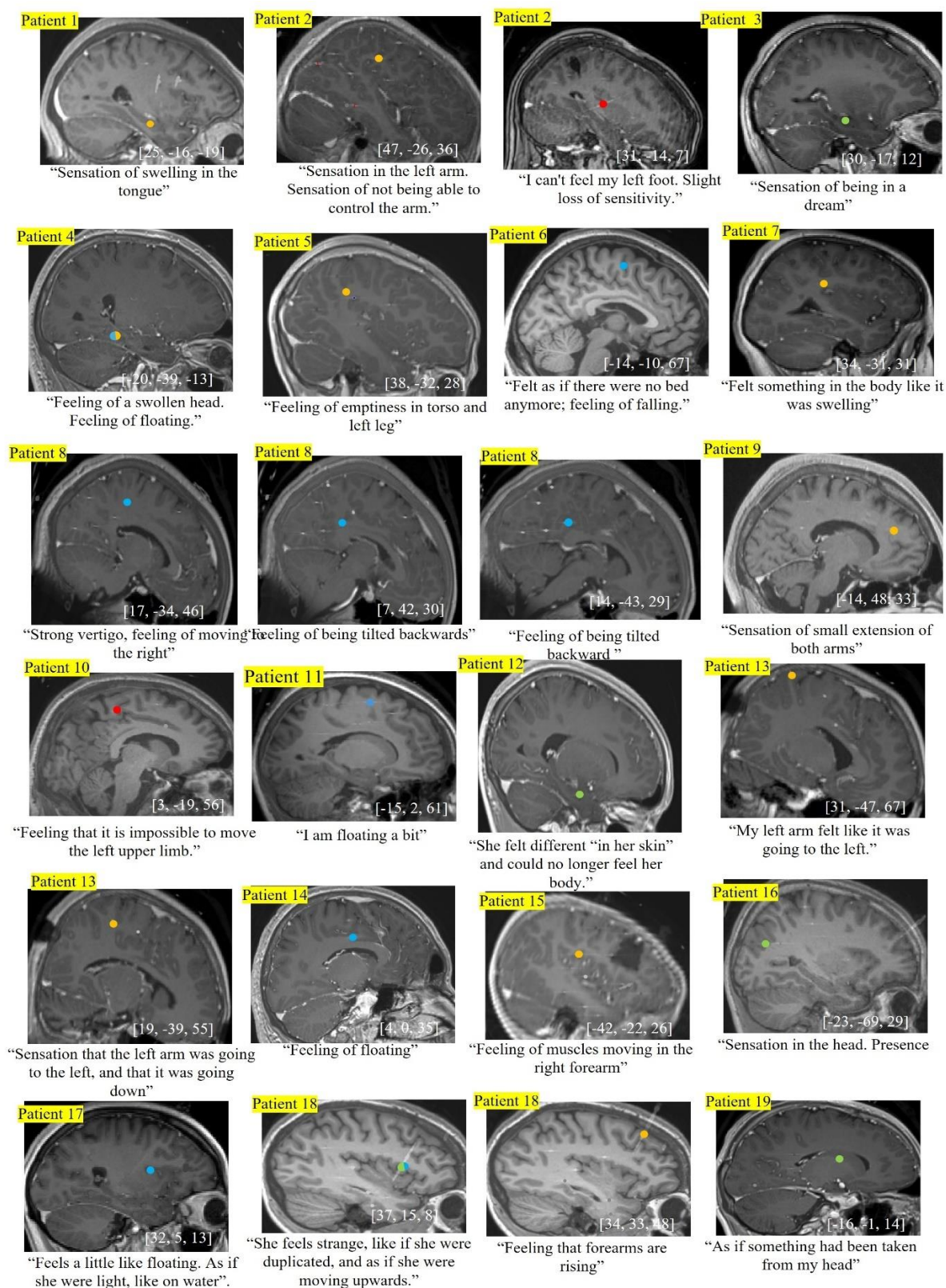
ID	Sex	Age (yrs)	Epileptogenic zone		MRI finding		Electrodes		EBS (n)
			Location	Side	Location	Side	n	Side	
1	F	54	Frontal operculum and posterior insula	R	FCD cingulo-opercular	R	11	R	69
2	F	12	Precentral sulcus, central operculum and anterior insula	R	FCD precentral sulcus	R	11	R	112
3	M	17	Inferior temporal gyrus and insula anterior	L	Normal		11	R	67
4	M	39	Superior temporal gyrus to angular gyrus	L	Head of the hippocampus and amygdala nucleus globular	L	16	B	127
5	M	11	Precuneus, posterior cingulate cortex	R	Normal		12	B	64
6	M	17	Temporal lateral	B	Bitemporal atrophy	B	17	B	131
7	M	12	Precentral region and SMA	R	Normal		11	R	67
8	F	18	Temporal-occipital	R	Normal		12	B	49
9	M	38	Parieto-opercular premotor network and mesial temporal (hippocampus)	L	Insular and hippocampal atrophy	L	16	B	33
10	M	29	Mesial premotor, precentral regions and SMA	L	Temporo-polar cyst	L	18	B	183
11	F	23	SMA	L	Normal		8	L	50
12	F	16	Amygdala, hippocampus, temporal pole, prefrontal and orbitofrontal cortex	R	Normal		16	B	62
13	F	14	Superior frontal sulcus	R	Normal		7	R	22
14	M	39	Orbitofrontal, frontal-mesial, anterior cingulate cortex, pre-SMA, F2 caudal	R	Post-traumatic frontal lesion	R	13	B	62
15	F	8	Prefrontal cortex	L	FCD middle frontal gyrus	L	13	B	57
16	M	16	Parietal operculum, posterior insula, motor cortex and S1	L	Normal		16	B	153
17	F	23	Temporal mesial (hippocampus)	R	Hippocampal sclerosis	R	13	R	51
18	F	35	Temporal mesial (hippocampus)	L	Normal		16	B	189
19	M	18	Posterior cingulate cortex	R	Normal		16	B	52
20	M	23	Temporal pole, amygdala, anterior hippocampus anterior, rhinal cortex	L	Normal		15	B	58
21	F	11	Precentral regions	R	FCD frontal	R			
22	M	53	Amygdala, hippocampus, temporal pole, rhinal cortex, insula	R	Hippocampal sclerosis	L	16	B	166
23	F	33	Mesial temporal (hippocampus)	R	Normal		14	B	108
24	F	17	Premotor cortex	R	Insulo-frontal cortical anomaly	R	12	B	76
25	F	38	Mesial temporal (hippocampus)	B	Periventricular heterotopia in temporal cortex	L	18	B	133
26	F	21	Superior temporal gyrus	R	Cortical anomaly in fronto-temporal cortex	R	9	B	42
27	M	31	Frontal mesial	L	Hypersignal in amygdala and hippocampus	L	17	B	124
28	M	35	Prefrontal cortex	R	Cortical dysplasia in pre-SMA	R	12	B	29
29	M	24	Precentral areas	R	Cortical anomaly insular	R	9	R	92
30	M	15	Posterior hippocampus	L	Temporal ganglioglioma	L	10	B	39
31	F	35	Temporal antero-mesial (anterior hippocampus)	L	Normal		15	B	34
32	F	21	Precentral gyrus	L	Cortical anomaly insular	L	5	L	23
33	M	31	Superior temporal gyrus and amygdala	R	Post-traumatic temporal lesion	R	11	R	58
33	F	17	Occipito-temporal cortex	R	FCD occipital	R	8	R	38
35	F	25	Lateral premotor and precentral regions	L	Fronto-parieto-insular dysplasia	L	10	L	135
36	M	13	Superior parietal lobule	L	Temporal pole lesion	L	7	L	30
37	F	18	Anterior cingulate cortex, premotor cortex	L	FCD precentral	L	8	L	49
38	M	12	SMA, superior frontal sulcus	L	Normal		7	L	35
39	F	23	Parietal lateral	L	Normal		10	B	68
40	M	39	Precentral regions and Heschl's gyrus	R	Post-traumatic fronto-temporal lesion	R	8	B	45
41	M	39	Premotor cortex	R	FCD frontal, temporal atrophy	L	10	B	19
42	F	25	Paracentral lobule	R	Abnormal cortical gyration in paracentral lobule	R	5	B	53
43	F	27	Mesial premotor cortex	R	Normal		10	B	23
44	F	14	Temporal lateral	L	DNET temporal	L	9	B	31
45	F	28	Temporal pole	R	FCD temporal	R	12	R	70
46	M	8	Amygdala, hippocampus and rhinal cortex	L	Hippocampal sclerosis	L	10	R	16
47	F	36	Temporal mesial (hippocampus)	R	Hippocampal sclerosis	R	10	R	37
48	F	22	Premotor cortex	R	Precentral sulcus FCD	R	7	R	41
49	F	25	Amygdala, temporal pole	R	Hippocampal sclerosis	R	11	B	26
50	M	41	Mesial temporal (hippocampus, rhinal cortex, parahippocampal cortex)	R	Normal		10	R	29

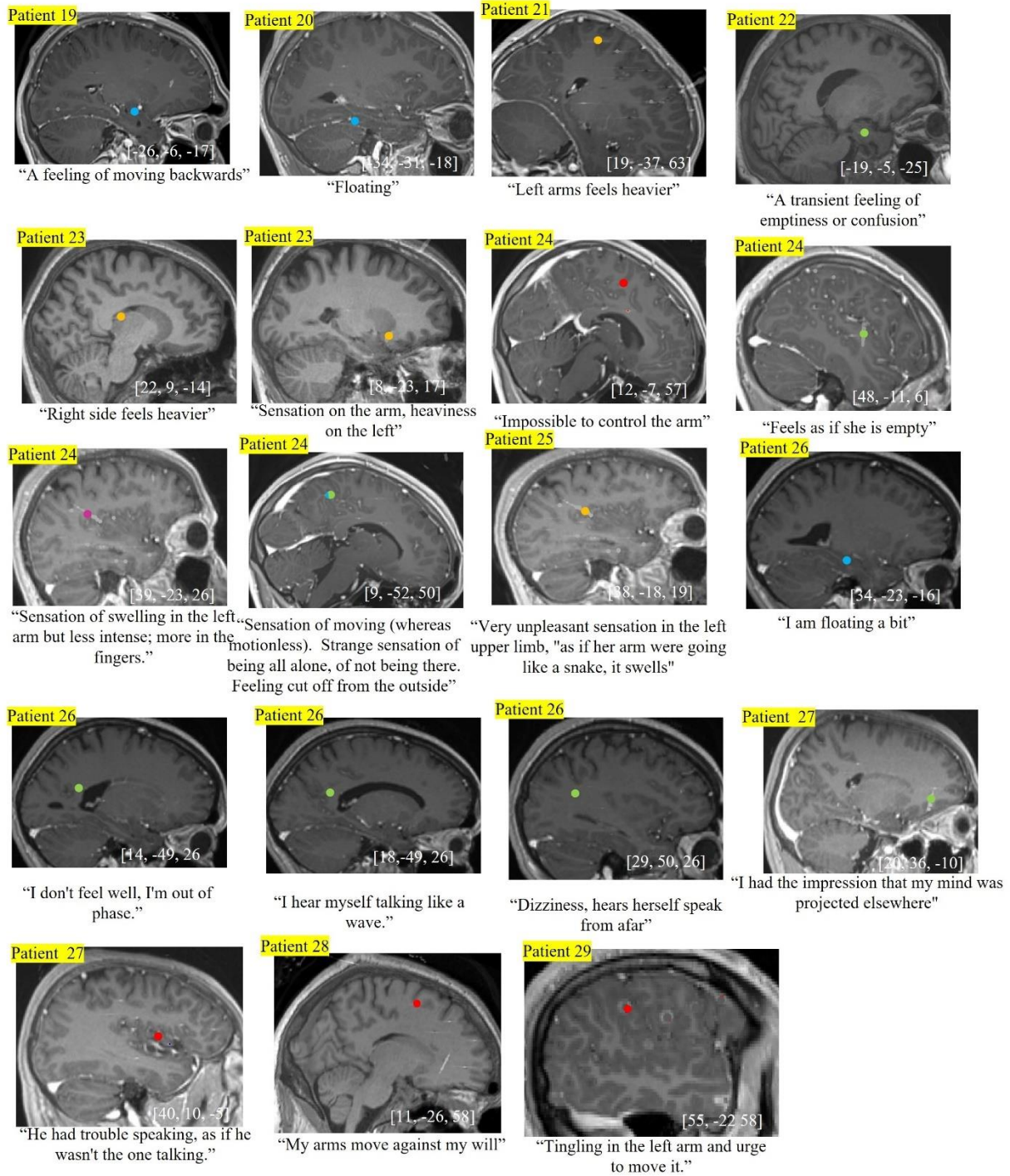
Supplementary Table 3. Summary of illusory changes in the bodily self evoked by EBS. Electrode location according to the VEP atlas: ACC: anterior cingulate cortex; IPS: intraparietal sulcus; MCC: middle cingulate cortex; PCC: posterior cingulate cortex; SMA: supplementary motor area; STS: superior temporal sulcus; WM: white matter. Stimulation parameters: F: frequency, I: intensity. Responses: Ag.: agency; BI: body image; DD: depersonalization disorder; SL: self-location.

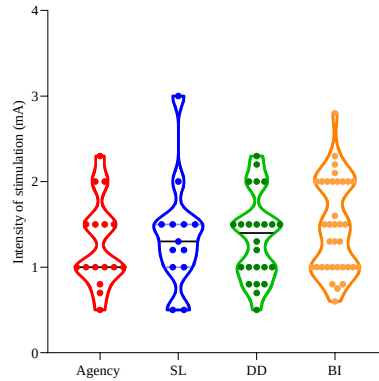
ID	Electrode contacts	S	Location	MNI coordinates (x, y, z)			I (mA)	F (Hz)	Illusory changes in the bodily self and associated sensations	Category
1	B 2-3	R	Anterior hippocampus	25	-16	-19	2.2	50	Sensation of swelling in the tongue.	BI
2	CP 10-11	R	Postcentral sulcus	47	-26	36	1	50	Sensation of not being able to control the arm.	Ag.
	I 7-8	R	Insula posterior	31	-14	7	1.3	50	"I can't feel my left foot". Slight loss of sensitivity. "I feel dizzy and it feels like my head is going to fall off".	BI
3	B' 1-2	L	Anterior hippocampus	-30	-17	-12	2	1	Sensation of being in a dream.	DD
4	GPH' 1-2	L	Parahippocampal cortex	-20	-39	-13	0.2	1	Feeling of a swollen head. Feeling of floating.	BI, SL
5	PI 7-8	R	<i>Planum temporale</i>	38	-32	28	2.8	50	Feeling of emptiness in torso and left leg.	BI
	PP 4-5	R	Intraparietal sulcus	17	-67	54	2.2	50	Feeling of emptiness below.	DD
6	SA' 2-3	L	SMA	-14	-10	67	1	1	Felt as if there were no bed anymore; feeling of falling. Sensation of moving.	SL
7	PI 1-2	R	WM near insula	32	-25	25	1.5	50	Felt something in the body (intercostal level on the left) like it was swelling.	BI
8	PA 3-4	R	WM near PCC	17	-34	46	1	50	Same type of vertigo, but weaker. Feeling of moving to the right	SL
							1.5	50	Strong vertigo, feeling of moving to the right.	SL
	GC 3-4	R	WM near PCC	14	-43	29	0.5	50	Weaker feeling of being tilted backwards. Feels a strange sensation.	SL
							1.5	50	Feeling of being tilted backwards.	SL
	GC 1-2	R	PCC	7	-42	30	1.5	50	Feeling of being tilted backwards.	SL
9	PM' 2-3	L	ACC	-14	14	33	2.3	50	Feeling of small extension of both arms.	BI
10	LP 1-2	R	Paracentral lobule	3	-19	57	1	50	Feeling that it is impossible to move the left upper limb.	Ag.
11	SA' 1-2	L	Precentral sulcus superior part	-15	2	61	0.5	50	"I am floating a bit".	SL
12	A' 1-2	L	Amygdala	-21	-10	-24	1.5	50	She felt different "in her skin" and could no longer feel her body.	DD
13	PA 1-2	R	WM near IPS	19	-39	55	1	50	Sensation that the left arm was going to the left, and that it was going down.	BI
	PA 6-7	R	Superior parietal lobule	31	-47	67	1	50	"My left arm felt like it was going to the left".	BI
14	CC 1-2	R	MCC	4	0	35	1.2	50	Feeling of floating. Blurred vision. Feeling of fear.	SL
15	OP' 3-4	L	Insula gyri longi	-33	-20	26	1	50	Feeling of muscles moving in the right forearm. No clear movement.	BI
16	PFG' 7-8	L	O1	-23	-69	29	1.5	50	Sensation in the head. Presence.	DD
17	OF 1-2	R	Insula	32	5	13	1.3	50	Feels a little like floating. As if she were light, like on water.	SL
18	Ia 4-5	R	F3 <i>pars opercularis</i>	37	15	8	1	50	She feels strange, like if she were duplicated, and as if she were moving upwards.	DD, SL
	Ia 11-12	R	Caudal F2	34	33	48	1	50	Feeling that forearms are rising.	BI
19	I' 7-8	L	Thalamus	-16	-1	14	1.5	50	"As if something had been taken from my head".	DD
	A' 1-2	L	Amygdala	-26	-6	-17	1.5	50	Like a vertigo, a feeling of moving backwards.	SL
20	GPH' 2-3	L	Parahippocampal cortex	-34	-31	-18	2	1	Floating.	SL
							3	1	Floating and vertigo.	SL
21	PA 4-5	R	Postcentral sulcus	19	-37	63	1.5	50	Left arm feels heavier.	BI
22	A' 1-2	L	Amygdala	-19	-5	-25	1	50	A transient feeling of emptiness or confusion.	DD
23	H 1-2	R	Thalamus	22	9	-14	1	30	Right side feels heavier.	BI
	OR 1-2	R	Putamen	8	-23	17	1	30	Sensation on the arm, heaviness on the left side.	BI
24	SA 1-2	R	Precentral sulcus	12	-7	57	1	50	Impossible to control the arm.	Ag.
	Im 3-4	R	Heschl's gyrus	48	-11	6	2	50	Feels as if she is empty. Hears sounds less.	DD
	PA 1-2	R	Precuneus	9	-52	50	2	50	Sensation of moving (whereas motionless). Strange sensation of being all alone, of not being there. Feeling cut off from the outside.	SL, DD

25	IP 2-3	R	Anterior supramarginal	38	-18	19	2	50	Very unpleasant sensation in the left upper limb, as if her arm were "going like a snake, it swells" plus flapping. Not painful, but surprising sensation.	BI
	IP 5-6	R	Anterior supramarginal	39	-23	26	2	50	Sensation of swelling in the left arm, but less intense; more in the fingers.	BI
26	PFG 2-3	R	WM near PCC	14	-49	26	0.7	50	"I don't feel well, I feel like I'm out of phase".	DD
	PFG 3-4	R	WM near PCC	18	-49	26	0.8	50	"I hear myself talking like a wave".	DD
	PFG 6-7	R	WM near posterior STS	29	-50	26	0.5	50	Dizziness, hears herself speak from afar.	DD
	B 1-2	R	Anterior hippocampus	34	-23	-16	0.5	50	"I am floating a bit".	SL
27	T 2-3	R	Insula (gyri brevi)	40	10	-5	1.5	50	He had trouble speaking, as if he wasn't the one talking.	Ag.
	OR 3-4	R	WM near orbitofrontal cortex	20	36	-10	2.3	50	"I had the impression that my mind was projected elsewhere". Unidentified olfactory hallucination.	DD
28	SA 1-2	R	WM near SMA	11	-26	58	0.7	50	"My arms move against my will".	Ag.
29	OP 5-6	R	Parietal operculum	55	-22	39	2	50	Tingling in the left arm and urge to move it.	Ag.
							2.3	50	Tingling in the left arm and urge to move it.	Ag.
30	OP' 1-2	L	Parietal operculum				0.8	50	Felt like he was all alone.	DD
31	TB 5-6	R	Fusiform gyrus				0.8	50	"Strange feeling, someone getting into my head, preventing me from doing something". Unpleasant feeling.	Ag.
32	SA 1-2	R	SMA				2	50	"Feeling that my belly has moved backwards".	BI
33	M 2-3	R	Central sulcus head-face				1	50	"It forced me to lower my arm". Involuntary movement of the left arm. "Impression that my arm has gone limp".	Ag., BI
	M 3-4	R	Central sulcus head-face				0.6	50	"The left arm becomes heavy and limp. It is a little prickling."	BI
34	GC 1-2	R	PCC				1.5	50	Feeling of a memory gap. Doesn't know what she's doing there, who she is, where she is.	DD
35	G' 1-2	L	ACC				2.5	1	Loss of sense of the body.	DD
	G'2-3	L	ACC				2.5	1	She could no longer feel her body. Feels as if the fingers inserted into the right hand.	DD, BI
	G'4-5	L	ACC				2	1	Impression of feeling nothing, of controlling nothing. Head version to the right.	DD, Ag.
	G'5-6	L	WM near ACC				2	1	"My hand froze and I couldn't speak".	Ag.
	P'2-3	L	Precuneus				2.5	50	She has no control over her body.	Ag.
	P'5-6	L	WM near precuneus				3	50	She can't control her right hand.	Ag.
36	SA'3-4	L	SMA				1.3	50	Sensation in the right eye (rising) and in the right arm as if it were twisting.	BI
37	CP' 1-2	L	MCC				2	50	Sensation of heaviness of the right upper limb.	BI
	M'7-8	L	Central sulcus				0.75	50	Feeling of paralysis in the right upper limb. Sensation that the arm is moving (nothing visible).	BI
							1	50	Feeling of forced deviation of the head to the left. Feeling of anesthesia of the right upper limb.	Ag., BI
38	CC' 1-2	L	ACC				2	50	Feeling of a forward pull of the right upper limb.	BI
39	SA' 2-3	L	SMA				1.5	50	Feeling of paralysis on the right side. Clenched right hand and throat with difficulty speaking.	Ag.
40	PA 7-8	R	Parietal operculum				1	50	Sensation in the index finger, as if it were twisting.	BI
41	CC 1-2	R	ACC				2	50	Felt something in the left upper limb, like electricity, unpleasant, and a sensation of movement.	BI
42	SA 5-6	R	F1 lateral premotor				2	1	Heaviness in the left forearm.	BI
43	PA 2-3	R	Precuneus				1.5	50	Feeling of strangeness, of unreality. "It's like déjà vu, but it's not".	DD
44	B' 2-3	L	Hippocampus posterior				1	50	Feels weird. Anxiety.	DD
45	H 10-11	R	STS				1	1	Feels weird.	DD
46	TB 2-3	R	Entorhinal cortex				1.3	50	Facial modification. She brings her hand to her eyes, "I feel weird".	DD
47	OP 7-8	R	Parietal operculum				1.3	50	Feeling of mouth shrinking. Taste in mouth.	BI
	OF 8-9	R	F3				1.2	50	Feeling of floating.	SL
48	SC 8-9	R	Postcentral sulcus				2	1	My fingers seem to move with electricity.	BI
49	PA 7-8	R	IPS				1.5	50	Feels like the eyes have moved.	BI
50	OT 1-2	R	Fusiform gyrus				1.5	50	Impression of seeing things differently.	DD

Supplementary Figures 3. Localization of EBS on the patients' MRI. Disturbances of self-location are indicated by blue points, body image responses in orange, depersonalization disorders in green, and agency in red.







Supplementary Figure 4. Stimulation intensity according to the disrupted component of the bodily self.

Localization of EBS sites altering the bodily self

A total of 1582 EBS were applied in these 50 patients (**Figure 2a**). The brain regions investigated through EBS are widely distributed across the lateral and medial aspects of the cerebral hemispheres, notably in the posterior parietal cortex and perisylvian regions, as well as in the cingulate and inferior frontal cortex. However, there was relatively less exploration of the posterior and inferior portions of the temporal-occipital cortex.

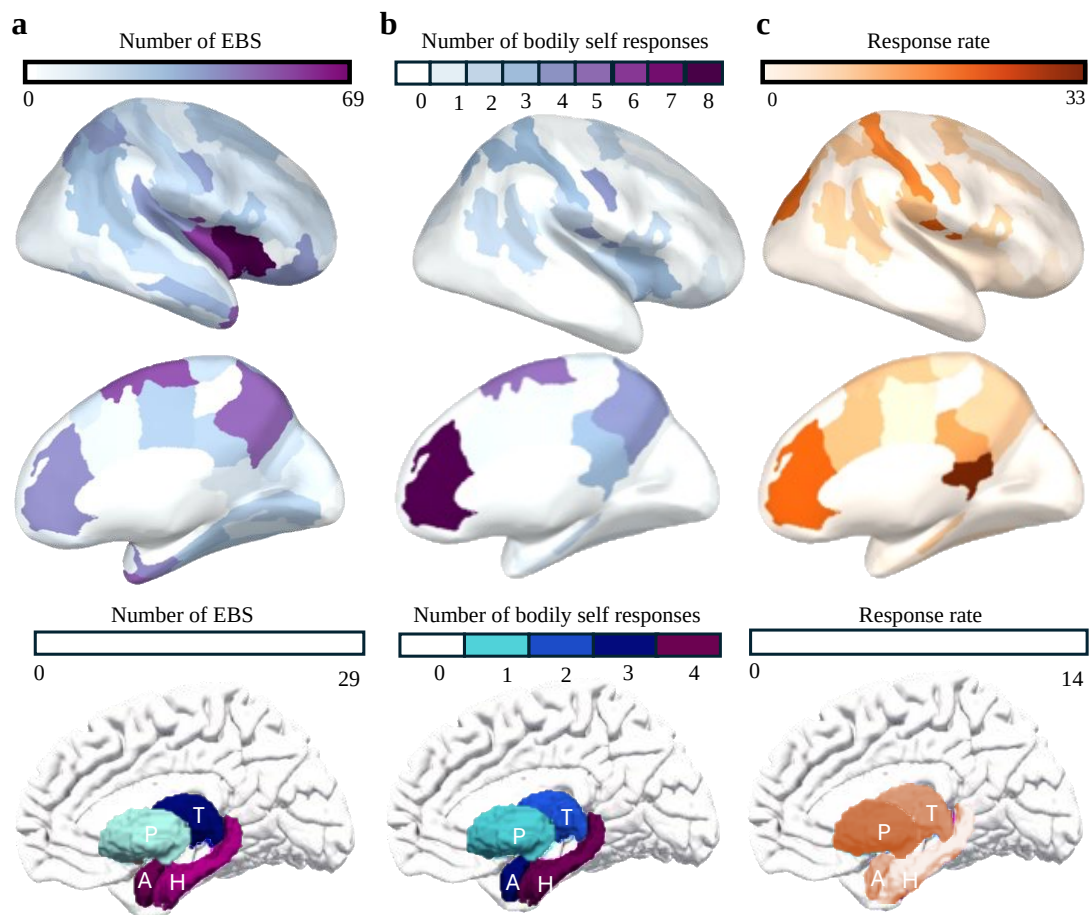
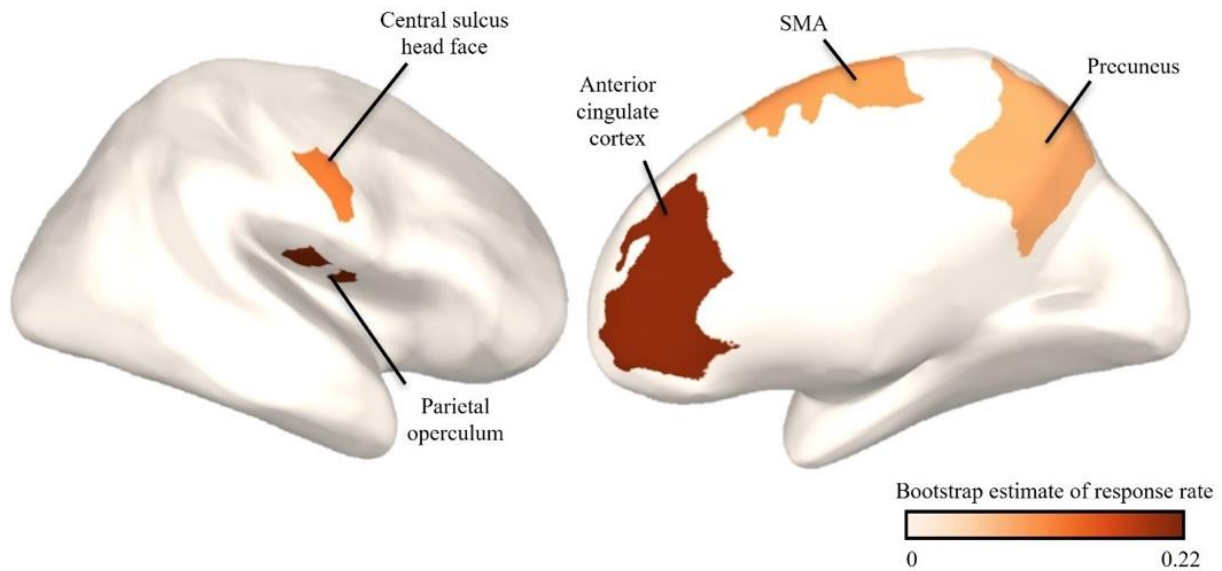


Figure 2. Localization of EBS and EBS-evoked bodily self disturbances. (a) Localization of all EBS administered in 50 patients. (b) Localization of EBS evoking bodily self disturbances. (c) Response rate. Localization of EBS is reported according to brain parcellation from the VEP atlas projected on 3D views of the right cerebral hemisphere *upper part*) and on separate depiction of the thalamus (T), putamen (P), amygdala (A) and hippocampus (H) (*lower part*).

Bodily self disturbances were primarily elicited by EBS within the anterior and posterior cingulate cortex, insula, hippocampus, SMA, and parietal operculum, as well as in the precuneus (**Figure 2b-c**). Statistical analyses with bootstrap procedure indicate that the response rate differed significantly from zero for the anterior cingulate cortex (bootstrap estimate of response rate: 0.22, 95% CI [0.08–0.35]), parietal operculum (0.22, 95% CI [0.06–0.44]), central sulcus head face (0.12, 95 %CI [0.03–0.24]), supplementary motor area (SMA) (0.10, 95%CI [0.02–0.20]), and precuneus (0.09, 95% CI [0.02–0.18]) (**Supplementary Table 4** and **Supplementary Figure 5**).



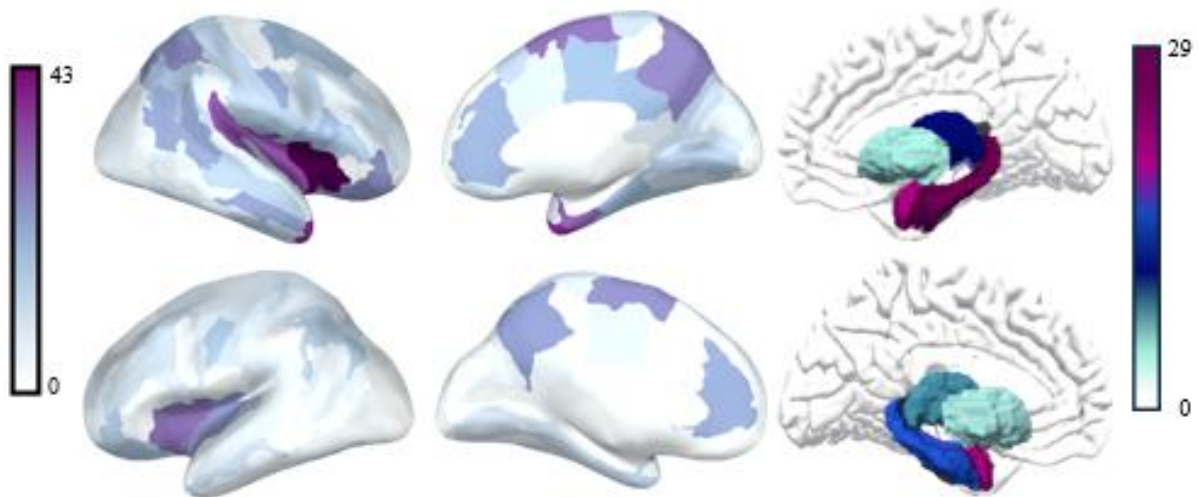
Supplementary Figure 5. Bootstrap estimate of response rate is color-coded only for areas showing a response rate significantly different from zero.

Supplementary Table 4: Statistical analysis of the response rate. * areas with a response rate significantly different from zero.

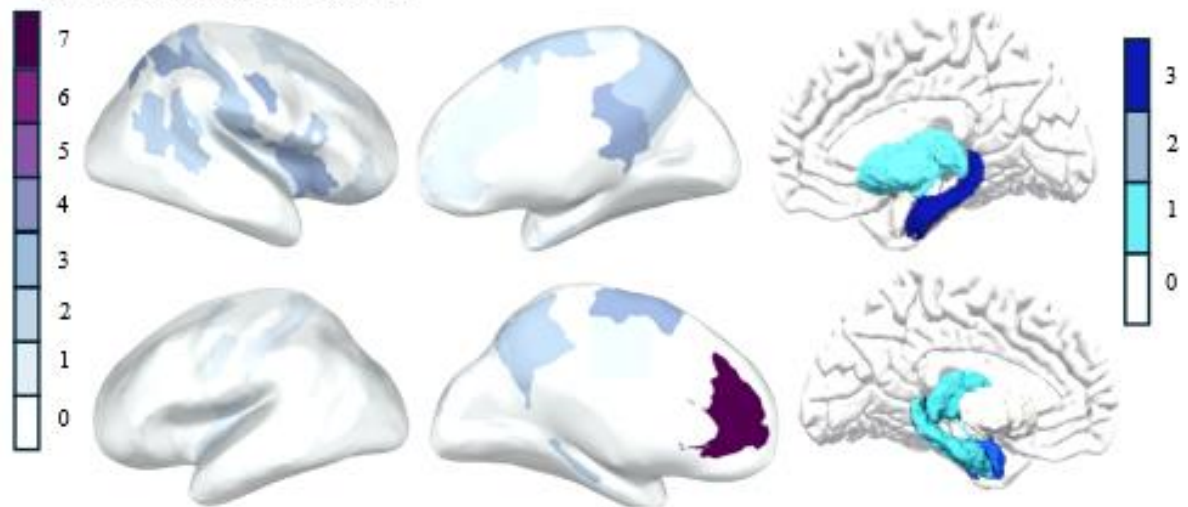
Brain area	EBS (n)	Bodily self disturbance (n)	Bootstrap estimate of response rate	95% CI (lower)	95% CI (upper)	$p < 0.025$
Amygdala	52	3	0,06	0,00	0,13	
Anterior cingulate cortex	37	8	0,22	0,08	0,35	*
Central sulcus head face	33	4	0,12	0,03	0,24	*
F1 lateral premotor	20	1	0,05	0,00	0,15	
F2 caudal	17	1	0,06	0,00	0,18	
F3 pars opercularis	24	2	0,08	0,00	0,21	
Fusiform gyrus	20	2	0,10	0,00	0,25	
Gyrus of Heschl	27	1	0,04	0,00	0,11	
Hippocampus anterior	27	3	0,11	0,00	0,26	
Hippocampus posterior	20	1	0,05	0,00	0,15	
Insula gyri brevis	69	3	0,04	0,00	0,10	
Insula gyri longi	53	2	0,04	0,00	0,09	
Intraparietal sulcus	33	3	0,09	0,00	0,21	
Middle cingulate cortex anterior part	9	1	0,11	0,00	0,33	
Middle cingulate cortex posterior part	23	1	0,04	0,00	0,13	
O1	5	1	0,20	0,00	0,60	
Orbito frontal cortex	35	1	0,03	0,00	0,09	
Paracentral lobule	17	1	0,06	0,00	0,18	
Parahippocampal cortex	22	2	0,09	0,00	0,23	
Parietal operculum	18	4	0,22	0,06	0,44	*
Postcentral sulcus	17	3	0,18	0,00	0,35	
Posterior cingulate cortex dorsal	21	3	0,14	0,00	0,29	
Posterior cingulate cortex retrosplenial gyrus	9	3	0,33	0,00	0,67	
Precentral sulcus superior part	22	2	0,09	0,00	0,23	
Precuneus	45	4	0,09	0,02	0,18	*
Putamen	7	1	0,14	0,00	0,43	
Rhinal cortex	38	1	0,03	0,00	0,08	
SMA	49	5	0,10	0,02	0,20	*
STS posterior	23	2	0,09	0,00	0,22	
Superior parietal lobule P1	28	1	0,04	0,00	0,11	
Supramarginal anterior	19	2	0,11	0,00	0,26	
T1 planum temporale	34	1	0,03	0,00	0,09	
Thalamus	21	2	0,10	0,00	0,24	

Analyses per hemisphere showed that 65% of bodily self disturbances ($n = 51$) were evoked by stimulation in the right hemisphere, while 35% ($n = 27$) occurred after left hemisphere stimulation (**Supplementary Figure 6**). Statistical analysis of proportion indicated a significant association between the stimulated hemisphere and the elicited responses ($\chi^2 = 13.6$, $p < 0.001$). Results from the z-test showed that the proportion of responses following EBS in the right hemisphere significantly exceeded those observed following EBS in the left hemisphere.

(a) Number of stimulation



(b) Number of bodily self responses



Supplementary Figure 6. Localization of EBS on 3D views on both hemispheres. (a) Localization of all EBS applied. (b) Localization of EBS evoking bodily self disturbances. The upper part illustrates the right hemisphere, the lower part the left hemisphere, and the rightmost part shows EBS sites within the thalamus, putamen, amygdala, and hippocampus.

Localization of EBS sites altering different components of the bodily self

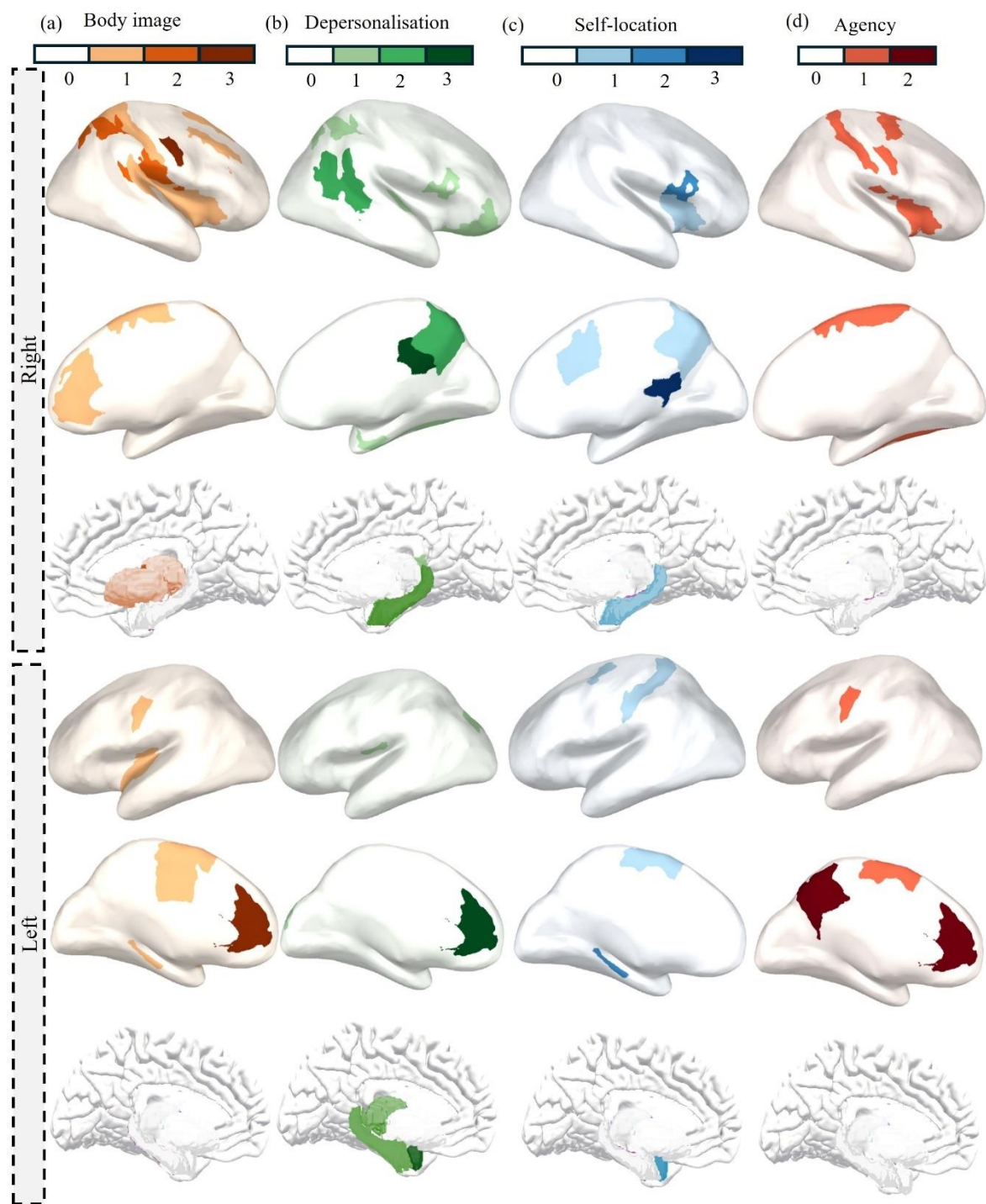
Body image. **Supplementary Figure 7a** illustrates that the central sulcus head face was the predominant site for eliciting body image responses, accounting for 14% of instances ($n = 4$), followed by the anterior cingulate cortex ($n = 3$, 10%), and the insula ($n = 3$, 10%). Additional stimulation sites yielding body image distortions included the parietal operculum ($n = 2$, 7%), as well as the supramarginal and intraparietal sulcus ($n = 2$, 7%) (**Supplementary Figure 8**). For instance, stimulation of the anterior cingulate cortex induced illusory movement of a body part (Patient 38), while sensations of body part distortion or absence were elicited following stimulation of the insula (Patient 15), supramarginal gyrus (Patient 25), central sulcus (Patient 33), and parietal operculum (Patient 40).

Depersonalization. **Supplementary Figure 7b** summarizes all stimulation-induced depersonalization, identifying five main areas: the anterior cingulate cortex ($n = 3$, 13% of all depersonalization), posterior cingulate cortex ($n = 3$, 13%), precuneus ($n = 2$, 9%), amygdala ($n = 2$, 9%), and posterior superior temporal sulcus ($n = 2$, 9%). For example, stimulation of the anterior cingulate cortex (Patient 35) led to a sensation of detachment from one's own body. Similar sensations were elicited after stimulation of the amygdala (Patient 12), precuneus, and posterior cingulate cortex (Patient 24 and 26). Additionally, one patient reported an out-of-body like experience following stimulation of the inferior frontal gyrus (*pars opercularis*) (Patient 18).

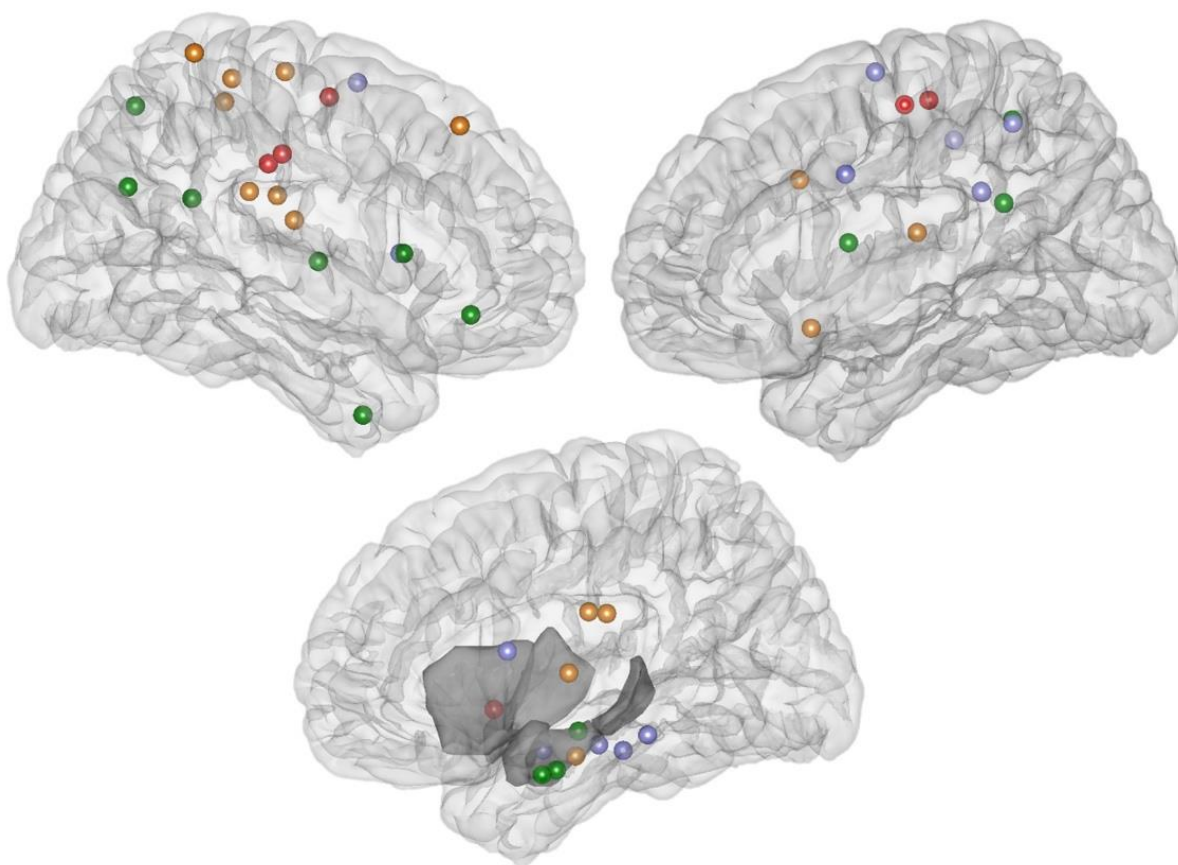
Self-location. Stimulation of the temporal cortex, notably in the hippocampal/amygdala complex ($n = 4$, 26%), elicited illusions of floating or falling in three patients. Comparable sensations were induced by insula stimulation and neighboring regions, including the inferior frontal gyrus (*pars opercularis*) ($n = 3$, 20%) (**Supplementary Figure 8**). Additionally, stimulation of the posterior cingulate cortex led to an illusory displacement of the entire body in one patient (Patient 8) (**Supplementary Figure 7c**).

Agency. Forty percent of sensations urging movement or resistance to movement were reported after EBS in the frontal cortex (SMA, precentral area, and anterior cingulate cortex), whereas 27% of responses were reported after parietal lobe stimulation, such as in the precuneus or somatosensory cortex. Disturbances in the sense of agency were evoked by EBS in the superior frontal gyrus (mesial part) and precentral gyrus, including the SMA and the anterior cingulate cortex (**Supplementary Figure 7d**). Stimulation of the mesial parietal lobe (precuneus; 14% of responses) induced, for example, in one patient, the sensation of lack of control over one's movements (Patient 35).

Hemispheric dominance of EBS-evoked responses. Analyses conducted per hemisphere revealed that 72% of body image responses ($n = 21$) were elicited in the right hemisphere (**Figure 7a**). A z-test demonstrated a significant difference in the proportion of responses between the right and left hemispheres after EBS ($\chi^2 = 9.9$; $p = 0.001$), with a higher proportion observed in the right hemisphere. For depersonalization, 60% of responses occurred following stimulation of the right hemisphere, with no significant difference between the two hemispheres ($\chi^2 = 1.4$; $p = 0.2$). No significant difference between the two hemispheres was found for self-location ($\chi^2 = 0.5$; $p = 0.5$) and agency ($\chi^2 = 0.1$; $p = 0.7$).



Supplementary Figure 7. Number of bodily self disturbances per category.



Supplementary Figure 8. Localization of EBS evoking bodily self disturbances in 29 patients. MNI coordinates were plotted on the ICBM space template European brains. EBS sites are summarized on 3D views of the right cerebral hemisphere. Orange: body image responses, green: depersonalization, red: agency responses and blue: self-location. The lower part shows EBS in the insula and the hippocampus/amygdala complex.

Functional connectivity analysis

Functional connectivity was calculated from SEEG signals recorded in a subsample of 21 patients, with more accurate location of SEEG contacts, during high-frequency (50 Hz) EBS (**Supplementary Table 5**).

Network underpinning the bodily self. First, we showed changes in functional connectivity associated in general with disruptions in any component of the bodily self. h^2 values were computed for 29 EBS representing 426 signals analyzed in 117 regions of the VEP atlas (**Supplementary Figure 2**). Two areas showed a significant decrease in node strength associated with disturbances of the bodily self, the inferior temporal gyrus (T3) ($p = 0.03$; Mean difference = -0.01)², and the inferior parietal lobule ($p = 0.03$; Mean difference = -0.008) (**Figure 3a**). There was a significant decrease in edge strength between the inferior temporal gyrus and the hippocampal complex ($p = 0.009$, Mean difference = -0.02), superior temporal sulcus ($p = 0.01$; Mean difference = -0.03), and middle temporal gyrus ($p = 0.01$; Mean difference = -0.04) (**Figure 3b**). In addition, there was a significant decrease in edge strength between the inferior parietal lobule and the middle temporal gyrus ($p = 0.03$; Mean difference = -0.03) (**Figure 3c**).

Body image. First, there was a significant decrease in node strength for the superior temporal sulcus (STS, $p = 0.04$; Mean difference = -0.01) after EBS (**Figure 4a**). When analyzing the STS connectivity with six other nodes, only central and precentral regions showed an increase connectivity, while other connected nodes tend to decrease their connectivity with STS. The decrease in edge strength was statistically significant only between the STS and amygdala ($p = 0.04$; Mean difference = -0.03) and the hippocampal complex ($p = 0.02$; Mean difference = -0.02). Second, there was a significant decrease in node strength for the middle temporal gyrus ($p = 0.007$; Mean difference = -0.01) (**Figure 4a**). However, no significant change in functional connectivity was found when analyzing the links between the middle temporal gyrus and seven nodes.

Depersonalization. No significant change in node strength was observed network (**Figure 4b**).

Self-location. We found a statistically significant increase in node strength in the insula ($p = 0.02$; Mean difference = 0.01) (**Figure 4c**). There was no significant change in the edge strength between the insula and seven other nodes sampled (**Figure 4c**).

Agency. **Figure 4d** shows that only the inferior parietal lobule showed a numerically lower connectivity. However, a significant increase in connectivity was observed only for the insula ($p = 0.03$; Mean difference = 0.03) (**Figure 4d**). There was no significant change in connectivity between the insula and nine other nodes sampled.

² All p-values reported here are not FDR corrected.

Supplementary Table 5. EBS used for functional connectivity analysis. Electrode location according to the VEP atlas. ACC: anterior cingulate cortex; IPS: intraparietal sulcus; MCC: middle cingulate cortex; PCC: posterior cingulate cortex; SMA: supplementary motor area; STS: superior temporal sulcus; WM: white matter. Stimulation parameters: F: frequency, I: intensity. Responses: Ag.: agency; BI: body image; DD: depersonalization disorder; SL: self-location.

ID	Electrode contacts	Side	Location	MNI coordinates (x, y, z)			I (mA)	F (Hz)	Category
1	B 2-3	R	Anterior hippocampus	25	-16	-19	2.2	50	BI
2	CP 10-11	R	Postcentral sulcus	47	-26	36	1	50	Ag.
	I 7-8	R	Insula posterior	31	-14	7	1.3	50	BI
5	PI 7-8	R	<i>Planum temporale</i>	38	-32	28	2.8	50	BI
	PP 4-5	R	Intraparietal sulcus	17	-67	54	2.2	50	DD
7	PI 1-2	R	WM near insula	34	-31	31	1.5	50	BI
9	PM'2-3	L	ACC	-14	14	33	2.3	50	BI
10	LP 1-2	R	Paracentral lobule	3	-19	57	1	50	Ag.
11	SA' 1-2	L	Precentral sulcus superior part	-15	2	61	0.5	50	SL
12	A'1-2	L	Amygdala	-21	-10	-24	1.5	50	DD
14	CC 1-2	R	MCC	4	0	35	1.2	50	SL
15	OP' 3-4	L	Insula gyri longi	-42	-22	26	1	50	BI
16	PFG' 7-8	L	O1	-23	-69	29	1.5	50	DD
17	OF 1-2	R	Insula	32	5	13	1.3	50	SL
18	Ia 4-5	R	F3 <i>pars opercularis</i>	37	15	8	1	50	DD, SL
	Ia 11-12	R	Caudal F2	34	33	48	1	50	BI
19	I'7-8	L	Thalamus	-16	-1	14	1.5	50	DD
	A' 1-2	L	Amygdala	-26	-6	-17	1.5	50	SL
21	PA 4-5	R	Postcentral sulcus	19	-37	63	1.5	50	BI
22	A'1-2	L	Amygdala	-19	-5	-25	1	50	DD
23	H 1-2	R	Thalamus	23	10	-13	1	30	BI
24	SA 1-2	R	Precentral sulcus	12	-7	57	1	50	Ag.
	Im 3-4	R	Heschl's gyrus	48	-11	6	2	50	DD
	PA 1-2	R	Precuneus	9	-52	51	2	50	SL, DD
25	IP 2-3	R	Anterior supramarginal	38	-18	19	2	50	BI
	IP 5-6	R	Anterior supramarginal	39	-23	26	2	50	BI
27	T 2-3	R	Insula (gyri brevis)	40	10	-5	1.5	50	Ag.
	OR 3-4	R	WM near orbitofrontal cortex	20	36	-10	2.3	50	DD
28	SA 1-2	R	WM near SMA	11	-26	58	0.7	50	Ag.

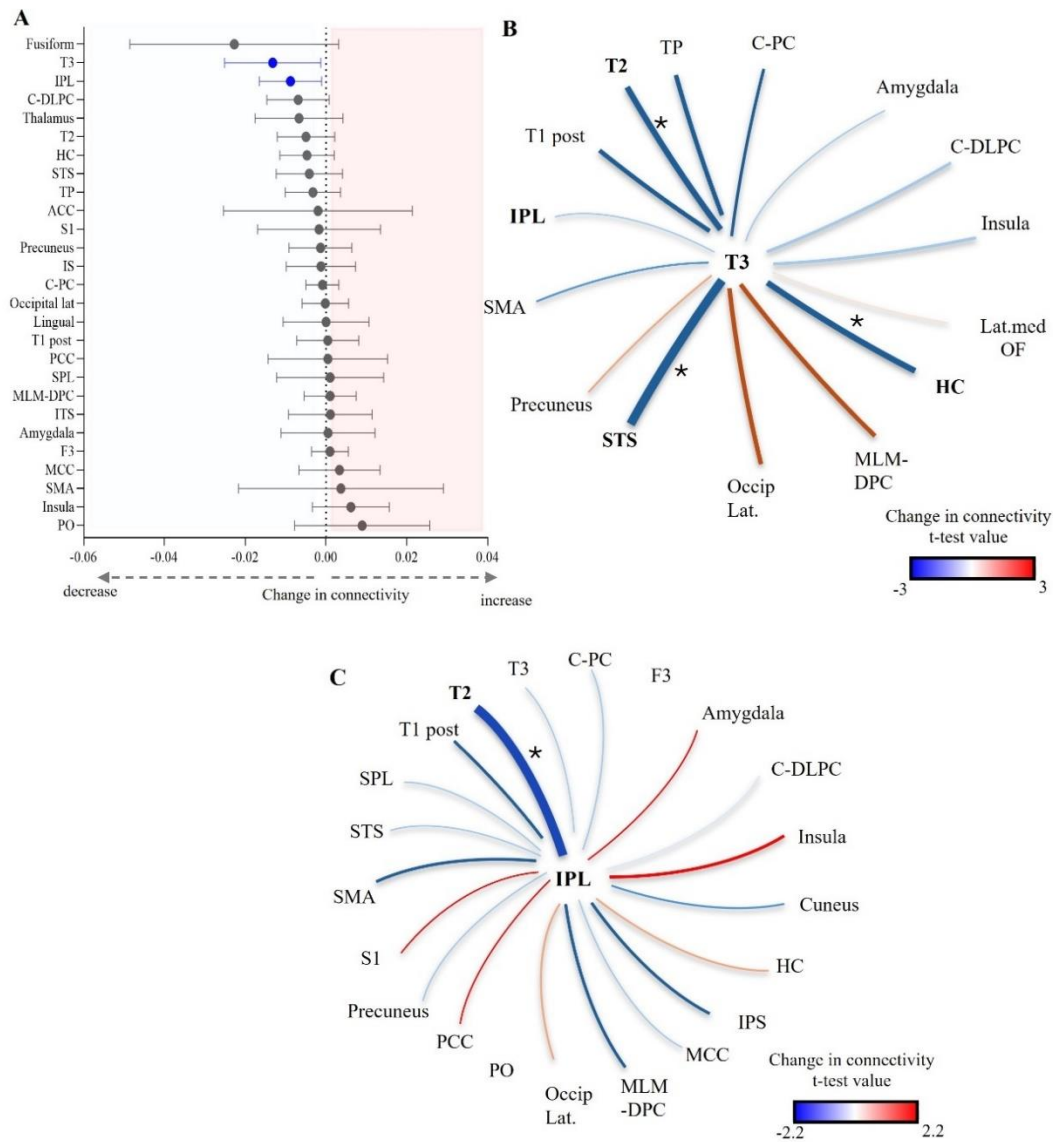
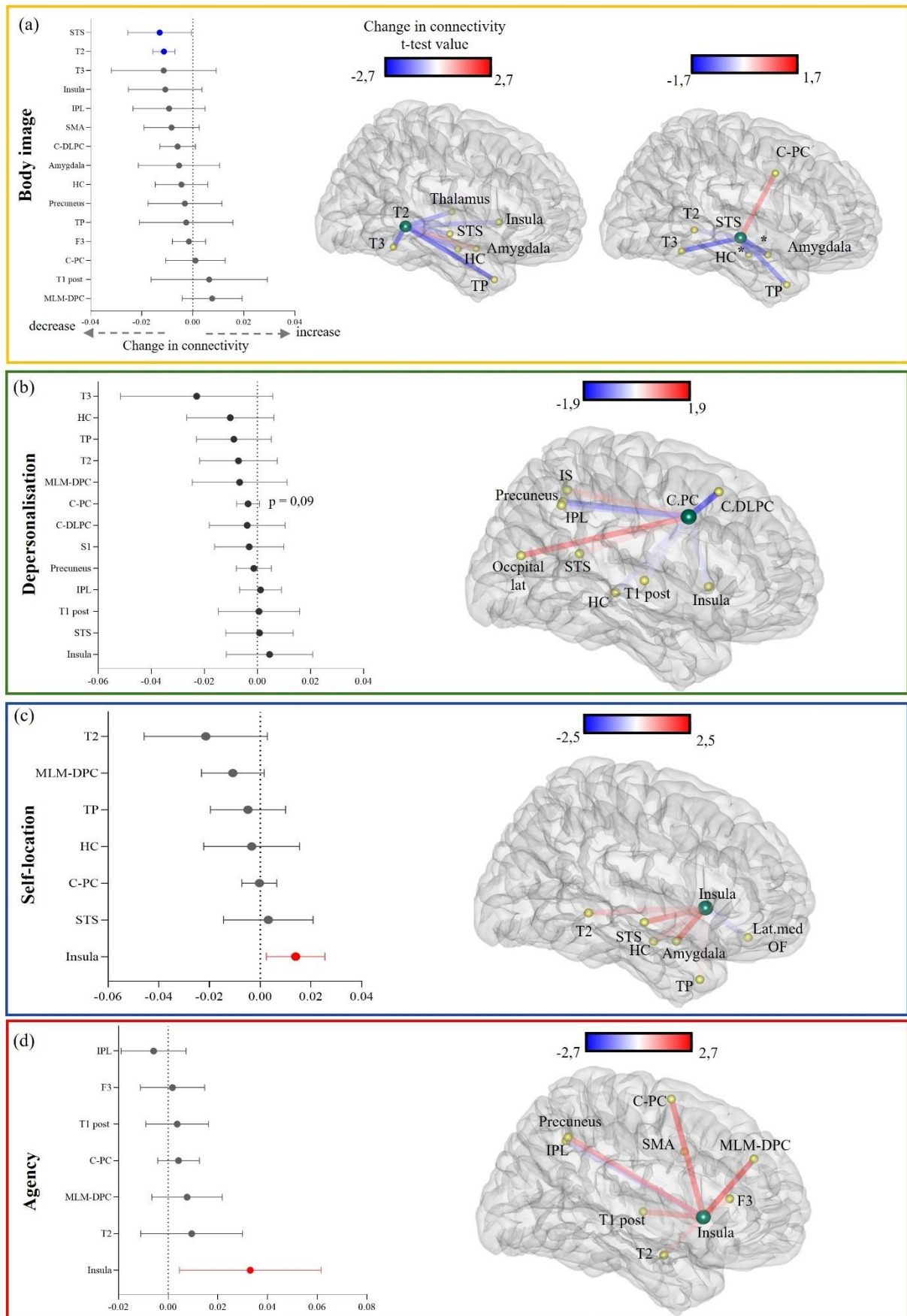


Figure 3. Functional connectivity related to overall bodily self disturbances. (a) Changes in node strength. Nodes exhibiting significant alterations in connectivity, determined by Student's *t*-tests prior to correction, are highlighted: increased strength is denoted in red, decreased strength in blue. (b) and (c) changes in edge strength on circular graphs. The results are represented by *t*-values derived from *t*-tests. Blue links signify decreased strength, while red links denote increased strength. * indicates significant change in connectivity without FDR correction. Lat.med OF: Lateral and medial orbitofrontal cortex; F3: Inferior frontal gyrus; C.DLPC: Caudal dorsolateral prefrontal cortex; MLM-DPC: Middle lateral and mesial dorsolateral prefrontal cortex; C-PC: Central and Precentral areas; SMA: Supplementary motor area; TP: Temporal pole; T1 post: Superior temporal gyrus posterior part; STS: Superior temporal sulcus; T2: Middle temporal gyrus; T3: Inferior temporal gyrus; HC: Hippocampal complex; S1: Somatosensory area; IPL: Inferior parietal lobule; PO: parietal operculum; MCC: Middle cingulate cortex; ACC: Anterior cingulate cortex; PCC: Posterior cingulate cortex; Occip Lat: Lateral occipital.

Figure 4 (opposite page). Functional connectivity results of sub-networks of bodily self components. Graph represents changes in node strength. Nodes exhibiting significant alterations in connectivity, determined by Student's *t*-tests prior to correction are highlighted: increased strength is denoted in red, decreased strength in blue. Brain schemas depict changes in edge strength. The results are represented by *t*-values. Blue links signify decreased strength, while red links denote increased strength.* significant change in connectivity without FDR correction. Lat.med OF : Lateral and medial orbito frontal cortex; F3: Inferior frontal gyrus; C.DLPC: Caudal dorso lateral prefrontal cortex; MLM-DPC: Middle lateral and mesial dorso lateral prefrontal cortex; C-PC: Central and Precentral areas, SMA: Supplementary motor area; TP: Temporal pole; T1 post: Superior temporal gyrus posterior part; STS: Superior temporal sulcus; T2: Middle temoprpal gyrus; T3: Inferior temporal gyrus; HC: Hippocampal complex; S1: Somatosensory area; IPL: Inferior parietal lobule.



Discussion

To the best of our knowledge, this study represents the first causal investigation, and currently the most comprehensive, of the brain networks underlying the bodily self. We present the results of EBS outside the epileptogenic zone in 73 brain regions in 50 patients. We reported all EBS that induced changes in one or more components of the bodily self (self-location, agency, depersonalization, or body image). Our findings indicate that EBS disrupting these different experiences occur at various locations in the brain but reveal overlapping functional networks.

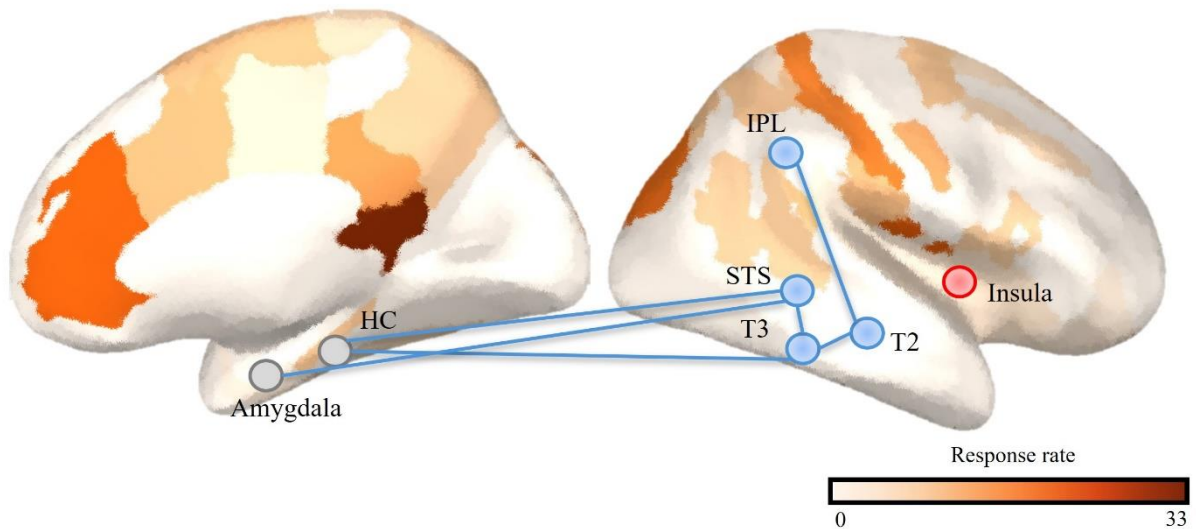


Figure 5. Schematic representation of the functional connectivity of the body self network. The network's nodes are depicted as circles in the figure, with colors indicating changes in strength: red for increase and blue for decrease. Grey circles represent nodes connected to the network, while blue lines illustrate decreased link strength between nodes.

Localization of the bodily self network

Our results identify a large neural network underpinning the bodily self, including the anterior and posterior cingulate cortex, insula, hippocampal complex (hippocampus, parahippocampus, rhinal cortex), precuneus, parietal operculum, and SMA. While we identify key regions previously described in the literature, our study highlights the involvement of medial parietal regions, particularly the posterior cingulate cortex and precuneus, in the bodily self network. Figure 5 summarises the functional connectivity of the body self network.

The Anterior Cingulate Cortex (ACC)

Our findings reveal that stimulations in the ACC led to changes in body image and depersonalization. Previous studies showed the role of the ACC in personal emotional expression and experience (Caruana et al., 2018; Northoff et al., 2006). This idea is supported by neuroimaging studies showing that at resting-state, the ACC is functionally connected to regions involved in affective processing. Indeed, the ACC is connected both to the emotional limbic system and the "cognitive" prefrontal cortex. The ACC is connected to regions important for emotions (amygdala), memory (hippocampus), and reward (orbitofrontal) (Oane et al., 2020; Stevens et al., 2011).

ACC connections with the limbic system could explain the emergence of depersonalization. Indeed, some patients reported "feeling nothing" or "feeling empty," reflecting emotional reduction. A decrease in connectivity in the ACC could explain these transient feelings of emotional emptiness during

EBS. Furthermore, as ACC activity is heavily regulated by the prefrontal cortex, a suppression of prefrontal activity could be responsible for emotional deficits.

Body image disturbances reported in our study referred to changes in the perception, absence, or proprioceptive illusion regarding a body part. It has been shown that the ACC is involved in illusory kinesthetic perception triggered by muscle tendon vibrations (Kavounoudias et al., 2008; Romaiguère et al., 2003), which could explain why stimulations in the ACC change the body image.

Retrosplenial Posterior Cingulate Cortex (PCC)

Our results indicate that stimulations in the retrosplenial PCC led to modifications in self-location. Sensations included feelings of whole-body displacement and are similar to vestibular sensations. The retrosplenial PCC is a small region around the splenium of the corpus callosum. It is known to be involved in spatial navigation and memory, as it is closely connected to the hippocampus (Vann et al., 2009). It has been proposed that the retrosplenial PCC, along with the hippocampus, is involved in the transformation from allocentric to egocentric representation (Vann et al., 2009). Thus, stimulation in the retrosplenial PCC could induce an error in updating the currently perceived self-location, causing an illusory movement of whole-body (Guterstam et al., 2015).

Dorsal Posterior Cingulate Cortex (dPCC)

Our findings reveal that stimulation of the dPCC leads to depersonalization. The dPCC is involved in detecting and responding to environmental events that may require a change in behavior (Leech and Sharp, 2014). It is linked to forms of internal and self-directed cognition. Clinical evidence also suggests the involvement of the dPCC in psychiatric disorders such as schizophrenia or depression (Leech and Sharp, 2014), conditions characterized by an inability to regulate the balance between internal and external attention. Our results are supported by other EBS studies, reporting depersonalization following PCC stimulation (Balestrini et al., 2015; Herbet et al., 2016, 2014).

Depersonalization could be explained by alterations in the functional connectivity of the dPCC, leading to an altered state of consciousness characterized by a lack of behavioral response or a loss of awareness of the external environment (Herbet et al., 2014). This hypothesis is supported by studies investigating the relationship between complete loss of consciousness and functional deactivation of the dPCC in states such as coma, epilepsy, or anesthesia. These data provide evidence that the PCC is essential in the neuronal network supporting conscious information processing (Alkire et al., 2008; Danielson et al., 2011; Norton et al., 2012). Indeed, the dorsal PCC exhibits significant functional connectivity within the default mode network (DMN), considered the network of internal consciousness, and the frontoparietal network involved in cognitive and attentional control, specifically external attention (Leech and Sharp, 2014; Raichle, 2015). Thus, EBS at the level of the dPCC could impact both networks.

Precuneus

Our results highlight that stimulations in the precuneus also lead to depersonalization. These findings are supported by previous studies on lesions (Herbet et al., 2019) or with intracranial EBS (Lyu et al., 2023; For a review, see Dary et al., 2023). Specifically, stimulation of the right precuneus resulted in dissociation phenomena (Lyu et al., 2023), suggesting right hemispheric dominance for depersonalization. Furthermore, some studies have shown that the precuneus is activated in response to a change of perspective in space, time and person (Peer et al., 2015). In this sense, a stimulation in the precuneus may lead to disturbances in these capacities and explain the feeling of depersonalisation.

Insula

Our results indicate that stimulations in the insula altered the perceptual body image. Unitary recordings in non-human primates have revealed the fundamental role of the insula in the representation of the body and its parts (Coq et al., 2004). Our findings are also supported by functional neuroimaging data in healthy subjects showing an increase in PET signal in the insula following a modification of body image during the rubber hand illusion (Tsakiris et al., 2007). These data are also supported by lesion studies showing that damage to the insula disrupts recognition of one's body as their own (Karnath et al., 2005; Karnath and Baier, 2010) and EBS studies (Nguyen et al., 2023; Penfield and Faulk, 1955; Yu et al., 2018). Moreover, studies also highlight that the insula is a multisensory region and is involved in

processing fundamental interoceptive information relevant to bodily self (Craig, 2002; Heydrich and Blanke, 2013). Recent data support this interrelationship between bodily self and interoception and show insula activation in interoception (Aspell et al., 2012; Monti et al., 2022; Park et al., 2016, 2018; Dary and Lopez, 2023).

The Hippocampal Complex

Our results show that stimulations in the hippocampal complex predominantly led to modifications in self-location and depersonalization. Numerous studies demonstrate the involvement of the hippocampus in self-location (Betka et al., 2022; Guterstam et al., 2015). EBS studies also revealed the involvement of the hippocampus in the bodily self (for a review, see Dary et al., 2023). Other mesial temporal regions such as the parahippocampal gyrus have been implicated in autoscopia phenomena (Blondiaux et al., 2021) or near-death experiences (Blanke et al., 2016). Thus, stimulations in the hippocampal complex could disrupt the neural bases of self-location. It is also important to note that self-location disturbances reported in this study refer to vestibular sensations (feeling of floating, whole-body displacement). There is ample evidence suggesting that the hippocampus processes crucial vestibular information for spatial navigation and thus self-location, especially otolithic signals (Dieterich and Brandt, 2024; Hitier et al., 2021; Smith, 2019). Furthermore, the hippocampal complex is implicated in depersonalization. Similar sensations have also been reported in other EBS studies (Mulak et al., 2008). Other studies have highlighted the link between identity disorders and a reduction in the cortical thickness of the hippocampus (Vermetten et al., 2006).

Supplementary Motor Area (SMA)

Our results indicate that stimulation of the SMA predominantly altered agency and body image. The SMA is involved in planning a voluntary action and the implicit sense of being the agent of this action. Previous studies have shown that lesions in the SMA can result in anarchic hand syndrome, where patients report being unable to control their limbs and that they move on their own (Giummarra et al., 2008). These descriptions resemble the sensations of "urge to move" reported by patients stimulated in the SMA in our study. Single-unit recordings in humans support this idea by showing that the SMA is activated in a pre-reflexive phase of voluntary action (Fried et al., 1991). This pre-reflexive phase refers to the sense of agency as defined for this study. Together, these results demonstrate the causal involvement of the SMA in agency (Kühn et al., 2013; Yomogida et al., 2010).

We also found modifications in body image during stimulation of the SMA. In our study, we included illusions of movement of a body part in the body image. Previous studies have highlighted that the SMA plays a role in kinesthetic functions (Kavounoudias et al., 2008).

The Parietal Operculum

Most stimulations in the parietal operculum induced modifications in body image, specifically changes in the size or shape of a body part. The parietal operculum, often considered as a secondary somatosensory area, is involved in the representation of body parts, including the head, legs, or hands (Eickhoff et al., 2007). Another study highlights that a lesion in the parietal operculum can lead to somatoparaphrenia (Gandola et al., 2012). Previous studies showed that EBS in the parietal operculum disturbed the body image, evoking for example the feeling that a body part is absent (Hao et al., 2022; Salanova et al., 1995).

Subdivision of functional networks to each bodily experience

Our functional connectivity analyses reveal subnetworks according to the type of bodily experiences. However, we note that these functional networks overlap and share common nodes.

Body image network

The body image network seems to involve mainly temporal, limbic and orbitofrontal regions. Surprisingly, our results highlight a disconnection of the superior temporal sulcus (STS) in the body image network. Studies in humans and non-human primates have shown the involvement of this region in the recognition of visually perceived biological motion (Grossman and Blake, 2001; Herrington et al., 2011; Pinsk et al., 2009; Sokolov et al., 2018; Vaina et al., 2001). However, in our categorization of

body image, it involves illusions of movement, hence proprioceptive movements. Therefore, a decrease in STS connectivity could be explained by the deficit in visual feedback in movement induction.

Our connectivity analyses also show a significant decrease edge strength between the STS and the hippocampal complex and the amygdala, two nodes involved in episodic memory and emotional processing. It has been shown that the amygdala and hippocampus are connected to the STS (Habas et al., 2011; Pitcher et al., 2017). Clinical evidence has shown that resection of the amygdala influences STS function in processing bodily expressions (Van de Vliet et al., 2018). Thus, a decrease in STS in the network may lead to a decrease in the amygdala as well, and therefore a decrease in emotional processing. Moreover, a decrease in connectivity between the hippocampal complex and the STS could indicate a disturbance in the non-recognition of one's body as one's own.

Our functional connectivity study also revealed a disconnection of the middle temporal gyrus (T2). T2 is known to be involved in language processing. However, recent studies have highlighted its involvement in the observation of movement and facial expression [Xu et al., 2015] and also in the detection of perceptual discrepancies during multisensory conflicts [van Kemenade et al., 2019; Yomogida et al., 2010]. A decrease in functional connectivity within the body image network might result from a lower ability to detect inconsistencies in body perception.

Self-location network

Our results from functional connectivity analysis support the involvement of several functional networks, such as the limbic network, the DMN, and the salience network, in self-location. We showed an increase in insula strength within this network. The insula is one of the most complex and least understood brain regions. All sensations reported in the modification of self-location are similar to vestibular illusions reported by patients with lesions in the vestibular otolithic system or central vestibular structures. Previous studies have shown that the posterior insula is considered a central region of the cortical vestibular network (Lopez et al., 2012; Mazzola et al., 2019, 2014). Moreover, several studies using artificial stimulation of the vestibular system or in clinical vestibular patients have shown transient disturbances in self-location (Lenggenhager and Lopez, 2014; Lopez and Elzière, 2018; Macaudo et al., 2019; Wu et al., 2024). It has also been proposed that the anterior insula plays a fundamental role in the unified and coherent perception of the sense of self in the present moment (Craig, 2009). The increase in insula strength in the self-location network could thus be explained in this way: whole-body movements are perceived as movements related to oneself, without a feeling of disembodiment. There is no conflict in the attribution of body movements, which would explain the increase in insula strength in the self-location network.

Agency network

The agency network involves a large functional network including the fronto-parietal network, the DMN and the limbic system. This hypothesis is supported by our connectivity results, which show an increase in the connectivity of the insula in the agency network.

The increase in insula strength in the agency network seems at first glance contradictory to results from functional neuroimaging studies in healthy subjects. Indeed, it has been shown that a decrease in insula activity is correlated with a decrease in the feeling of movement control. In other words, a decrease in insula activation led to a sensation of observing someone else's movements (Farrer et al., 2003; Farrer and Frith, 2002). However, a recent study on the analysis of lesions causing disturbances in the ability to initiate action (similar to sensations of being unable to move, feeling stuck) shows that this type of response involves the ACC and its functional network in such responses (Darby et al., 2018). Moreover, it has been determined by resting-state functional neuroimaging studies that the insula, particularly the anterior insula, is connected with the ACC, the amygdala, the entorhinal cortex, the orbitofrontal cortex, and the middle and inferior temporal cortex (Almashaikhi et al., 2014; Cauda et al., 2011; Seghezzi et al., 2019). This network is involved in the control of voluntary movements, intentionality, reward, and emotions. Therefore, an increase in insula strength in the agency network could be explained by an increase in the intention to perform a movement and a stronger anchoring to the self.

On the other hand, it has been shown that lesions causing disturbances related to being the origin of the action involve a brain network defined by the connectivity of the precuneus (Darby et al., 2018). Moreover, it has been shown that the posterior insula is connected with the premotor cortex, the SMA,

the PCC, the precuneus, the pre- and postcentral gyrus, and the superior temporal sulcus (Almashaikhi et al., 2014; Cauda et al., 2011; Seghezzi et al., 2019). As the precuneus was involved in perspective taking (Cavanna and Trimble, 2006; Ruby and Decety, 2001), the increase in node strength in the insula could be explained by an increase in the weight given to third-person information. Indeed, patients do not perceive themselves as the agents of the action, leading to an overactivation of regions involved in self-representation, particularly the insula.

Functional Network of the Bodily Self

Inferior Parietal Lobule (IPL)

An important finding from our functional connectivity analysis of the bodily self network, encompassing various experiences, reveals a decrease in the node strength for the inferior parietal lobule (IPL). Previous research emphasizes that the IPL's pivotal role in explicitly attributing actions and in the awareness of one's own movements (Desmurget et al., 2009). It also participates in estimating object dimensions and bodily proportions (Hashimoto and Iriki, 2013). Thus, a decrease in connectivity in this region could reflect an error in maintaining a coherent perception of body size and awareness of action execution. Electrical stimulation in this area could disrupt this cognitive process. This aligns with recent findings on brain lesions linked to Alice in Wonderland syndrome, where patients experience distortions in body image perception, with many regions being disconnected from the IPL (Friedrich et al., 2024). Furthermore, disruptions or lesions in the IPL have been associated with various pathologies, including anorexia nervosa (Pietrini et al., 2011), somatoparaphrenia [Vallar and Ronchi, 2009], and feelings of disembodiment (Blanke et al., 2002; Blanke and Mohr, 2005). Together, we highlight the fundamental role of the IPL in the bodily self network.

Given the significant number of connections with the IPL in our connectivity analysis, the IPL can be considered a hub, i.e., a particularly connected node. It has been shown that the IPL is at the crossroads of several functional networks (Caspers et al., 2011). At rest, the IPL is particularly integrated into the default mode network (DMN), the frontoparietal network, and the salience network. Our results reveal a decrease in connectivity between the IPL and the middle temporal gyrus. Functional neuroimaging studies have shown that the IPL connects to lateral temporal regions by joining the inferior longitudinal fasciculus (Caspers et al., 2011). While the middle temporal gyrus (T2) is involved in language processing, recent studies have highlighted its involvement in motion observation, facial expression (Xu et al., 2015), and detection of perceptual divergences during multisensory conflicts (van Kemenade et al., 2019; Yomogida et al., 2010). Therefore, a decrease in connectivity between the IPL and T2 could indicate a decrease in the ability to perceive perceptual divergences, leading to alteration in bodily self.

Inferior temporal gyrus (T3)

We also found a decrease in the strength of the inferior temporal gyrus. This region is involved in visual object recognition, decision-making, and the visual ventral pathway, as well as language (Lin et al., 2020). Tractography studies revealed the engagement of local association fibers within white matter, distinguished by their U-shaped morphology. These fibers establish connections between neighboring cortical areas through sulci (Briggs et al., 2021). Specifically, in the lateral temporal lobe, U-fibers establish connections between T3 and T1 as well as T2. The inferior longitudinal fasciculus connects T3 with limbic regions including the hippocampus and parahippocampus, highlighting the role of T3 in emotions and memory. Studies on lesions show that damage to the inferior longitudinal fasciculus could lead to a loss of emotional response to visual stimuli as well as deficits in visual recognition (Lin et al., 2020). Therefore, a decrease in functional connectivity within the T3 network may stem from an impairment in perceiving the body coherence. This interpretation finds support in instances where T3 stimulations induced sensations of dissociation, such as feeling detached from one's body, or alterations in self-location reported by patients (Andelman-Gur et al., 2020).

Study limitations

While our study causally demonstrates the body self-network for the first time, several limitations need to be addressed. First, the variable spatial sampling between patients and structures directly impacts the number of connections probed in our functional connectivity analysis. Secondly, our anatomical

grouping used for our functional connectivity analysis may conflict with functional region groupings. For instance, it has been shown that the inferior parietal lobule (IPL) encompasses both the angular gyrus, a central node of the default mode network (DMN), and the supramarginal gyrus, a node of the salience network. It would be interesting in future studies to group regions according to functional networks (Yeo et al., 2011) and identify changes in connectivity between functional networks. Additionally, due to the low number of signals analyzed for functional connectivity, we did not consider hemispheric laterality. However, functional connectivity may vary depending on hemispheric laterality (Zhang and Li, 2014).

Conclusion

This is the first study, to our knowledge, to demonstrate the bodily self network through causal approaches. Our extensive patient sampling allowed us to locate EBS resulting in modifications of one or several bodily experiences in over 50 patients. Through the localization of EBS, we identified six regions that were most consistently involved in bodily self disturbances, including the ACC, PCC, insula, SMA, precuneus, parietal operculum, and hippocampal complex. Our functional connectivity analyses revealed a decrease in connectivity in the IPL, a core node for bodily self network. Our study highlights the existence and overlap of sub-networks for each bodily experience. Together, our findings contribute to understanding the neural basis of the bodily self, which is particularly important for better assessment of patients with brain lesions, psychiatric disorders (such as depersonalization), or for more accurately predicting the consequences of brain surgery on different components of the bodily self.

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Etudier les bases multisensorielles du soi corporel : influence du système vestibulaire

Article 4 : Influence d'une vestibulopathie bilatérale sur la localisation du soi et le sentiment d'appartenance

L'influence du système vestibulaire dans le soi corporel est encore trop peu étudiée. Dans cette étude, nous nous sommes intéressés à l'impact d'une perte vestibulaire bilatérale sur le soi corporel et plus précisément sur le sentiment d'identification et de localisation du soi. Pour cela, nous avons conduit une expérience en réalité virtuelle, une Full-body-illusion (FBI), chez 34 patients atteints d'une perte vestibulaire bilatérale et chez 34 contrôles appariés. Comme les patients et contrôles étaient relativement âgés (moyenne âge $\pm$ SD : 58 ± 12 ans) et que la FBI a essentiellement été utilisée sur une tranche d'âge plus jeune, nous avons également inclus 19 autres contrôles plus jeunes sans troubles otoneurologiques (moyenne âge $\pm$ SD : 34 ± 8 ans). Pour rappel, une perte vestibulaire bilatérale se caractérise par une réponse vestibulaire absente ou sévèrement diminuée des deux côtés. Dans notre étude, cela se traduit par la perte bilatérale des canaux semi-circulaires. L'objectif est donc plus précis : il s'agit d'étudier le rôle des organes otolithiques dans le soi corporel.

La Full-body illusion dans un environnement virtuel, que j'ai entièrement programmée en C# dans Unity 3D (Unity 3D 2020.1, Unity Technologies), a été adaptée pour que les participants n'aient pas de nausée, ni ne ressentent d'instabilités posturales. Ils étaient donc assis sur un tabouret et immergés dans un environnement virtuel, dans lequel ils observaient un avatar de dos qui avait été adapté à leur morphologie. Nous avons utilisé une tâche d'imagerie mentale comme mesure implicite pour évaluer la modification de la localisation du soi et l'identification à l'avatar après une stimulation visuo-tactile synchrone ou asynchrone. Des questionnaires relatifs au sentiment d'identification, d'agentivité, de localisation du soi ont également été proposés comme mesure explicite.

Nos résultats montrent que les résultats aux mesures explicites sont plus faibles chez les patients que chez les contrôles, suggérant que les patients sont moins sensibles à l'illusion que les volontaires sains. Ce résultat contre-intuitif au premier abord, du fait de la dépendance visuelle des patients rapportée dans d'autres études, peut cependant être expliqué par l'ancrage plus fort sur des références égocentrées (somesthésiques et intéroceptives) pour l'orientation spatiale et donc pour coder la localisation du soi.

Les résultats des mesures implicites de la tâche de localisation du soi ne montrent pas de différence significative entre les deux groupes et pas d'effet significatif de la stimulation visuo-tactile. Ces résultats négatifs peuvent être expliqués par un effet de

l'âge. En effet, dans le groupe de contrôles plus jeunes, nous retrouvons un effet largement significatif de la stimulation visuo-tactile.

Enfin, nos analyses sur le rôle des informations otolithiques dans la localisation du soi n'a pas permis de montrer de résultats significatifs. Nous relevons seulement que dans les mesures explicites, les patients avec des cVEMPs ont des scores d'identification plus faibles que leurs contrôles respectifs, ce qui n'est pas le cas des patients avec des cVEMPs. Cependant, nos résultats doivent être interprétés avec prudence du fait de la petite taille des échantillons une fois que les groupes de patient ont été partagés en sous-groupe.

Influence of a bilateral vestibulopathy on the bodily self as measured by a full-body illusion

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Abstract

The vestibular contribution to own body and self perception is suggested by the effects of artificial vestibular stimulation in healthy subjects as well as by the consequence of otoneurological disorders, which sometimes manifest as depersonalization-like symptoms. Despite this, the influence of the vestibular system on the bodily self, an immediate and pre-reflective form of self, remains relatively unexplored. In this study, we investigated the multisensory bases of the bodily self by conducting a full-body illusion in virtual reality in 34 patients with a bilateral vestibulopathy and 34 matched controls. Our findings revealed that the intensity of the illusion measured by questionnaires was lower in patients compared to controls. Implicit measures of the self-location using a mental imagery task showed no significant difference between the two groups. These negative results may be attributed to a compensation mechanism for vestibular loss that mitigates multisensory conflict. Furthermore, we observed that sensitivity to the illusion was influenced by age.

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Introduction

The experience of 'I' as a subject is intricately linked to the experience of owning and inhabiting a body. Thus, bodily self-consciousness is often regarded as relying on a set of bodily experiences, such as *self-location*—defined as the sense of occupying a volume of space at a given time, typically within the physical confines of the body—or the sense of *body ownership*, where one identifies with a body and regards its parts as one's own (Blanke, 2012). Other bodily experiences, such as *first-person perspective*—characterized by an egocentric viewpoint—and *agency*—characterized by the sense of being the agent of actions and thoughts—have also been linked to the bodily self (Blanke, 2012). Both longstanding neurological studies and more recent cognitive neuroscience research have demonstrated that these various facets of the bodily self rely on coherent integration of sensorimotor signals from the body and the extracorporeal environment (Blanke et al., 2015; Dieguez and Lopez, 2017; Park and Blanke, 2019; Serino et al., 2013; Seth, 2013). Indeed, focal epilepsies (Blanke et al., 2004), focal brain lesions (Gandola et al., 2012; Heydrich and Blanke, 2013; S. Ionta et al., 2011), as well as invasive electrical stimulation in multisensory brain regions (Blanke et al., 2002; Dary et al., 2023; De Ridder et al., 2007; Desmurget et al., 2009), have been reported to alter the bodily self by affecting self-location, body ownership, first-person perspective, and agency.

While the contributions of the visual and somatosensory systems (touch and musculoskeletal proprioception) to the bodily self have been extensively studied (e.g., Botvinick and Cohen, 1998; Tsakiris and Haggard, 2005; Lenggenhager et al., 2007a; Palluel et al., 2011; Petkova et al., 2011; Chancel et al., 2022), the contributions of less “overt” sensory systems have received less attention. In recent years, focus has shifted to the role of interoceptive signals in the bodily self, demonstrating links between cardiac, respiratory, and gastrointestinal signals and the bodily self (Adler et al., 2014; Aspell et al., 2013; Monti et al., 2022; Park et al., 2016; Park and Blanke, 2019; Tsakiris et al., 2011). Conversely, far less attention has been paid to the vestibular system, despite its crucial role in encoding translations and rotations of the body through sensors in the inner ear and vestibulo-thalamo-cortical pathways involved in perception, emotion, and cognition (Gurvich et al., 2013; Lopez, 2016; Lopez and Blanke, 2011). It has even been suggested that vestibular information provides an unparalleled type of information regarding self-motion, particularly by enabling an absolute coding of movement that other senses cannot provide (Lenggenhager and Lopez, 2015).

The role of vestibular information in the bodily self is evidenced by the effects of caloric and galvanic vestibular stimulations, which increase the frequency and intensity of depersonalization-like symptoms in healthy volunteers, wherein the self appears strange and unreal (Jauregui-Renaud, 2015; Jauregui-Renaud et al., 2008; Lopez et al., 2018). These same artificial stimulations of vestibular sensors also seem to alter self-location and perspective taking (Ferrè et al., 2014; Pavlidou et al., 2018), as well as identification with body parts in the rubber hand illusion (Lopez et al., 2010). Similarly, some patients with peripheral vestibular impairments appear to exhibit a distorted sense of self (Lopez, 2013), with a threefold higher chance of experiencing an out-of-body illusion (Lopez and Elzière, 2018), and more frequent and intense depersonalization-derealization symptoms than neurotypical individuals (Elyoseph et al., 2023a; Grigsby and Johnston, 1989; Jauregui-Renaud et al., 2008; Toupet et al., 2019; Tschan et al., 2013). Moreover, vestibular disorders are frequently associated with alterations in the bodily self in neurological conditions characterized by illusory self-location, such as out-of-body illusions or autoscopic phenomena (Blanke et al., 2004; Heydrich et al., 2011; Nakul and Lopez, 2017).

Multisensory illusions developed in immersive virtual environments or through head-mounted displays offer means to study the contribution of sensorimotor systems to the bodily self in a well-controlled laboratory setting (Ehrsson, 2007; Lenggenhager et al., 2007, 2009; Nakul et al., 2020b; Pfeiffer et al., 2013, 2014; Preuss and Ehrsson, 2019a; Tekgün and Erdeniz, 2021). The Full-Body Illusion (FBI) in virtual reality (VR) is particularly convenient, as it enables the investigation of self-location, body ownership and agency (Nakul et al., 2020b). During the FBI in VR, participants observe either their own back or the back of an avatar positioned a few meters ahead in the VR environment. Tactile stimulation is applied to the participants' back and replicated on the avatar's back, synchronously, or asynchronously with a time delay. Typically, participants tend to self-identify with the avatar after synchronous visuo-tactile stroking and localize themselves closer to the avatar they self-identify with, which can be measured using mental imagery tasks (Lenggenhager et al., 2009; Nakul et al., 2020b; Pfeiffer et al., 2013).

Despite its potential, few studies have utilised the FBI alongside vestibular stimulation to demonstrate that visuo-vestibular stimulation can induce illusory identification with the observed body (Macauda et al., 2015; Mattsson et al., 2022; Preuss and Ehrsson, 2019b). Thür et al. (2019) integrated FBI with conflicting visuo-graviceptive information by presenting a virtual body tilted with respect to gravity, showing that the strength of the illusion weakened during visuo-graviceptive conflict. They also observed that during the illusion, the perception of one's own body orientation was modulated only in visual-field dependent participants. Recently, Wu et al. (2024) used mixed reality with a whole-body motion platform to manipulate visual-vestibular integration, inducing out-of-body like experiences in healthy participants. Their findings suggest that congruent visual-vestibular stimulation in a self-centered reference frame triggered such experiences. Although these studies provide empirical support for the role of vestibular signals in the bodily self, its precise contribution remains poorly understood, with limited research focusing on the importance of otolithic function in the bodily self.

To assess the vestibular influence on the bodily self, we conducted a study involving patients with a bilateral vestibulopathy (BVP), a disorder characterized by severe bilateral loss of vestibular functions. The diagnostic criteria for BVP primarily focus on the loss of semicircular canal functions, potentially overlooking preserved otolithic functions (Rosengren et al., 2018). Individuals with BVP often experience instability, especially in dim lighting or on uneven surfaces, and they may experience oscillopsia during movements (Fujimoto et al., 2019). BVP patients tend to rely more on visual signals for balance control (Cutfield et al., 2014; Dieterich et al., 2007; Lacour et al., 2018; Pogson et al., 2020), and recent research has highlighted deficits in spatial navigation and memory among BVP patients (Brandt et al., 2005; Dobbels et al., 2020, 2019; Gammeri et al., 2022; Smith, 2022). However, despite the strong alteration in multisensory processing in these patients and their inability to correctly encode self-motion and self-orientation (Cohen, 2000; Schöberl et al., 2021), there is a paucity of studies investigating the sense of self in patients with BVP, with the few exception of interoceptive acuity, self-reported self-location (Nakul et al., 2020a), and first-person perspective (Deroualle et al., 2017).

The primary objective of our study was to examine the role of the vestibular system in self-location and self-identification by comparing the experience of BVP patients and carefully matched healthy controls during the FBI from a third-person perspective in VR (Lenggenhager et al., 2007; Nakul et al., 2020b). We anticipated that BVP patients, owing to their higher reliance on visual signals, would exhibit increased self-identification to the avatar and illusory self-location towards the avatar. The secondary aim of our study was to assess the contribution of otolithic function to self-location and self-identification by comparing the performance of BVP patients with and without otolithic responses.

Materials and methods

Participants

We tested 34 participants with idiopathic BVP (19 females; mean age $\pm$ SD: 58 ± 13 years) and 34 healthy volunteers (19 females; mean age $\pm$ SD: 58 ± 12 years) volunteers matched for age, sex, education level, and socio-professional status (controls group 1). Sociodemographic data are summarized in **Table 1**.

The diagnosis of BVP was based on comprehensive neuro-otological examinations (**Supplementary Table 1**). The semicircular canal functions were assessed with the bithermal caloric test and the video head impulse test (VHIT). All patients demonstrated caloric nystagmus parameters below the threshold, indicative of BVP as outlined in the Barany's Society diagnostic criteria. Most patients presented severe deficits at the VHIT (i.e., gain <0.69 for the vertical canals, and <0.8 for the lateral canals). Further evaluation of vestibular function included saccular assessment through the recording of cervical vestibular-evoked myogenic potentials (cVEMPs) over the sternocleidomastoid muscles. Of the total patient cohort, 20 exhibited bilateral cVEMPs, while 14 showed no cVEMPs. Additionally, utricular function was assessed through the recording of ocular vestibulo-evoked myogenic potentials (oVEMPs). Among the patients, 8 displayed bilateral or unilateral oVEMPs, while 26 showed no oVEMPs.

As the FBI in VR has never been evaluated within the age spectrum matching our BVP patients and their respective controls, we incorporated 19 additional younger controls (control group 2) devoid

of self-reported otoneurological disorders (**Table 1**). This inclusion aimed to meticulously investigate the impact of age on the elicitation of the FBI.

Ethical approval and participant's consent

Ethical approval was granted by Institutional Review Boards (for the patients: CPP Région Ouest I, ID-RCB 2022-AO1513-40; for the controls: ID-RCB 2022-A00098-35) and procedures were in accordance with the Declaration of Helsinki. All participants gave their written consent before being involved in the study. Only healthy controls received a 10 € compensation for their participation.

	BVP (n =34)	Controls group 1 (n = 34)	Controls group 2 (n =19)
Age (years)	59 ± 13	59 ± 13	34 ± 8
Females/Males (n)	19/15	19/15	9/10
Right handedness (n)	33	33	18
Highest education level (%)			
Level 1	6.2	8.9	0.0
Level 2	15.6	11.9	0.0
Level 3	15.7	8.4	11.1
Level 4	21.9	5.9	33.3
Level 5	40.6	64.9	55.6
Employment status (%)			
Student	0.0	0.0	26.3
Employed	43.8	55.9	73.7
Retired	46.8	44.1	0.0
Unemployed	9.4	0.0	0.0
Marital status (%)			
Single	15.6	11.8	5.9
Married/Couple	68.8	76.5	53.0
Divorced/widowed	15.6	11.7	41.1
Smoker (%)	15.6	29.4	27.8
Migraine (%)	37.5	11.8	11.1
Vision problems (%)	93.8	81.9	27.8
Game experience score	2.5 ± 3.8	3.1 ± 2.8	8.4 ± 3.7
Depersonalization (CDS)	18.1 ± 16.5	18.3 ± 21.6	36.3± 21.1
State of anxiety (HADS)	7.2 ± 3.2	7.0 ± 3	7.2 ± 2.6
State of depression (HADS)	3.9± 2.6	4.1± 2.6	4.6± 2.6
Empathy (EQ)	47.0 ± 11.3	45.4 ± 14.3	53.0 ± 11.5

Table 1. Socio-demographic data and questionnaire scores. Mean ± SD is reported for age, game experience, CDS, HADS and EQ. Percentage of participants is reported for education level, employment, marital status, smoking habits. Education level is based on the French education system: Level 1 (before high school), Level 2 (accomplished high school), Level 3 (two years after high school), Level 4 (Bachelor's degree), Level 5 (Master's degree, Engineering degree, PhD, MD). Game experience score was rated using a five-point Likert scale (0: never, 1: sometimes, 2: every month, 3: every week, 4: almost every day, 5: every day).

Patients	Score VHIT	cVEMP Right	cVEMP Left	oVEMP Right	oVEMP Left
P1	0	1	1	1	1
P2	0	1	1	0	0
P3	2	1	1	1	1
P4	2	0	0	1	0
P5	1	0	0	0	0
P6	0	0	0	0	0
P7	3	1	1	0	0
P8	1	1	1	0	0
P9	0	1	1	0	0
P10	0	1	1	1	1
P11	0	1	1	0	0
P12	0	0	0	0	0
P13	0	0	0	1	1
P14	0	1	1	0	1
P15	0	0	0	0	0
P16	0	0	0	0	0
P17	0	0	0	0	0
P18	1	1	1	0	0
P19	0	1	1	1	1
P20	1	1	1	1	1
P21	0	0	0	0	0
P22	0	1	1	0	0
P23	0	1	1	0	0
P24	0	1	1	0	0
P25	0	0	0	0	1
P26	3	1	1	0	0
P27	0	1	1	0	0
P28	1	0	0	0	0
P29	6	0	0	0	0
P30	1	0	0	0	0
P31	2	1	1	0	0
P32	0	1	1	0	0
P33	1	0	0	0	0
P34	0	1	1	0	0

Supplementary Table 1. Results from the neuro-otological assessment. Video Head Impulse Test (VHIT) scores was calculated by attributing a score (0 for abnormal gain; 1 for normal gain) for each semicircular canal and each side. The total VHIT scores for both sides are reported. Gain was considered normal when >0.69 for the vertical canals, and >0.8 for the lateral canals. cVEMP: cervical vestibular-evoked myogenic potential; oVEMP: ocular vestibulo-evoked myogenic potential.

Experimental setup

Participants were immersed in a VR environment created in Unity 3D 2020.1 (Unity Technologies) using a head-mounted display (HTC Vive, HTC Corporation) with a horizontal visual field of 110° ($\sim 90^\circ$ per eye). Participants were “placed” at the centre of a virtual room (3.8 x 2.9 x 6.8 m) with blank walls. They held a VR controller in their right hand. Two laser emitters and inertial units encoded 3D coordinates of the head-mounted display, VR controllers and the tracker, which were all recorded at 90 Hz with Unity. Participants wore headphones playing white noise during the experiment to avoid distractions and spatial auditory information. An avatar wearing a pair of jeans and a white t-shirt (created with Blender) was displayed as if it were approximately 2 m in front of the participants in the VR room. The experimenter gently stroked the participants’ back with a VR controller, irregularly so that they could not predict the tactile stimulation on their back, while the controller movement was reproduced by a virtual representation of the controller on the avatar’s back. During synchronous visuo-tactile stimulation, the movement of the virtual controller on the avatar’s back matched the movement and position of the controller on the participant’s back. During asynchronous visuo-tactile stimulation,

the virtual controller reproduced the movement of the controller on the participant's back with a 1 s delay. Synchronous and asynchronous visuo-tactile stimulations were each applied for 2 min in separate blocks of trials (**Figure 1**).

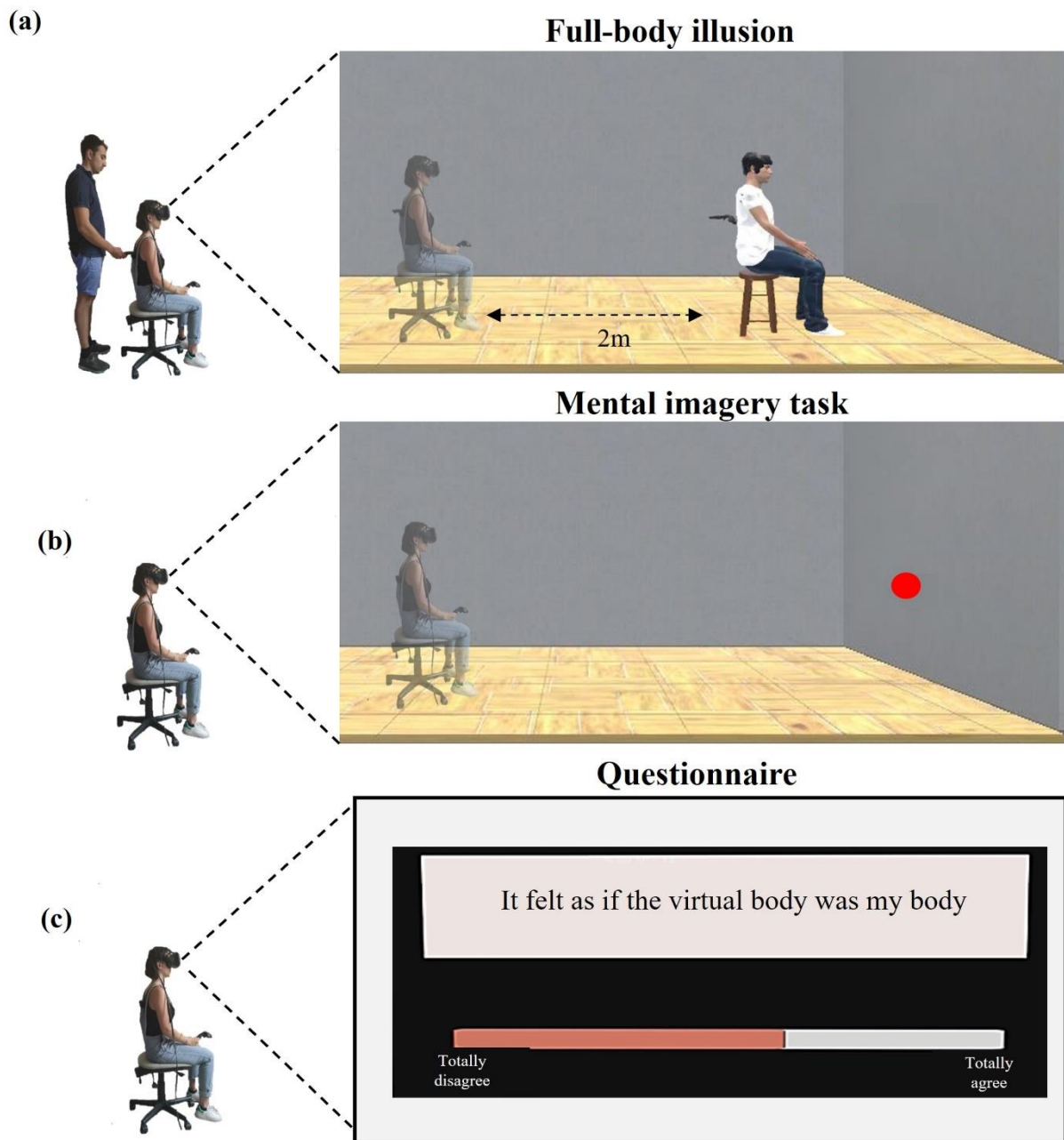


Figure 1: Experimental setup. (a) An avatar wearing a pair of jeans and a white t-shirt was presented approximately 2 m in front of the participants in a VR room. The experimenter stroked the participants' back with a VR controller while the controller movement was reproduced by a virtual representation of the controller on the avatar's back. (b) After 2 minutes of visuo-tactile stimulation, the avatar was "removed" from the VR room and a beep tone in the headphones indicated the start of the mental imagery task. A red ball at the far end of the VR room, presented at the height of the participant's chest, moved linearly towards the participant for 3 s. (c) After each block of visuo-tactile stimulation, a four-item or eleven-item questionnaire was presented in VR to measure the strength of the illusion.

Measure of illusory self-location using a mental imagery task

The mental imagery task aims to measure the perceived self-location by asking participants to indicate when a ball presented in the VR environment felt at the level of their self. All procedures were adapted from (Nakul et al., 2020b).

Assessment of visual mental imagery ability. We first aimed at controlling that the ability to estimate self-location based on visual mental imagery did not differ between patients with BVP and controls, as BVP has been linked to impaired visual and motor imagery (Demougeot et al., 2011; Péruch et al., 2011) and visual motion detection (Shallo-Hoffmann and Bronstein, 2003). Participants were immersed in a VR room and a beep tone played in the headphones signaled the start of the mental imagery task. A red ball appeared at the far end of the VR room at a height corresponding to the participant's chest. The ball moved linearly towards the participant for 3 s at one out of six predetermined velocities (V1 = 0.3 m/s; V2 = 0.4 m/s; V3 = 0.5 m/s; V4 = 0.6 m/s; V5 = 0.7 m/s; V6 = 0.8 m/s). A black screen was then displayed, and participants were instructed to imagine the ball continued to move linearly towards them at the same constant velocity and to indicate when the ball would reach "them", by pressing on a button on the VR controller. To infer participants' self-location, we recorded the coordinate of the (hidden) ball along the anterior-posterior axis when participants responded. Participants performed the task 3 times for each of the randomly presented ball velocity (V1–V6). When the ball moved for 3 s at velocities ranging from V1 to V6, the distances between the position where the ball disappeared and the participants location were: 4, 3.7, 3.4, 3, 2.8, and 2.4 m, respectively. Thus, if participants correctly estimated their self-location, they should press a button on the VR controller when the ball has travelled these exact distances (**Figure 1** and **Figure 2a**).

Effect of the full-body illusion on perceived self-location. After 2-min visuo-tactile stimulation, the avatar was removed from the VR room and a beep tone in the headphones signaled the start of the mental imagery task. A red ball at the far end of the VR room, presented at the height of the participant's chest, moved linearly towards the participant for 3 s at V2 (0.4 m/s) or V4 (0.6 m/s). After a black screen was displayed, participants imagined the ball continued to move linearly towards them at the same speed and to indicate when the ball would reach "them", by pressing on a button on the VR controller.

Self-reports during the full-body illusion

Short questionnaire. After each block of visuo-tactile stimulation, a four-item questionnaire was presented in VR to measured experiences (**Table 2**). Questions focused on self-identification and self-location. Participants responded to the sequentially presented questions using a sliding scale ranging from "Totally disagree" to "Totally agree". They used a trackpad on the controller to select their answers and validated their choice by pressing the trigger on the controller. Before each question the slider was presented at randomly chosen position along the scale to avoid a bias in the response.

Long questionnaire. After three consecutive blocks of each visuo-tactile stimulation, another eleven-item questionnaire was presented to measure the average experience regarding the whole series of visuo-tactile stimulation (**Table 2**). The questions related to different aspects of the self highlighted in previous research, such as self-identification, touch referral, disembodiment, agency, illusory movement, bi-location and presence.

Additional questionnaires

After the experiment, participants filled-out several questionnaires with paper and pencil.

Demographics. Basic demographic information was collected, including age, sex, handedness, education level, marital status, and employment status. We also collected information about smoking and drinking habits, and history of migraine (**Table 1**).

Anxiety and Depression. States of depression and anxiety were measured using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith, 1983), a self-reported scale with 7 items tapping

into anxiety and 7 items tapping into depression. Answers to each item are rated from 0 to 3, contributing to an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Each subscale has scores ranging from 0 to 21. The HADS shows high sensitivity and reliability to assess the symptom severity of anxiety disorders and depression in various clinical populations, as well as in the general population (Bjelland et al., 2002).

Depersonalization and derealization. Experiences of depersonalization-derealization were assessed using the Cambridge Depersonalization Scale (CDS) (Lopez and Elzière, 2022; Sierra and Berrios, 2000), designed to provide a comprehensive overview of potential distortions of self, own-body, surrounding, senses, emotions and memories. The CDS includes 29 items about depersonalization and derealization symptoms. Participants were asked whether they have had these 29 experiences during the last six months. For each item, participants indicated the frequency of the experience on a scale ranging from 0 (“never”) to 4 (“all the time”), and the duration of the experience on a scale from 1 (“few seconds”) to 6 (“more than a week”). For each item, the global score (sum of the frequency and duration) ranged from 0 to 10. The total score for the CDS ranges from 0 to 290. The CDS shows high internal consistency and good reliability (Sierra and Berrios, 2000).

Empathy. Participants filled out the Empathy quotient (EQ), a 60-item questionnaire designed to measure individual empathy traits. Scores were given on a four-point scale ranging from “strongly disagree” to “strongly agree”. The total score for the EQ ranges from 0 to 80. The EQ is a valid and reliable scale, and the various subscales have been adapted for clinical populations (Baron-Cohen and Wheelwright, 2004; Lawrence et al., 2004).

Computer and game experience. Participants completed a gaming experience questionnaire to measure their experience with VR, as well as with 2D and 3D games.

Category	Questionnaire item
Self-identification	Q1*: It felt as if the virtual body was my body.
	Q6: It seemed as if I might have had more than one body.
Touch referral	Q2: It seemed as if I were feeling the touch of the VR controller in the location where I saw the virtual body (hence on the virtual body).
	Q3: It seemed as though the touch I felt was caused by the virtual controller touching the virtual body.
	Q5: It seemed as if the touch I was feeling came from somewhere between my own body and the virtual body.
Self-location	Q4*: It felt as if my (real) body was drifting toward the front (toward the virtual body).
	Q11*: It appeared as if the virtual body were drifting backward (toward my body).
	Q7*: It seemed as if I were in two places at the same time.
Agency	Q8: It seemed as if I could animate (put in motion) the virtual body as my own body if I had wanted
Presence	Q9: It seemed as if I were located in the virtual scene.
Nausea	Q10: I felt sick to my stomach (nausea).

Table 2. Questions used to assess the intensity of the full-body illusion. *Question also presented in the short questionnaire.

Session organization

1) Before the experiment proper, the size of the avatar (width and height of the back) was adapted to each participant.

- 2) Participants underwent three training sessions for the mental imagery task, each conducted at varying speeds, aimed at acquainting them with the task instructions and procedures. They were also trained to manipulate the VR controller to answer questionnaires using the slider.
- 3) To assess their visual mental imagery ability, participants performed the mental imagery task eighteen times (3 times per velocity).
- 4) Each session of visuo-tactile stimulation lasted 2 min. After each type of visuo-tactile stimulation (synchronous and asynchronous), participants (1) completed one trial of the mental imagery task at a given speed and (2) filled out a four-item questionnaire (here referred to as “short questionnaire”). Each stimulation condition was repeated twice. At the end of the two stimulation blocks for a same condition (synchronous or asynchronous), participants completed the eleven-item questionnaire (here referred to as ‘long questionnaire’) about their subjective experience during the visuo-tactile stimulation. The visuo-tactile stimulation was presented in a quasi-counterbalanced order across participants.
- 5) Participants took a five-minute break between the two stimulation conditions.
- 6) Participants completed the EQ, CDS, HADS, and game experience questionnaires on paper sheets at the end of the experiment.

Data processing and statistical analyses

Statistical analyses were carried out in GraphPad Prism (version 10.1.0) and RStudio (version 4.3.1).

Assessment of visual mental imagery ability. Simple linear regressions were calculated to investigate the relationship between the distance between the location of the ball before it disappeared from the VR scene and the participant’s location, and the distance imagined by the participant. R^2 values, indicative of the goodness-of-fit of the regression, were compared between participants using Mann-Whitney tests.

Self-reports about the FBI. As questionnaire ratings were not normally distributed, we used Kruskal–Wallis tests for between-group comparisons (controls group 1, controls group 2 and patients) and Dunn tests for post-hoc multiple comparisons. Further between-group comparisons were calculated after patients were stratified based on the presence or absence of cVEMPs. Participants were categorized into four groups: patients with cVEMPs and their matched controls, and patients without cVEMPs along with their respective controls.

Illusory self-location after the FBI. Drifts in self-location after the FBI were calculated as the coordinate of the ball recorded after synchronous visuo-tactile stimulation minus the coordinate recorded after asynchronous visuo-tactile stimulation. Due to the non-normal distribution of the data, between-group comparisons were analyzed using Mann-Whitney and Kruskal-Wallis tests. In instances where the Kruskal-Wallis test yielded significant results, post-hoc multiple comparisons were performed with non-parametric Dunn tests. One-tailed Wilcoxon tests were calculated to assess whether self-location in the synchronous condition was significantly larger (i.e., more towards the avatar) than in the asynchronous conditions.

Results

Assessment of visual mental imagery ability

Figure 2b shows the linear regressions between the distance travelled by the ball to reach the participant’s location and that imagined by the participants, for all patients and controls (group 1). Overall, participants from all groups showed a tendency to underestimate the distance, as regressions lines were below the theoretical line (red line on **Figure 2b**). In addition, there was a very large variability in the ability to perform the mental imagery task. However, despite this variability, there was no statistical difference between the R^2 values calculated for the BVP patients and the controls ($U = 453$, $p = 0.06$), indicating that both groups performed equally in the mental imagery task (**Figure 2c**).

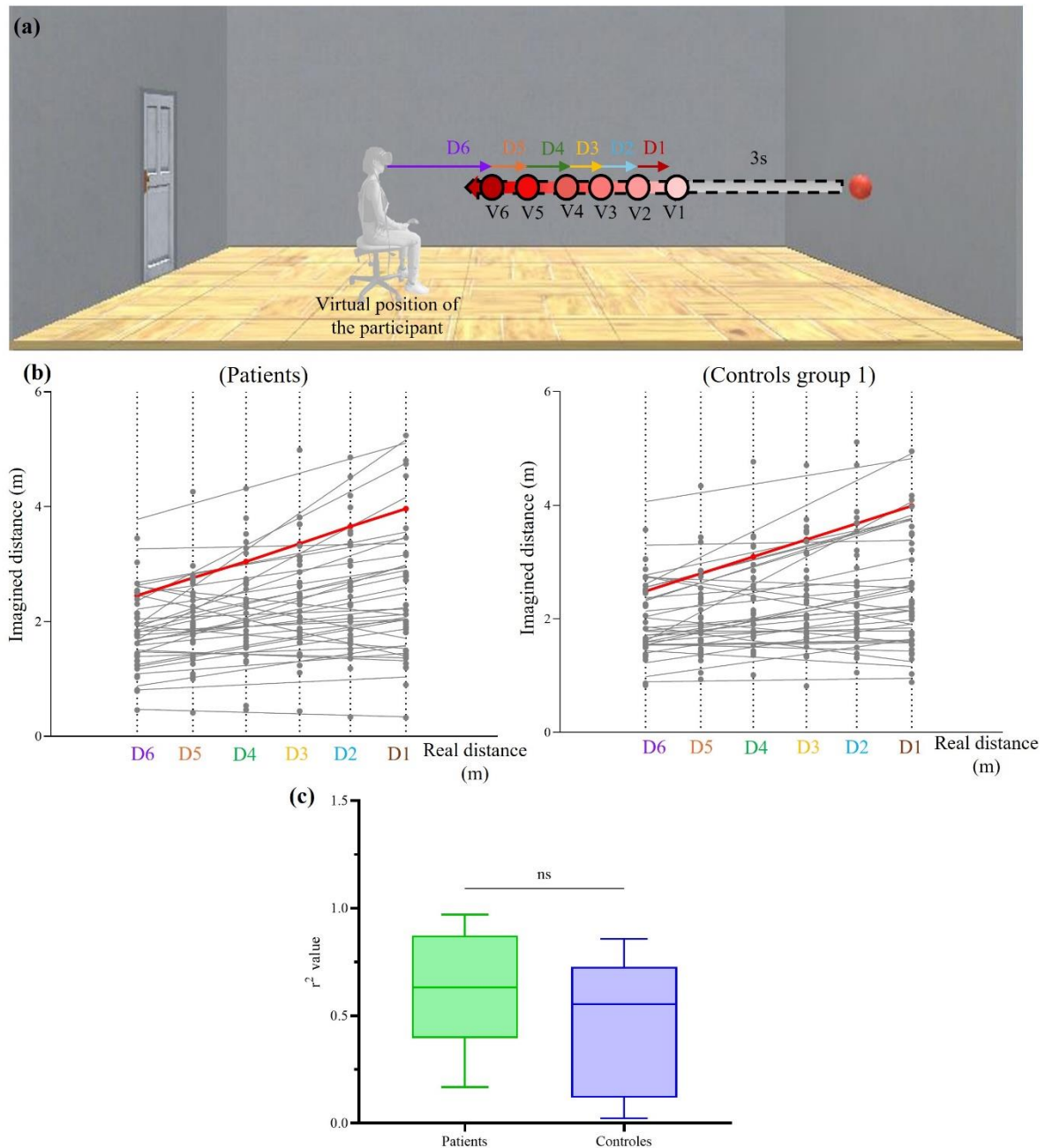


Figure 2. Mental imagery task to measure self-location in VR. (a) Procedures. Participants were immersed in a VR room and a beep tone played in the headphones signaled the start of the mental imagery task. A red ball appeared at the far end of the VR room at a height corresponding to the participant's chest. The ball moved linearly towards the participant for 3 s at one out of six predetermined velocities (V1 = 0.3 m/s; V2 = 0.4 m/s; V3 = 0.5 m/s; V4 = 0.6 m/s; V5 = 0.7 m/s, V6 = 0.8 m/s). Participant estimates when the ball reaches "them", by pressing on a button on the VR controller. Participants performed the task 3 times for each of the randomly presented ball velocity (V1–V6). When the ball moved for 3 s at velocities ranging from V1 to V6, the distances between the position where the ball disappeared from the VR scene and the participants' location were: D1, D2, D3, D4, D5, and D6. **(b)** Linear regression for all patients and controls. The red line represents the ideal scenario, in which participants precisely pressed the button corresponding to their actual location. Grey dots represented the participant's estimated position (averaged across 3 trials) and grey lines are linear regressions. **(c)** Individual R^2 values estimated from the linear regressions in controls and patients (Mann-Whitney's test was not significant).

Self-report about the FBI

Short questionnaire. Controls reported a significantly stronger illusory sense of self-location (bilocation) than BVP patients (Mann-Whitney tests, Q7; $U=804$, $p=0.005$). There were no significant between-group differences for the other questionnaire items.

When patients were stratified according to the presence of cVEMPs, there was no difference between patients without cVEMPs and their respective matched controls for all questionnaire items. However, there was a significant difference between patients with cVEMPs and their matched controls regarding self-identification (Q1; $U = 122$, $p = 0.03$) and self-location (bilocation) (Q7; $U = 82$, $p = 0.001$).

Long questionnaire. Interestingly, BVP patients reported significantly lower illusion than controls participants for items pertaining to self-identification (Q1; $U = 394$, $p = 0.0177$; Q6; $U = 412$, $p = 0.03$), and to self-location (bilocation) (Q7; $U = 307$, $p = 0.005$) (**Figure 3a**).

When patients were stratified according to the presence of cVEMPs, we found no significant difference between patients without cVEMPs and their matched controls for all questionnaire items. However, there were significant differences between patients with bilateral cVEMPs and their matched controls regarding questions pertaining to self-identification (Q1, $U = 92.5$, $p = 0.003$; Q6, $U = 115.5$, $p = 0.02$) and self-location (bilocation) (Q7, $U = 96$, $p = 0.004$). In each instance, controls exhibited a greater susceptibility to the illusion than patients (**Figure 3b**).

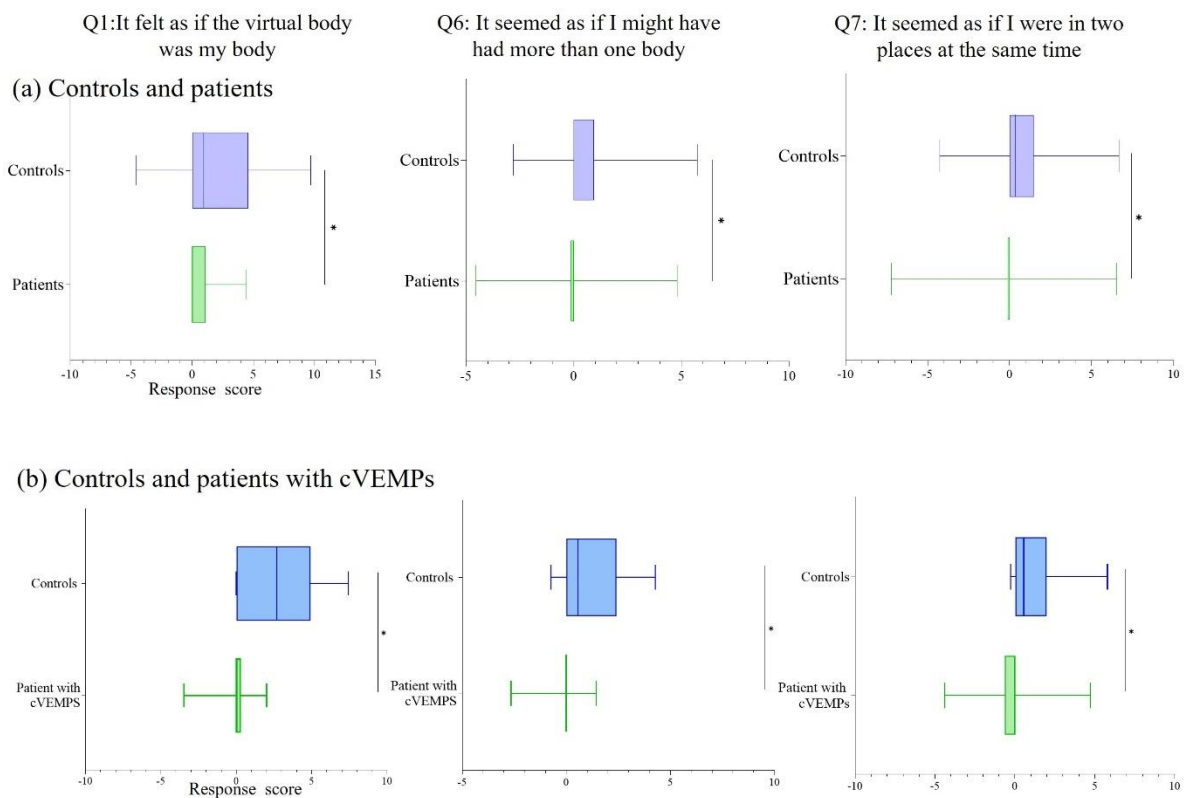


Figure 3. Results for the self-report. Box and whiskers plots illustrate medians and interquartile ranges (10–90) of the difference between synchronous and asynchronous for each questionnaire item.

Then, Kruskal-Wallis tests with three groups (patients, matched controls group 1, younger controls groups 2) revealed a significant effect of the group on the intensity of illusory self-identification (Q1; $\chi^2 = 6.04$, $p = 0.04$), self-location (bilocation) (Q7; $\chi^2 = 12.8$, $p = 0.001$), and presence in VR (Q9; $\chi^2 = 6.6$, $p = 0.03$). Notably, the significant difference for Q1 was exclusively observed between matched controls (group 1) and patients (p adj. = 0.04), consistent with prior findings. Significant differences for

Q7 were evident between patients and controls, as well as between matched controls and younger controls (p adj = 0.02). Moreover, significant differences for Q9 were found only between younger controls and patients (p adj. < 0.03).

Table 3 and **Figure 4** summarize results from two-tailed Wilcoxon tests comparing ratings for the synchronous and asynchronous visuo-tactile stimulation for each group separately. Most significant differences were found for controls matched with patients (group 1).

Questions	Controls matched with patients (group 1)	Patients	Controls group 2
Q1	W=300, z=3.7, p<0.001*	W=72, z=1.8, p=0.06*	W=94, z=2.6, p=0.01*
Q2	W=467, z=3.8 p<0.001*	W=273, z=3.0, p=0.003*	W=168, z=3.6, p<0.001*
Q3	W=362, z=3.1, p=0.002*	W=155, z=2.4, p=0.02*	W=133, z=3.4, p<0.001*
Q4	W=96, z=0.4, p=0.663	W=83, z=1.3, p=0.2	W=81, z=2.5, p=0.014
Q5	W=175, z=3.4, p<0.001*	W=54, z=0.09, p=0.9	W=33, z=0.1, p=0.9
Q6	W=215, z=2.3, p=0.02*	W=49, z=-0.9, p=0.3	W=44, z=0.4, p=0.7
Q7	W=352, z=3.4, p<0.001*	W=47, z=-0.3, p=0.7	W=38, z=0.4, p=0.7
Q8	W=265, z=2.8, p=0.006*	W=115, z=0.8, p=0.4	W=71, z=1.2, p=0.2
Q9	W=366, z=2.7, p=0.006*	W=122, z=1.0 p=0.3	W=142, z=3.1, p=0.002*
Q10	W=6, z=-0.4, p=0.8	W=23, z=0.7, p=0.5	W=16, z=-0.2, p=0.8
Q11	W=111, z=1.6, p=0.108	W=31, z=1.0, p=0.3	W=39, z=2.0, p=0.058

Table 3: Self-reports. Results of Wilcoxon signed-rank test per groups. Significant differences between ratings for synchronous and asynchronous visuo-tactile stimulation is indicated by an asterisk.

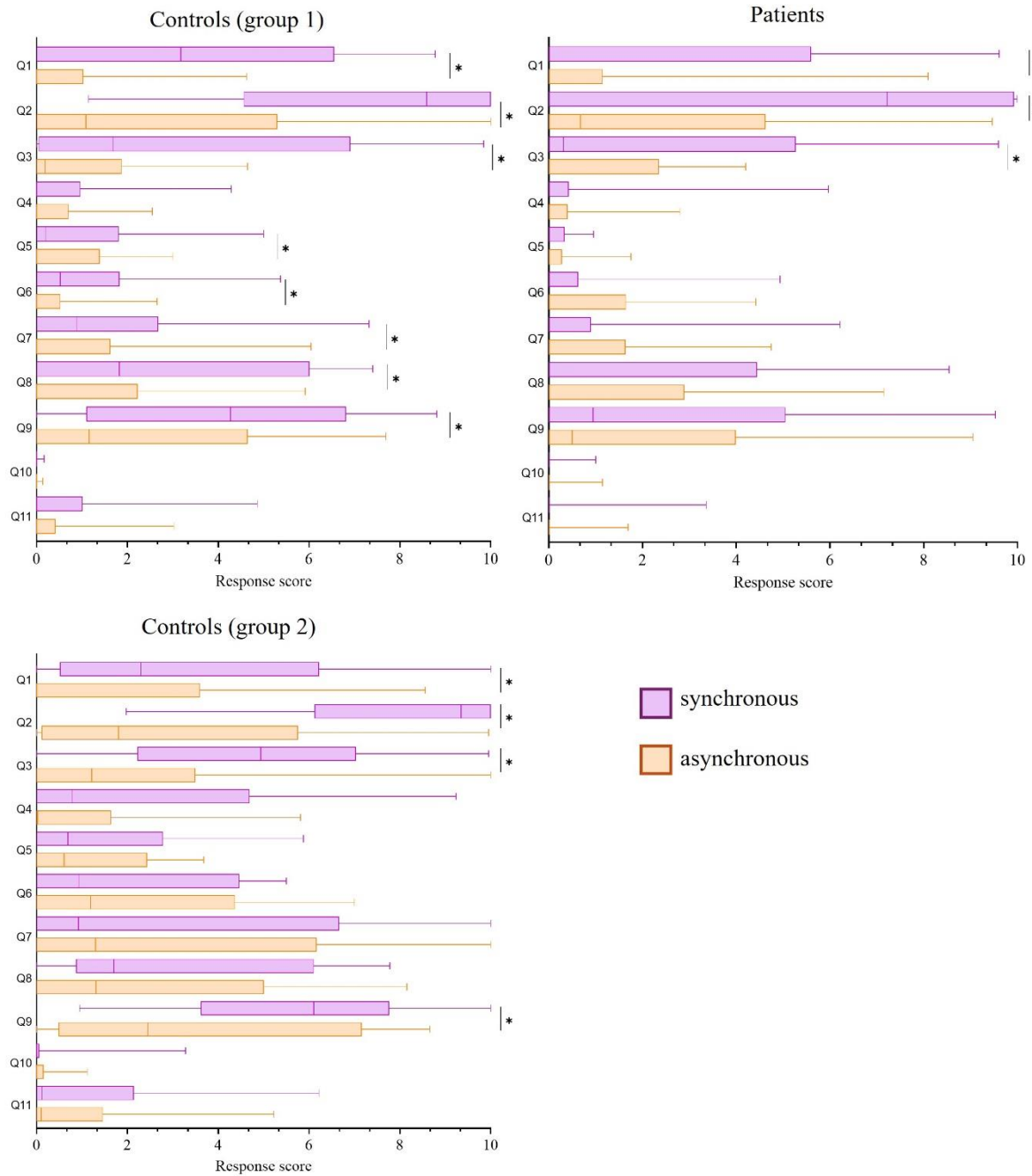


Figure 4: Self-reports. Results of Wilcoxon signed-rank test per groups. Significant differences between ratings for synchronous and asynchronous visuo-tactile stimulation is indicated by an asterisk.

Illusory self-location after the FBI

The two older groups of participants (BVP patients and controls group 1) showed no significant effect of the visuo-tactile stroking on illusory self-location. There was no significant difference in the drift in self-location between patients and controls for both ball velocities, V2 (Mann-Whitney test, $U = 496$, $p = 0.7$), and V4 ($U = 5578$, $p = 0.9$). Similarly, there was no statistically significant difference between synchronous and asynchronous conditions for either velocity in controls (V2: Wilcoxon test, $W = 128$, $p = 0.12$; V4: $W = 19$, $p = 0.4$) and patients (V2: $W = 77$, $p = 0.25$; V4: $W = 171$, $p = 0.06$) (**Figure 5**).

However, as expected, we found in the younger participants (controls group 2) a significant effect of the visuo-tactile stimulation on self-location. Self-location was significantly more directed towards the avatar after synchronous than asynchronous visuo-tactile stroking, for V2 ($W = 120$, $p = 0.007$) as well as for V4 ($W = 134$, $p = 0.026$) (Figure 5).

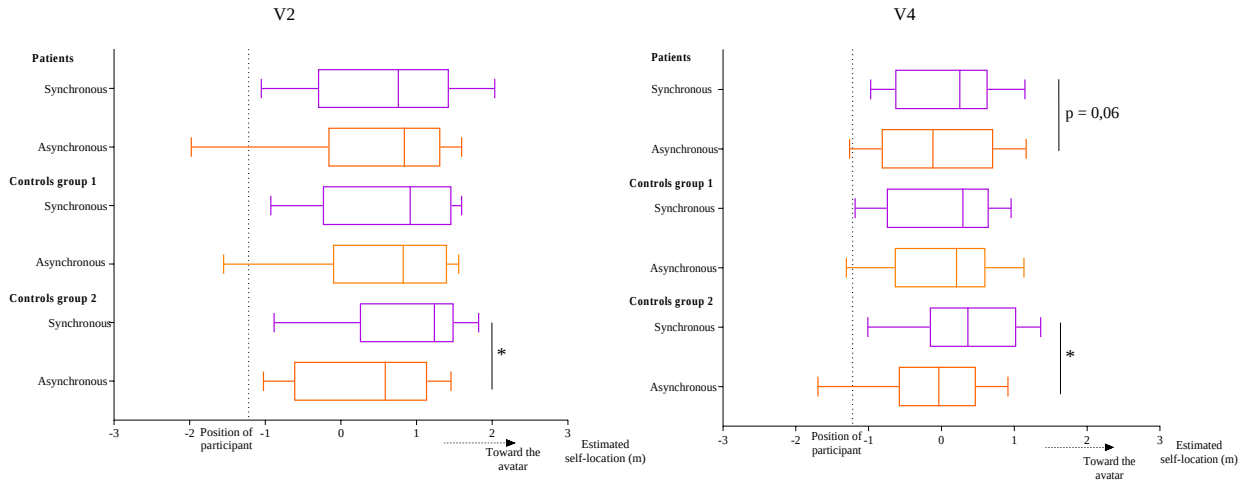


Figure 5: Self-location measured by the mental imagery task. Box and whiskers plots show medians and interquartile ranges (10–90) for the perceived self-location measured with the mental imagery task for both velocities of the ball.

Next, we analyzed the drift in self-location (difference between estimates for the synchronous and asynchronous stimulations). A Kruskal-Wallis's test revealed a significant effect of the group for V2 ($\chi^2 = 7.4$, $p = 0.02$). Post-hoc Dunn tests showed a significant difference between drifts in BVP patients and younger control group (p adj = 0.03), as well as between control group matched with patients and younger control group (p adj = 0.04) for V2. These effects were not found for V4 ($\chi^2 = 2.7$, $p = 0.3$) (Figure 6).

When patients were stratified according to the presence of cVEMPs, self-location did not differ between patients with cVEMPs and their respective age- and sex-matched controls for V2 ($U = 138$, $p = 0.3$) and V4 ($U = 180$, $p = 0.8$). Similarly, there was no difference between patients without cVEMPs and their controls for V2 ($U = 91$, $p = 0.8$) and V4 ($U = 62$, $p = 0.1$).

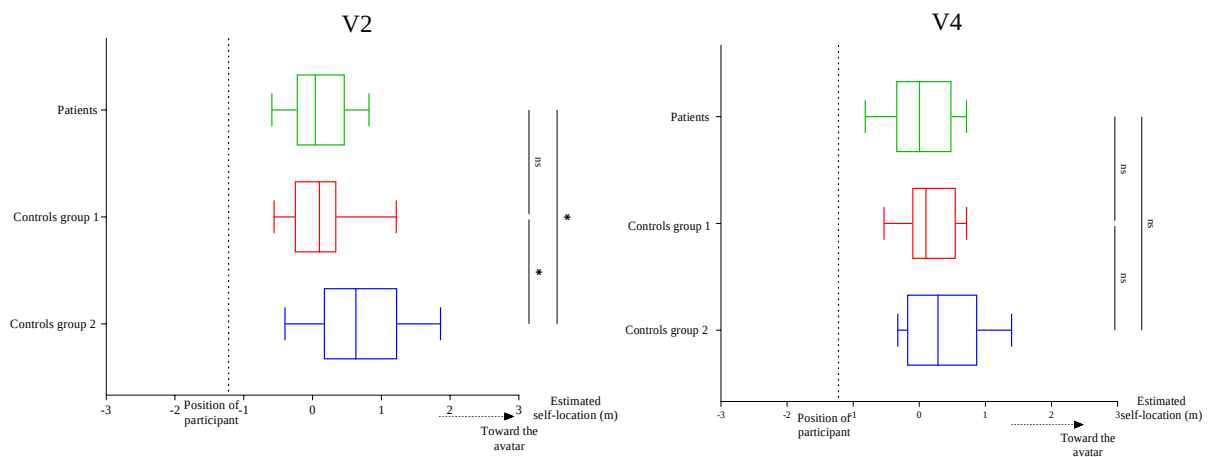


Figure 6. Drift in self-location calculated as the difference between estimates for the synchronous and asynchronous visuo-tactile stimulation. Box and whisker plots illustrate the medians and interquartile ranges (10–90) for the drifts.

Depersonalization-derealization and empathy. No statistical difference was found between BVP patients and controls regarding their depersonalization-derealization scores ($U = 539.5$, $p = 0.6$) and empathy quotients ($U = 521.5$, $p = 0.8$).

Discussion

Mental imagery

We observed similar performance in mental imagery in both groups, excluding the possibility that this ability to engage in mental imagery was responsible for the observed effects on perceived self-location. It was important to control for this factor as previous behavioral studies have shown decreased performance in motor imagery and visuo-spatial imagery in patients with unilateral and bilateral vestibular impairments (Borel et al., 2008; Demougeot et al., 2011; Deroualle et al., 2019; Péruch et al., 2011). Our well-matched groups in terms of age, sex, and level of education exclude confounding effects reported in the literature of sex and age on mental imagery abilities (Butler et al., 2006; Dror and Kosslyn, 1994; Hugdahl et al., 2006).

Self-reports on the illusion of self-identification and localization in the full-body illusion

Here, we found that self-identification with the avatar, the feeling of having two bodies, and the sense of being in two places at once (bilocation) are significantly weaker in BVP patients compared to control participants. Thus, BVP patients appear less prone to report the FBI than healthy volunteers. These differences cannot be explained by age, sex, cultural level, self-reported anxiety, depression, empathy, and depersonalization-derealization state, which do not differ significantly between the two groups. At first glance, this result may seem counterintuitive because BVP patients have increased visual dependence (for postural control and perception of visual vertical) (Bronstein et al., 1996; Guerraz et al., 2001; Lopez et al., 2007) and because the FBI, like the rubber hand illusion, has traditionally been interpreted in terms of visual capture (Botvinick and Cohen, 1998; Pavani et al., 2000; Pfeiffer et al., 2013). Although visual dependence was not measured in participants in our study, we might have expected stronger visual capture in BVP patients. However, this is not the case, and the reduced self-identification with the avatar can be interpreted in several alternative ways. First, it is possible that patients, seated on a stool during visuo-tactile stimulation received on their back, instead favored the use of an egocentric spatial reference frame for self-location coding rather than an allocentric one. If BVP patients are described as more visually dependent, there is also abundant evidence that they use somesthetic information for spatial orientation (Cutfield et al., 2014; Strupp et al., 1998). Second, our team has identified an increase in egocentric spatial navigation strategies and a decrease in allocentric navigation strategies in patients with BVP (Gammeri et al., 2022). Third, in BVP patients equipped with an eye tracker system during 3D spatial navigation tasks in free environment, it has been reported that these patients had different visual exploration strategies and extracted fewer visual cues than healthy volunteers (Schöberl et al., 2021). Overall, all these results seem consistent with a stronger reliance of spatial orientation and self-location coding on egocentric references in BVP and could account for the weaker FBI reported here.

Illusory self-location during the FBI

Our results in the two groups of older participants – BVP patients and their respective controls – do not confirm previously reported effects in younger subjects, where synchronous visuo-tactile stimulation tends to induce an illusory self-relocation toward the avatar participants self-identify with (Ionta et al., 2014; Silvio Ionta et al., 2011; Lenggenhager et al., 2007; Nakul et al., 2020b; Pfeiffer et al., 2013). We propose that these negative results are mainly due to age effects. Indeed, in a group of healthy volunteers tested with identical experimental procedures (control group 2), we find a significantly larger effect of coherent visuo-tactile stimulation on illusory self-location. It is noteworthy that most studies on the FBI and the rubber hand illusion have been conducted in young and healthy volunteers. However, there is experimental evidence that older individuals are less likely to report the rubber hand illusion than younger individuals (Campos et al., 2021; Ferracci and Brancucci, 2019; Marotta et al., 2018) consistent

with the results of our study. Moreover, in non-neurotypical individuals, such as patients with schizophrenia, it has also been reported a lack of significant effect of visuo-tactile synchrony on the illusion of self-relocation (i.e., drift measures) (Shaqiri et al., 2018). Shaqiri and colleagues (2018) indicate that the wide range of ages of participants in clinical groups could account for the variability in self-location measures, and this conclusion may apply to our sample of participants. The intensity of illusions based on visuo-tactile coherence changes with age in neurotypical children and adolescents (Cowie et al., 2018; Raoul et al., in prep). Finally, it has been reported that subjective reports about self-identification with the avatar, body ownership and self-location measures are different facets of self-body awareness and may be modulated differently from each other (Lopez et al., 2010; Rohde et al., 2011; Serino et al., 2013).

Role of otolithic vestibular information

Stratification of patients based on the presence of cVEMP did not show that otolithic information played a predominant role in illusory self-location as measured with the FBI. We only note that patients with cVEMPs have weaker scores self-identification with the avatar and bilocation than their respective controls, which is not the case for patients without cVEMPs. The fact that patients without cVEMPs show an illusion intensity that does not differ from their own controls seems at odds with recent clinical data indicating that patients with peripheral vestibular pathologies preserving saccular otolithic functions (tested by cVEMPs) do not differ from healthy volunteers in terms of depersonalization-derealization scores (Elyoseph et al., 2023b). However, one should be cautious when interpreting our data due to small sample sizes once the group of BVP patients was divided into two subgroups. Additional studies will be necessary in larger groups of patients, through multicenter studies, and probably in younger age groups, to more finely analyze the impact of otolithic functions on the bodily self.

Conclusions on the impact of BVP on the bodily self

Some BVP patients suffer from cognitive impairments, spatial disorientation, and anxiety related to the risk of falling due to deficient vestibulospinal reflexes (Dobbels et al., 2019; Lucieer et al., 2020; Strupp et al., 2017). However, it has been reported that these patients do not exhibit an anxiety-depressive syndrome (Brandt and Dieterich, 2020), nor as we have seen in our study, higher levels of depersonalization-derealization symptoms (article in preparation from our group; Gobinet et al.), than healthy volunteers. These results contrast with those reported in individuals with acute or chronic unilateral impairments, who are more likely to report an anxiety-depressive syndrome as well as depersonalization-derealization symptoms (Decker et al., 2019; Jauregui-Renaud, 2015; Lahmann et al., 2015; Lopez and Elzière, 2018). Unlike patients with fluctuating peripheral vestibular functions, sending erroneous messages to the brain about body orientation and movements in space, patients with vestibular areflexia are not subject to repeated sensory conflicts and perceptual incoherence. It has been proposed that exposure to perceptual incoherence could account for changes in the bodily self in peripheral vestibular impairments (Lopez, 2013; Lopez et al., 2018; Lopez and Elzière, 2018). These explorations should be continued by studying the FBI in patients with acute or chronic vestibular impairments, such as patients with Menière's disease or recurrent benign paroxysmal positional vertigo, where the sense of bodily self should be more altered than in patients with a bilateral vestibular deafferentation.

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Discussion et perspectives

L'ensemble de ce travail de thèse apporte de nouveaux éclairages sur le lien entre les mécanismes cérébraux et sensoriels qui sous-tendent le soi corporel. Nos résultats étant déjà discutés dans leurs articles respectifs, cette discussion mettra en perspectives certains résultats saillants de notre travail.

I. Le réseau du soi corporel révélé par des approches causales

Dans notre article d'opinion (Dary et Lopez 2023), nous pointions un ensemble de défis à relever dans la recherche sur les bases neurales du soi corporel. Parmi les points cités, un explicitait le manque de preuve causale dans l'étude des bases neurales du soi corporel. Nos études 2 et 3 ont permis de répondre à ce manque.

I.1. Des régions cérébrales causalement impliquées dans le réseau du soi corporel

Les études 2 et 3 apportent des résultats majeurs et complémentaires sur les bases neurales du soi corporel. La [Figure 20](#) met en perspective ces résultats. De cette comparaison, six régions clés émergent dont le précuneus, l'insula, l'hippocampe, l'aire motrice supplémentaire, le cortex cingulaire et l'opercule pariétal. L'implication de chaque région dans le réseau du soi corporel a été discutée dans les articles. Nous souhaitons cependant revenir sur les différences qui émergent entre les deux études.

Nous observons une première différence concernant la stimulation du lobule pariétale inférieur (gyrus angulaire et supramarginal). Notre revue systématique souligne qu'un nombre important de modifications du soi corporel ont été rapportées à la suite de stimulations dans cette région. La plupart de ces stimulations induisaient des modifications dans la localisation du soi, notamment des expériences de sortie du corps, des modifications de l'image du corps, ou encore de l'agentivité (Salanova et al. 1995; Blanke et al. 2000, 2002; Desmurget et al. 2009; Balestrini et al. 2015). Cette région est considérée comme une région clé dans le réseau du soi corporel (Tsakiris et al. 2008; Blanke 2012; Ionta et al. 2014). Cependant, dans notre étude rétrospective, nous ne rapportons que deux stimulations dans le lobule pariétale ayant induit une modification du soi corporel. Ce résultat peut s'expliquer par le faible nombre de stimulations appliquées dans cette région. En effet, chez les 50 patients de l'étude, seulement 3% de toutes les stimulations appliquées se situaient dans le lobule pariétal inférieur.

L'étude 2 soulignait une forte implication de gyrus cingulaire moyen (MCC) dans les modifications de la localisation du soi (Caruana et al. 2018; Popa et al. 2019; Oane et

al. 2020). Dans notre analyse rétrospective, une seule stimulation dans cette région évoquait des modifications du soi corporel. Une telle différence pourrait s'expliquer par le nombre de stimulations appliquées dans cette région. En effet, la stimulation de du MCC représentait seulement 2 % de toutes les stimulations appliquées chez les 50 patients de l'étude.

Un résultat intéressant révélé par notre analyse rétrospective était l'implication du cortex cingulaire antérieur dans le réseau du soi corporel. Des études précédentes ont mis en évidence que des stimulations électriques dans cette région entraînaient le plus souvent des réponses émotionnelles (rires, sourires), intéroceptives, et neurovégétatives (vide dans l'estomac, sensation de brûlures abdominales, etc.) (Caruana et al. 2018; pour une revue, voir Pelliccia et al. 2023). Les résultats de l'étude 3 montrent que les stimulations dans cette région ont induit des modifications du soi corporel liées notamment à la dépersonnalisation. Les patients rapportaient « ne rien ressentir » ou « se sentir vide », traduisant une forme apathie. Il serait intéressant dans de futures études d'examiner avec plus de précision le rôle du cortex cingulaire antérieur dans le soi corporel et notamment sa connectivité fonctionnelle avec le réseau limbique (Stevens et al. 2011). Une telle relation mettrait en évidence le rôle du système émotionnel dans le soi corporel (Damasio 1999, 2003).

A) Nombre de réponses évoquant une modification du soi corporel de l'étude 2



B) Nombre de réponses évoquant une modification du soi corporel de l'étude 3



Figure 20 : Localisation des stimulations électriques intracérébrales modifiant le soi corporel. (a) Localisation des stimulations dans notre revue systématique de la littérature (étude 2). (b) Localisation des stimulations dans notre analyse rétrospective (étude 3).

Un point important à noter est que dans nos deux études, certaines expériences fondamentales pour le soi corporel n'étaient que rarement évoquées par une stimulation. En effet, l'étude 2 présente un seul cas de modification du sentiment d'appartenance du corps, défini comme l'incapacité à reconnaître une partie de son corps comme sienne et seulement quatre cas de modification de la perspective en première personne. Une explication serait que ces types d'illusion soient beaucoup plus complexes que, par exemple, de simples sensations de flottement. Elles pourraient en effet impliquer un réseau plus vaste témoignant de l'intégration de plusieurs sens. Par exemple, de récentes méta-analyses conduites sur des résultats d'études de neuroimagerie ont mis en évidence l'implication du cortex prémoteur ventral, du sillon intrapariétal ainsi que l'insula dans le sentiment d'appartenance d'un membre (Grivaz et al. 2017; Salvato et al. 2020; Nilsson et Kalckert 2021). D'autres études en IRMf ont également rapporté des activations au niveau le cortex cingulaire postérieur et de l'aire corporelle extrastriée lors d'illusion multisensorielle modifiant le sentiment d'appartenance (Limanowski et al. 2014; Guterstam et al. 2015b). Enfin, des études de lésion et de neuroimagerie ont également suggéré l'implication de régions sous-corticales telles que l'amygdale, le cervelet, l'hippocampe, les noyaux gris centraux et le thalamus (Ehrsson et al. 2004; Gandola et al. 2012; Guterstam et al. 2015a; Matsumoto et al. 2020; Chancel et al. 2022b; Crucianelli et al. 2024). Ensemble, ces résultats suggèrent l'implication d'un vaste réseau cortical et sous-cortical impliqué dans le traitement d'informations visuelles, proprioceptives, tactiles et intéroceptives, ce qui pourrait expliquer la faible occurrence des modifications du sentiment d'appartenance lors de stimulations électriques intracérébrales. Les régions décrites précédemment sont peu stimulées à l'exception de l'hippocampe et de l'amygdale, ce qui pourrait également expliquer cette observation. Nous avons trouvé seulement deux études qui étudient le sentiment d'appartenance en combinant une illusion multisensorielle avec des enregistrements intracrâniennes (Collins et al. 2017; Guterstam et al. 2019).

I.2. Quelle force de causalité ?

Nos études 2 et 3 s'inscrivent dans une dynamique de recherche qui tend à décrire l'implication causale de régions cérébrales dans des mécanismes sensori-moteurs ou cognitifs en utilisant l'analyse des lésions cérébrales ou de stimulations électriques intracérébrales. Nous avons utilisé les stimulations électriques intracérébrales pour mettre en évidence le réseau du soi corporel. D'après le continuum décrit dans le chapitre 2 de l'introduction de ce travail (partie II.2, p.29), cette technique possède un degré de causalité élevé. La première preuve de cette causalité est soutenue par le lien établi entre une réponse observée et une région stimulée.

Cependant, notre méthodologie pourrait être améliorée afin d'augmenter l'inférence causale de notre étude. Tout d'abord, pour montrer la spécificité des stimulations dans certaines régions du réseau, il faudrait comparer nos résultats de

connectivité fonctionnelle avec des stimulations « contrôles », c'est-à-dire des stimulations dans la même région qui n'induiraient pas de modification du soi corporel.

Pour accroître la force de notre inférence causale, nous pourrions également nous intéresser à la relation dose/effet. Dans le cadre des stimulations électriques intracérébrales, il est possible de manipuler l'intensité des stimulations – la dose – et d'observer la complexité de l'illusion – l'effet. C'est ce que Blanke et collaborateurs (2002) ont mis en évidence. Ils ont montré que des stimulations à 3 mA de la jonction temporo-pariétale entraînaient des modifications de l'image du corps et que des stimulations de plus haute intensité (3,5 mA) engendraient une illusion de sortie du corps. Étant donné la nature rétrospective de notre étude, il est difficile de mettre en place un tel paradigme. En effet, seulement 4 patients ont reçu des stimulations avec des intensités de plus en plus élevées, modulant leur réponse. De plus, les stimulations ont été réalisées dans un but clinique. Nous noterons seulement qu'il serait intéressant d'étudier une telle relation entre intensité et complexité de l'illusion dans le soi corporel. La mise en évidence du seuil d'activation traduirait cette *zone grise* intrinsèque au soi corporel, c'est-à-dire le passage du niveau préréflexif ou niveau réflexif.

Enfin, il serait également intéressant d'approfondir l'inférence causale de notre étude en développant des analyses de connectivité effective qui mettraient ainsi en évidence la directionnalité des connections entre les régions, ce que nous n'avons pas étudié.

I.3. Le réseau fonctionnel du soi corporel

Il est bien renseigné que les stimulations électriques entraînent une inhibition ou une excitation d'une population de neurones localement (à l'endroit de la stimulation) mais également à distance (Borchers et al. 2011; Mohan et al. 2020). Le point de stimulation peut ainsi être considéré comme une porte d'entrée du réseau (Mandonnet et al. 2010). Notre étude 3 a mis en évidence cet aspect. Nos analyses de connectivité fonctionnelle, quel que soit le type d'expérience corporelle considéré, ont révélé une diminution de la connectivité du lobule pariétal inférieur. Or, comme nous l'avons souligné dans la partie précédente, seulement deux stimulations dans le lobule pariétal inférieur entraînaient des modifications du soi corporel. Ce résultat traduit bien l'idée selon laquelle l'effet de la stimulation électrique se répercute sur un réseau plus large et pas uniquement au niveau du site stimulé (Borchers et al. 2011; Parvizi et Kastner 2018). L'approche par réseaux apparaît donc fondamentale lors de cartographie cérébrale par stimulations électriques intracérébrales (Mandonnet et al. 2010).

I.3.A. Un réseau multifonctionnel ...

Nos analyses de connectivité fonctionnelle de l'étude 3 et les résultats de localisation des stimulations des études 2 et 3 indiquent que le réseau du soi corporel est

un réseau multimodal comprenant le réseau fonctionnel limbique, le réseau de saillance, le réseau fronto-pariétal et le réseau du mode par défaut. Cette idée est soutenue par une littérature, encore discrète, qui étudie l'interconnexion de ces différents réseaux fonctionnels dans le soi corporel et plus généralement dans la conscience de soi (Fox et al. 2020; Raccach et al. 2021; Ribeiro da Costa et al. 2022; Asakage et Nakano 2023; Lyu et al. 2023). Ainsi, une perspective intéressante pour notre étude serait de réanalyser les données de connectivité fonctionnelle en regroupant nos régions par réseaux fonctionnels (Yeo et al. 2011; Fox et al. 2020). Une telle analyse révélerait pour la première fois la contribution des différents réseaux fonctionnels dans le soi corporel.

Il serait également intéressant de comparer nos résultats de connectivité fonctionnelle de signaux intracrâniens enregistrés pendant que les patients rapportaient des sensations de modification du soi corporel avec des résultats de connectivité fonctionnelle en IRMf. Cette approche complémentaire permettrait de fournir, pour la première fois, une analyse détaillée du réseau fonctionnel du soi corporel. Elle augmenterait notre degré d'inférence causale en proposant une autre technique pour affirmer ou infirmer nos résultats.

1.3.B. ... qui traduit des recouvrements fonctionnels avec le soi cognitif ?

Cette relation étroite entre les réseaux fonctionnels soulève l'idée d'un possible recouvrement du réseau du soi corporel avec celui du soi cognitif (autobiographique, narratif) (Damasio 1999; Gallagher 2000; Schaller et al. 2021). Bien que notre article d'opinion (étude 1) aborde déjà cette question (Dary et Lopez 2023), il nous semblait important de revenir sur quelques points au vue de nos résultats. Pour rappel, le soi cognitif implique des processus cognitifs tels que la reconnaissance de soi (apparence, voix), la mémoire autobiographique, le langage ou la capacité mentale de voyager dans le temps (Schaller et al. 2021). Premièrement, nos résultats de connectivité fonctionnelle supportent cette idée. Nous avons montré l'implication de régions temporelles telles que le sillon temporal supérieur, le gyrus temporal latéral inférieur et moyen, le lobule pariétal inférieur ainsi que l'hippocampe et l'amygdale. Ces régions font également partie du réseau fonctionnel de la conscience auto-noétique (Markowitsch et Staniloiu 2011; Bartolomei et al. 2017a). Deuxièmement, des études récentes se sont intéressées à ces possibles chevauchements en étudiant le lien entre la conscience auto-noétique, définie comme l'expérience subjective de soi dans le temps, et le soi corporel (Bréchet et al. 2018; Gauthier et al. 2020; Bréchet 2022). Ces études ont mis en évidence un recouvrement des réseaux au niveau du lobule pariétal inférieur, plus précisément dans le gyrus angulaire (Bréchet et al. 2018), et du lobe temporal mésial (Gauthier et al. 2020), régions multisensorielles impliquées dans le réseau du soi corporel, comme nous l'avons montré dans les études 2 et 3. Troisièmement, bien que nous distinguions conceptuellement et phénoménologiquement ces deux aspects du soi, ontologiquement ils sont indissociables (Zahavi 2005; Legrand 2007; Gallagher 2013). En d'autres termes, la conscience de soi émergerait de leurs interactions réciproques (Legrand 2007; Gallagher 2013).

Ensemble, ces résultats soulignent le chevauchement des réseaux neuronaux entre le soi corporel et le soi cognitif et plus généralement, ils mettent en évidence l'interconnexion entre le soi-sujet (le soi est le sujet de l'expérience consciente) et le soi-objet (le soi est l'objet de l'expérience consciente). Très peu d'études se sont intéressées à ce chevauchement d'un point de vue empirique (Farmer et Tsakiris 2012). Pourtant, cette investigation aurait des implications cliniques et philosophiques importantes. En effet, dans certaines maladies neurovégétatives, comme la maladie d'Alzheimer, le soi cognitif est atteint ; les patients perdent peu à peu leur mémoire autobiographique (Martinelli et al. 2013). Certaines expériences du soi corporel peuvent également être perturbées, notamment le sentiment d'agentivité ou d'appartenance du corps (Arzy et Schacter 2019). Étudier la relation entre les deux formes de soi permettrait ainsi de comprendre dans quelle mesure la dégradation d'une forme de soi peut influencer l'autre. D'un point de vue philosophique, cet approfondissement apporterait des éclaircissements sur les fondements de la conscience de soi. Il serait dès lors intéressant dans de prochaines études de révéler cette relation par exemple, en analysant la connectivité fonctionnelle entre ces deux réseaux.

I.4. Limites de notre approche

Bien que l'approche par stimulations électriques intracérébrales soit considérée comme le « gold-standard » dans les analyses de causalité des bases neurales (Mandonnet et al. 2010), cette approche comporte certaines limites. Une des limites repose sur l'implantation inégale des électrodes dans les différents cortex. Étant donné que le modèle clinique dicte le type d'implantation et que la grande majorité des épilepsies focales proviennent des lobes temporaux et frontaux, les régions occipitales ou pariétales sont beaucoup moins échantillonnées (Parvizi et Kastner 2018). Ainsi, comparativement à l'IRM fonctionnelle, les méthodes de stimulations électriques ne peuvent pas couvrir l'ensemble du cerveau. Une étude a d'ailleurs montré que pour échantillonner l'ensemble du volume cérébral avec une résolution spatiale de 3,5 mm, qui correspond à l'espace entre contacts le long d'une électrode, il faudrait environ 10 000 sites d'enregistrement (Halgren et al. 1998; Lachaux et al. 2003). Or, chez les patients implantés, le nombre de sites varie entre 80 et 120.

Une deuxième limite repose sur le fait que les stimulations électriques sont appliquées sur des cerveaux de patients présentant un fonctionnement anormal du tissu cérébral. Ceci pourrait poser un problème quant à la généralisation des résultats à des individus sains. Il est en effet légitime de se demander dans quelle mesure les cerveaux des patients épileptiques fournissent un modèle approprié pour étudier les mécanismes neuronaux qui sous-tendent la cognition et le comportement chez des personnes saines (Parvizi et Kastner 2018). Pour que les résultats de ce modèle soient généralisables, trois conditions devraient être respectées : 1) l'analyse des données devrait être effectuée en dehors des tissus épileptiques ou lésionnels 2) l'étude devrait exclure toute activité électrophysiologique pathologique telle que la présence de post-décharges 3) les effets observés devraient être similaires à ceux rapportés dans des études non-invasives sur des

sujets sains, ou devraient être cohérents avec ceux observés chez d'autres patients avec une région épileptogène différente. Notre avons porté une attention particulière à ces différents points dans notre étude 3. En effet, nous avons exclu de notre analyse toutes les stimulations qui étaient dans la zone épileptogène ou dans une lésion identifiée par IRM, favorisant ainsi la généralisation de nos analyses de connectivité fonctionnelle à une population saine.

La dernière limite discutée se rapporte davantage à nos études qu'à la technique même. La plupart des évaluations effectuées au cours d'une séance de stimulation sont orientées vers l'évaluation du langage, de la mémoire ou des capacités visuo-spatiales du patient. Les modifications du soi corporel seraient donc possiblement sous-évaluées, notamment si les patients n'expriment pas spontanément leurs sensations. La mise en place de questionnaires ou d'entretiens subjectifs pendant une séance de stimulation pourrait être un avantage pour que les patients décrivent avec précision une éventuelle modification du soi corporel. Des études prospectives permettraient donc de pallier cette limite. Cependant, aux vues de la rareté des modifications du soi corporel, une telle étude s'étalerait sur plusieurs années.

II. Système vestibulaire et soi corporel

Nos études 2, 3, et 4 mettent en perspective l'influence réciproque entre le système vestibulaire et le soi corporel. Les études 2 et 3 illustrent un chevauchement du réseau cortical vestibulaire et celui du soi corporel. L'étude 4 interroge sur une possible implication du système vestibulaire dans le soi corporel.

II.1. Des réseaux corticaux qui se chevauchent

Nos études 2 et 3 mettaient en évidence que des stimulations dans le cortex insulaire, le cortex cingulaire moyen et l'hippocampe entraînaient des modifications de la localisation du soi caractérisée par des illusions de mouvement du corps entier et des sensations de tomber ou de flotter dans l'aire. Ces sensations étaient similaires à celles rapportées par des patients avec des lésions au niveau des récepteurs otolithiques ou des régions centrales du réseau vestibulaire (Blanke et al. 2002; Blanke et Arzy 2005; Murofushi et al. 2013; Park et al. 2019). Des travaux chez l'Homme et l'animal ont révélé que ces régions traitaient des informations vestibulaires (Dieterich et al. 2003; Horii et al. 2004; Lopez et al. 2012a; Smith et al. 2012; Hitier et al. 2021; Smith 2022). Il serait ainsi intéressant de comparer causalement le chevauchement de ces deux réseaux.

II.1.A. Révéler causalement le cortex vestibulaire et sa connectivité fonctionnelle

Il s'avère que la localisation anatomique des aires corticales impliquées dans le traitement des informations vestibulaires chez l'Homme est encore en développement, notamment du fait des contraintes méthodologiques liées à la stimulation du système vestibulaire dans des scanners d'IRM. Utiliser les stimulations électriques intracérébrales permettrait d'identifier causalement le réseau cérébral vestibulaire.

Nous avons répertorié dans notre base de données (cf : Avant-propos p.61), un total de 82 réponses vestibulaires à la suite d'une stimulation électrique chez 53 patients. Une étude ultérieure consistera à mettre en évidence causalement les bases neurales du système vestibulaire, et ce, en nous appuyant sur la méthode décrite dans l'étude 3 et résumée par la [Figure 19](#).

II.1.B. Révéler la connectivité fonctionnelle du cortex vestibulaire

Un second objectif de cette prochaine étude sera de révéler la connectivité du réseau vestibulaire pendant que les patients rapportent des sensations vestibulaires. Une rapide analyse de la littérature sur la connectivité fonctionnelle en IRMf à l'état de repos a révélé une diminution de la connectivité dans l'insula postérieure et dans l'opercule pariétal chez des patients atteints d'une vestibulopathie bilatérale (Göttlich et al. 2014). Une augmentation de la connectivité fonctionnelle entre l'opercule pariétal et le lobule pariétal inférieur, le cortex cingulaire antérieur et le cortex somatosensoriel primaire a également été rapportée pendant des stimulations vestibulaires caloriques chez des volontaires sains (Ibitoye et al. 2022). Ces régions ont été mises en évidence dans nos études 2 et 3. Nous pourrions ainsi analyser le recouvrement fonctionnel entre le réseau vestibulaire et celui du soi corporel.

II.2. Contribution vestibulaire au soi corporel

Les résultats de notre étude 4 ne montrent pas de différence significative dans la tâche de localisation du soi entre les patients avec vestibulopathie bilatérale et les contrôles. Ces résultats traduisent l'idée que les patients ne sont pas sensibles à l'illusion du corps entier, tout comme leurs contrôles appariés en âge et en sexe. Ils sont conformes avec de résultats trouvés par notre équipe chez des patients similaires. Deux études ont en effet montré que les résultats de ces patients testés dans des tâches de mesure de localisation de soi sur des silhouettes humaines, de sensibilité intéroceptive et émotionnelle, d'ancrage auto-rapporté du soi sur le corps et de prise de perspective spontanée, n'ont pas différé des groupes contrôles (Deroualle et al. 2017; Nakul et al.

2020a). Nous ne montrons pas de score de dépersonnalisation-déréalisation plus élevé chez les patients que chez les contrôles. Une des hypothèses retenues pour expliquer ces résultats négatifs repose sur un modèle neuroscientifique qui stipule que des modifications du soi corporel émergeraient de conflits multisensoriels (Lopez 2013). Or, la plupart des patients, lors de l'expérience, ne présentaient pas de vertiges et donc auraient compensé leur perte vestibulaire, ce qui n'induirait potentiellement pas d'incohérence sensorielle. À l'inverse, des patients avec des atteintes unilatérales chroniques (par exemple, maladie de Menière) pourraient montrer une plus grande susceptibilité à l'illusion. Cette idée est d'ailleurs soutenue par des études qui montrent que des patients avec des atteintes vestibulaires aiguës unilatérales présentent des modifications du soi corporel (Saj et al. 2013; Allum et al. 2017; Lopez et al. 2018; Lopez et Elzière 2018) ou par des travaux utilisant des stimulations artificielles vestibulaires chez des sujets sains (Lopez et al. 2010, 2012b, 2018). Il serait ainsi intéressant de poursuivre cette étude chez des patients avec atteinte vestibulaire unilatérale, qui rapportent encore des sensations de vertige, et qui n'auraient pas compensé leur perte vestibulaire. Nous nous attendons à ce que l'illusion de relocalisation du soi et d'identification à l'avatar dans la full-body illusion soit plus forte chez ces patients.

II.3. Différences interindividuelles et soi corporel

Notre article d'opinion montrait qu'un des défis pour la recherche sur le soi corporel était de comprendre quels pouvaient être les facteurs explicatifs de l'occurrence de l'illusion du corps ou de la main en caoutchouc. Comprendre les différences inter-individuelles qui sous-tendent ce type d'expérience, permettrait d'appréhender la malléabilité du soi corporel.

II.3.A. *Malléabilité du soi corporel selon l'âge*

Nos résultats ne confirment pas les effets classiquement rapportés de la congruence de la stimulation visuo-tactile sur la localisation illusoire du soi (Lenggenhager et al. 2007; Ionta et al. 2011a; Nakul et al. 2020b). Ces résultats peuvent s'expliquer par l'âge plus élevé de notre cohorte relativement aux études antérieures ayant utilisé le même paradigme (Nakul et al. 2020b). Un premier facteur explicatif serait que l'avatar présenté, d'apparence relativement jeune, ne permettrait pas aux sujets de s'identifier. Un second facteur explicatif est proposé par une littérature qui s'interroge sur l'effet de l'âge dans l'induction d'une illusion multisensorielle. La plupart des études sur les illusions de type full-body illusion ont porté chez des jeunes adultes entre 20 et 30 ans (Marotta et al. 2018). Des études avec l'illusion de la main en caoutchouc montrent que la force de l'illusion diminue à partir de 50 ans. Kallai et collaborateurs (2017) comparent deux groupes de 50 participants, un de 20 à 40 ans, et un autre de 56 à 72 ans. Les auteurs montrent que les sujets du deuxième groupe ont une illusion beaucoup moins forte que le

groupe plus jeune. Ces résultats ont été corroborés par d'autres études (Serino et al. 2018). Ensemble, ces études tendent à souligner une diminution de la malléabilité du soi corporel avec le vieillissement. Cela pourrait s'expliquer par la dégradation des systèmes sensoriels au cours du vieillissement. Cette hypothèse est d'ailleurs étayée par les travaux sur le temps de réaction à des stimuli visuels ou auditifs chez des personnes jeunes et plus âgées (Diederich et al. 2008). De manière générale, le temps de réaction des personnes âgées (65-75 ans) était plus lent que celui des jeunes (20-22 ans). Ce phénomène s'expliquerait notamment par un ralentissement du traitement sensoriel chez les personnes âgées. Une fenêtre temporelle plus longue au cours de laquelle l'intégration d'un stimulus a lieu ne peut que partiellement compenser ce ralentissement et donc entraîne une réduction du stimulus ressenti (Diederich et al. 2008; Chancel et al. 2018). Ces résultats suggèrent que l'illusion semble diminuer en terme de force et en terme de latence d'apparition en fonction de l'âge des participants (Serino et al. 2018). Ces travaux expliqueraient ainsi les différences dans la force de l'illusion entre nos deux groupes contrôles de notre étude 4.

D'autres résultats semblent plus nuancés. L'étude de Marotta *et al.* (2018) montre que le sentiment d'appartenance lors de l'illusion de la main en caoutchouc suit une forme en U : une illusion plus forte a été observée chez les jeunes adultes (20-25 ans) et chez les personnes plus âgées (60-72), comparativement aux adultes d'âge moyen (44-55 ans). Les auteurs expliquent ce résultat par une malléabilité réduite de la représentation du corps chez le groupe adulte d'âge moyen. Les jeunes adultes et les personnes âgées sont dans une période de leur vie où ils sont confrontés à des changements d'apparence physique plus importants qu'à l'âge moyen, ce qui nécessiterait une plus grande malléabilité de leur représentation corporelle (Marotta et al. 2018). Ces résultats sont soutenus par des travaux qui ont utilisé une illusion dite « d'enfacement » (Tajadura-Jiménez et al. 2012). Dans cette illusion, le participant regarde un écran dans lequel il voit un visage inconnu de face et une stimulation tactile est appliquée sur son visage et est reproduite soit de façon synchrone ou asynchrone sur le visage observé. Les auteurs montrent que des sujets plus jeunes (entre 17 et 25 ans) ont une illusion plus forte que les sujets d'âge moyen (25-38 ans). Enfin, certains résultats vont à l'encontre des travaux préalablement décrits et suggèrent qu'il n'y a pas d'effet de l'âge (Palomo et al. 2018).

La littérature sur l'influence de l'âge dans les illusions semble donc controversée. D'une part, les différentes études ne justifient pas de façon claire le choix des tranches d'âge utilisées pour caractériser les jeunes, l'âge moyen ou les personnes âgées. D'autre part, la majorité des études se sont penchées sur la question en utilisant le paradigme de la main en caoutchouc, seules quelques études ont étudié cette question dans une illusion du corps entier (Serino et al. 2018; Weijs et al. 2021). Il serait ainsi intéressant de tester notre illusion du corps entier sur une grande cohorte de participants pour déterminer l'effet de l'âge sur la sensibilité aux illusions et donc si le soi corporel varie selon l'âge.

II.3.B. Empathie, dépersonnalisation, anxiété et dépression dans le soi corporel

Certains traits de personnalité pourraient également influencer la sensibilité d'une personne à l'illusion. Il a été précédemment montré que des scores d'empathie élevés seraient susceptibles d'entraîner une illusion plus forte (Lopez et al. 2013; Nakul et al. 2020b). Des scores d'anxiété ou de dépression ainsi que de dépersonnalisation élevés pourraient également jouer un rôle dans l'induction de l'illusion. Chez une population de patients avec des déficits vestibulaires, des scores de dépersonnalisation plus élevés étaient associés à des changements du soi corporel (Jáuregui Renaud 2015; Lopez et Elzière 2016, 2018). Dans notre étude 4, nous avons seulement utilisé les scores des questionnaires relatifs à ces états pour montrer que nos groupes de patients et de contrôles ne différaient pas. Il serait également intéressant de mener cette analyse chez une plus grande cohorte, notamment des personnes plus jeunes.

II.3.C. Pratiques sportives et soi corporel

La force de l'illusion, et donc la malléabilité du soi corporel, pourrait également être influencée par la pratique sportive. En effet, des études ont mis en évidence que la pratique sportive à haut niveau entraînait de meilleures capacités intéroceptives et proprioceptives, notamment chez des danseurs professionnels (Legrand et Ravn 2009; Jola et al. 2011; Christensen et al. 2018; Virtanen et al. 2022). Il serait ainsi intéressant dans de futures études de mettre en évidence ce lien entre la pratique sportive et la malléabilité du soi corporel.

Conclusion

Ce travail de thèse avait pour ambition d'approfondir notre connaissance sur les bases neurales et multisensorielles du soi corporel. Nous avons mis en évidence dans les chapitres introductifs de cette thèse et dans notre article d'opinion (étude 1, Dary et Lopez 2023), un ensemble de pistes de recherches sur le soi corporel. Notre thèse s'est focalisée sur trois objectifs :

1) Apporter une preuve causale des bases neurales qui sous-tendent le soi corporel.

Nous étudions, pour la première fois causalement, les bases neurales du soi corporel en prenant en considération les différentes expériences corporelles. Pour réaliser cette cartographie, nous avons utilisé les techniques de stimulations électriques intracérébrales permettant d'établir ainsi un lien de causalité entre une région stimulée et une réponse observée. Nos résultats démontrent l'existence d'un vaste réseau cérébral s'étendant principalement dans les régions pariétales latérales (lobule pariétal inférieur, gyrus postcentral) et médiales (précuneus, cortex cingulaire moyen et postérieur), temporales mésiales (complexe amygdalien-hippocampique) et pariéto-insulaires (insula et opercule pariétal).

2) Décrire le réseau fonctionnel du soi corporel

Ce travail de thèse a également contribué à décrire le réseau fonctionnel du soi corporel. Pour cela, nous avons analysé les changements de connectivité fonctionnelle pendant que les patients rapportaient une modification du soi corporel. Pour tirer des conclusions sur le fonctionnement d'un cerveau sain, nous avons exclu les stimulations dans la région épileptogène et dans le tissu lésionnel. Nos résultats ont montré une diminution significative de la force de plusieurs nœuds, dont le lobule pariétal inférieur, les gyrus temporaux inférieurs et moyens, ainsi que le sillon temporal supérieur. Seule l'insula montrait une augmentation de force de connectivité dans le réseau. Nos analyses sur la force des liens ont montré une diminution significative de connectivité entre le lobule pariétal inférieur et le gyrus temporal moyen, entre le gyrus temporal inférieur, le sillon temporal supérieur, l'hippocampe et le gyrus temporal moyen. Nous avons également trouvé une diminution significative de la force des liens entre le sillon temporal supérieur, l'amygdale et l'hippocampe. Nos analyses suggèrent donc l'implication majeure des régions temporales dans le réseau du soi corporel. Cependant, une limite majeure de cette étude est le manque de puissance statistique notamment dû au faible nombre de structures échantillonnées qui impacte directement le nombre de connexions analysées. Une prochaine étude pourrait mettre en évidence les connexions par réseau fonctionnel (DMN, etc.), ce qui augmenterait considérablement le nombre de connexions.

3) Apporter un éclairage sur le lien entre le soi corporel et le système vestibulaire

Enfin, ce travail s'est intéressé aux bases multisensorielles sous-tendant les expériences corporelles, en se focalisant principalement sur le rôle du système vestibulaire dans le soi corporel. Notre étude avait également un objectif secondaire plus précis, à savoir, comprendre le rôle du système otolithique dans le soi corporel. Pour répondre à cela, nous avons étudié à une population présentant une vestibulopathie bilatérale, c'est-à-dire une perte du fonctionnement des canaux semi-circulaires. Nous avons testé ce groupe de patients dans une illusion du corps entier développée à la troisième personne en réalité virtuelle. Nous n'avons pas trouvé de différence significative dans les mesures implicites d'imagerie mentale entre les patients et les contrôles. Il est possible que ces patients aient compensé leur perte vestibulaire, ce qui n'induirait aucun conflit multisensoriel. Par ailleurs, nous proposons que la sensibilité à l'illusion du corps entier soit fortement affectée par l'âge. En effet, l'illusion est rapportée par notre groupe de témoins plus jeunes. Il serait intéressant dans de prochaines études d'étudier l'effet de l'âge sur la sensibilité à l'illusion.

L'ensemble de ce travail contribue ainsi à mieux comprendre, par le prisme des neurosciences cognitives, le lien entre le cerveau et le corps. Nous avons essayé dans cette thèse de créer un dialogue entre les travaux théoriques sur le soi corporel, proposés par la phénoménologie, et les travaux empiriques et cliniques des neurosciences. Nous soutenons qu'un dialogue transdisciplinaire est nécessaire pour appréhender la complexité du soi corporel et plus généralement la conscience de soi. Ce dialogue ne s'arrête pas aux disciplines exposées dans cette thèse. Au contraire, il implique la psychologie, la sociologie et même l'art. Après tout, « *la vraie vie, la vie découverte et éclaircie, la seule vie par conséquent réellement vécue, c'est la littérature [...]* [l'art c'est] *le retour aux profondeurs où ce qui a existé réellement gît inconnu de nous* » (Proust, *Le temps retrouvé*, 1927).

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Annexes

Annexe 1

The origin of pleasant sensations: Insight from direct electrical brain stimulation

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Research Report

The origin of pleasant sensations: Insight from direct electrical brain stimulation

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ABSTRACT

Research into the neuroanatomical basis of emotions has resulted in a plethora of studies over the last twenty years. However, studies about positive emotions and pleasant sensations remain rare and their anatomical-functional bases are less understood than that of negative emotions. Pleasant sensations can be evoked by electrical brain stimulations (EBS) during stereotactic electroencephalography (SEEG) performed for pre-surgical exploration in patients with drug-resistant epilepsy. We conducted a retrospective analysis of 10 106 EBS performed in 329 patients implanted with SEEG in our epileptology department. We found that 13 EBS in 9 different patients evoked pleasant sensations (.60% of all responses). By contrast we collected 111 emotional responses of negative valence (i.e., 5.13% of all responses). EBS evoking pleasant sensations were applied at 50 Hz with an average intensity of $1.4 \pm .55$ mA (range .5–2 mA). Pleasant sensations were reported by nine patients of which three patients presented responses to several EBS. We found a male predominance among the patients reporting pleasant sensations and a prominent role of the right cerebral hemisphere. Results show the preponderant role of the dorsal anterior insula and amygdala in the occurrence of pleasant sensations.

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Abbreviations: EBS, direct electrical brain stimulation; SEEG, stereoelectroencephalography; AI, anterior insula.

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1. Introduction

Emotions are a major part of our psychic life and brain function. They can be defined by the triad of: (1) affect (conscious experience), (2) motor and behavioral adaptation and, (3) autonomic nervous system response (Hamann, 2001; Lang, 1995). Emotions with positive valence have an important impact on quality of life and well-being. They can improve cognitive and social capacities by facilitating decision making, problem solving, social interaction and creativity (Ashby et al., 1999; Carpenter et al., 2013; Fredrickson, 2004; GROSS, 2002)). The genesis and regulation of positive emotions have been mainly studied using functional MRI with different tasks evoking pleasant sensations, including sensory experiences (Koelsch & Skouras, 2014), viewing of images of loved ones (Bartels & Zeki, 2000; Nitschke et al., 2004) or other images or films (Brassen et al., 2011; Garavan et al., 2001; Kim & Hamann, 2007), recollection or imagination of pleasant situations (Matsunaga et al., 2016; Pelletier et al., 2003; Zotev et al., 2011) or social relationships (Scharnowski et al., 2020). Despite some variability depending on the paradigm used, these studies highlighted the implication of ventral, “emotional” cortico-subcortical networks including the orbitofrontal cortex, the anterior cingulate cortex, the insula, the amygdala, as well as the caudate, the putamen, the globus pallidus and the brainstem.

The neural underpinnings of pleasant conscious sensations have also been studied using direct electrical brain stimulation (EBS) in the context of pre-surgical evaluation of patients with drug-resistant epilepsy using electrocorticography or stereotactic electroencephalography (SEEG). Brain explorations through EBS in awake patients offer several advantages. SEEG has better temporal resolution than functional MRI (Mercier et al., 2022) and targeted EBS allows to establish a direct causal “stimulation–clinical event” relationship. However, only few studies showed that EBS can evoke emotional sensations, reproducing usual ictal symptoms or more rarely sensations not encountered during seizures. Penfield and his collaborators were among pioneers in describing experiential and emotional phenomena in response to EBS during per-operative stimulations in patients (Penfield & Jasper, 1954). More recent studies on the effects of EBS on emotion have provided a functional brain map of the cortical regions involved (Drane et al., 2021; Gordon et al., 1996). In particular, the amygdala has repeatedly been involved in triggering emotional responses, which were mainly perceived as negative (Bujarski et al., 2022; Inman et al., 2020; Lanteaume et al., 2007). Other brain regions have been shown to produce emotional affects, such as other medial temporal regions (rhinal and temporal pole cortices) (Bartolomei et al., 2004; Meletti et al., 2006; Smith et al., 2006a) and the insula (Bartolomei et al., 2019; Mazzola et al., 2019). However, studies on positive emotions triggered by EBS remain very sparse when compared to stimulation-based studies of brain areas involved in other cognitive and emotional functions (Drane et al., 2021) and we are lacking causal evidence of brain network implications in pleasant sensations.

The aim of the present study was to identify the brain areas underlying conscious perception of pleasant sensations using direct EBS in a large, unselected cohort of patients with epilepsy. For this purpose, we retrospectively analyzed the effects of all EBS performed during SEEG in our department over the past twenty years.

2. Materials and methods

We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. Patients

The analysis of clinical responses to EBS was performed from a database established on EBS collected from 329 consecutive patients (167 females, 162 males; mean age: 24.9 ± 13.38 years) who underwent SEEG for pre-surgical evaluation of drug-resistant epilepsy between August 2000 and September 2020 in the Epileptology Unit—Clinical Neurophysiology Department of the Timone University Hospital in Marseille, France. The left cerebral hemisphere was explored in 254 patients (6.93 ± 4.44 electrodes per patient) and the right cerebral hemisphere was explored in 269 patients (7.14 ± 4.52 electrodes per patient).

This study was approved by the local ethics committee (the institutional review board of the Assistance Publique Hôpitaux de Marseille, C3BHV2), and informed written consent was obtained from all patients. Three patients of the present series have been reported in two publications about ecstatic feelings during anterior insula stimulation (Bartolomei et al., 2019; Picard et al., 2013).

2.2. SEEG

SEEG was performed using intracerebral multi-contact electrodes (Dixi Medical or Alcis), which had 10, 15, or 18 contacts with a length of 2 mm, a diameter of .8 mm, and a spacing of 1.5 mm. Electrodes were placed stereotactically using the Talairach technique for older implantations, or with the aid of the ROSA™ robotic surgical assistant for implantations performed after 2016 (Contento et al., 2021). SEEG was recorded with a 128- or 256-channel Natus system depending on the year of recording, sampled at 256, 512, or 1024 Hz, and recorded on a hard drive (16 bits/sample) without digital filters. Two computer filters were applied during data acquisition: a high-pass filter (cutoff frequency = .16 Hz at 3 dB), and an anti-aliasing low-pass filter (cutoff frequency = 97 Hz for a 256 Hz sampling rate, 170 Hz for a 512 Hz sampling rate, 340 Hz for a 1024 Hz sampling rate). The implantation scheme of electrodes was determined in a multidisciplinary meeting in the presence of neurologists specialized in epileptology as well as neurosurgeons. Electrodes number and their implantation sites were established in relation to the suspected epileptogenic zone on the basis of clinical examination, semiology of usual seizures, morphological and functional

imaging data (cerebral MRI, PET scan), neuropsychological tests and scalp video-EEG recorded previously.

2.3. Identifying contacts of interest

The electrode contacts which stimulation induced pleasant sensations were localized on the patient's MRI using a co-registration process based on the automatic SEEG electrode localization, segmentation and reconstruction GUI GARDEL (Medina Villalon et al., 2018) (freely available at <https://meg.univ-amu.fr/wiki/GARDEL:presentation>). First, a co-registration of the preoperative MRI on the post-implantation CT-scan including images of the electrodes was performed. Then, the co-registered MRI was segmented in order to extract the white matter, the grey matter and the cerebrospinal fluid. Following steps comprised automated localization of each electrode and the associated contacts and their labeling as belonging to the gray matter, white matter or the cerebrospinal fluid. Finally, the reconstruction and labeling of each contact was verified visually on MRI by expert clinicians. For older SEEG, where post-implantation CT scan was not available, electrodes were manually reconstructed from MRI post-implantation followed by automatic labeling and visual verification as previously mentioned.

2.4. Electrical brain stimulation

EBS were performed while patients were lying in bed and instructed to keep their eyes open and relax. A current-regulated neurostimulator designed for diagnostic purposes delivered EBS according to routine procedures used in our department and according to French guidelines on SEEG (Isnard et al., 2018). Square current pulses were applied between two adjacent contacts at 50 Hz, with a pulse duration of 1 ms and a train duration of 3–5 s. These parameters were used to avoid tissue damage (charge density per square pulse $<55 \text{ mC/cm}^2$). The stimulus intensity was increased from .3 mA by .2 mA increments, until sensation or after-discharge was evoked, and up to a maximum of 3 mA. Due to the clinical purpose of EBS, a stimulation evoking a response was usually not repeated to assess the reproducibility of the response with the same stimulation parameters. However, for two patients the same electrode contacts where a positive sensation was evoked were stimulated twice at different intensities, showing reproducible responses (Table 1).

2.5. Data collection and assessment

Subjective reports and behavioral responses to cortical EBS in 329 epilepsy patients were recorded with video-SEEG. They were carefully analyzed and entered into an Excel database.

A total of 10 106 EBS using 50 Hz electrical stimulation (train duration: 3–5 s) were collected. After each stimulation, the patients were systematically asked to express the sensations and symptoms that may have been evoked by that stimulation. The effects on the EEG (after-discharge) as well as the clinical effects were routinely collected and systematically documented in dedicated notebooks, and the video-EEGs of positive responses were stored. For the present study, all the reported emotional responses of positive valence (feelings of

happiness, well-being, joy, pleasant sensation of any intensity) were systematically retained and verified on the video-EEG by two expert clinicians (CV and FB). The patient's baseline emotional status was estimated from the video-EEG immediately preceding each selected stimulation and the patient's status regarding psychiatric co-morbidities was verified from the medical records. No analysis code was used in this study.

No part of the study procedures or analysis plans was preregistered prior to the research being conducted.

3. Results

3.1. Frequency and phenomenology of pleasant sensations evoked by EBS

Of the 10 106 EBS performed in our department between August 2000 and September 2020 in 329 patients, 2 165 evoked one or several responses or sensations, 1 286 during stimulation of the right cerebral hemisphere and 879 during stimulation of the left hemisphere. A pleasant sensation was reported during only 13 of these stimulations (i.e., .60% of all responses) in nine patients (i.e., 2.74% of the sample), making it a very rare experiential phenomenon evoked by EBS. By contrast, 111 emotional responses of negative valence (i.e., 5.13% of all responses) were observed in the same cohort of patients in 50 patients (i.e., 15.2% of the sample).

Among the nine patients (P1 to P9) who reported pleasant sensations, three (P4, P6 and P8) showed responses to several EBS (Table 1). Regarding the experienced phenomena, a pleasant sensation was reported by six patients, well-being by six patients, positive emotion or joy was reported by two patients and bliss by one patient. These positive sensations were accompanied by sensations of floating (three patients), warmth (one patient) or shivering (one patient). Of note, patient P5 presented a change in emotional valence of his semiology during the same stimulation, starting with a pleasant floating sensation and well-being followed by an unpleasant sensation of anxiety.

The reproducibility of the responses was not systematically assessed because EBS was delivered only for clinical. However, for patient P2 two EBS of the same electrode contacts (CC2–3) successively at 1.6 and 2 mA evoked the same feeling of well-being; for patient P6, two stimulations of the same bipolar contacts (OF1–2) successively at 1.3 and 1.6 mA, evoked the same pleasant sensation (Table 1). In conclusion, in two patients where the same electrode contacts were stimulates twice, the responses were reproducible.

3.2. Patients' characteristics

We found a male predominance among the patients reporting pleasant sensations (one 1 female, eight 8 males; sex ratio: .13), although the sex ratio was close to 1 in the whole cohort (167 females, 162 males; sex ratio: 1.03). This is in contrast with the female predominance for emotional responses of negative valence in the same cohort of patients (31 females, 19 males; sex ratio: 1.63). There was a significant effect of sex on the valence of the emotional response evoked by EBS

Table 1 – Table showing the features of the patients who had pleasant sensations during electrical 50 Hz (3–5 s) brain stimulations.

Patient (sex)	Age (years)	Subjective seizure semiology	MRI	Epileptogenic zone	Electrodes nb (right/left)	Stimulation site	Intensity (mA)	Induced clinical response	After-discharge
P1 (M)	31	Chest tightness	Left amygdala& hippocampus hypersignal	Undetermined (no seizures recorded)	17 (15/2)	Left AI	2.0	Pleasant warm sensation in the body, well-being	no
P2 (M)	35	Well-being, euphoria, floating	Right temporal FCD	Right temporal lateral	17 (14/3)	Right ACC	1.6 & 2.0	Feeling of well-being	no
P3 (M)	41	Visual illusion, well-being	Normal	Right mesial temporal	10 (10/0)	Right amygdala	.5	Pleasant sensation	no
P4 (M)	24	Well-being, numbness of the left hemibody, auditory illusion	Normal	Right temporal mesio-lateral	10 (10/0)	Right TP Right amygdala	1.0 .5	Feeling of well-being Feeling of well-being	no yes
P5 (M)	18	Well-being, reminiscence of memory, auditory illusion, déjà-vu	Left mesial temporal hypersignal	Left mesial temporal and insula	11 (0/11)	Left AI	2.0	Pleasant floating, well-being followed by anxiety and lipothymia	yes
P6 (F)	23	Pleasant epigastric sensation, floating, space distortion, auditory hallucination	Normal	Right mesial temporal and insula	10 (10/0)	Right AI	1.3 & 1.6	Pleasant floating, well-being, pleasant shivering	no
P7 (M)	24	Modification of temperature perception	Left temporal Ganglioglioma	Left mesial temporal	12 (1/11)	Right amygdala	1.0	Pleasant epigastric sensation	yes
P8 (M)	45	Well-being, bliss, floating, pleasant sensation, chest tingling	Normal	Right mesial temporal	16 (13/3)	Left amygdala Left AI Right AI	1.0 2.0 2.0	Joy, pleasant sensation Bliss Positive emotion, well-being	yes yes yes
P9 (M)	40	Positive emotion, bliss, tachycardia	Right fronto-opercular lesion	Right prefrontal	12 (11/1)	Right amygdala Right AI	1.0 1.6	Positive emotion, well-being Pleasant sensation, floating	yes no

Abbreviations; AI: anterior insula; ACC: anterior cingulate gyrus; TP: temporal pole; FCD: focal cortical dysplasia.

($\chi^2 = 7.96$; $P = .005$). The mean age of these patients reporting pleasant sensations was 31.2 ± 9.5 years.

Five out of nine patients had abnormal brain MRI. The epileptogenic zone was mainly located in the right hemisphere (six patients). The epileptogenic zone defined by SEEG included the mesial temporal regions in six patients. The epileptogenic zone was limited to these regions in three cases, extended to the temporal lateral in one case, and extended to the insula in two cases. The epileptogenic zone was temporal lateral in one case, prefrontal in one and remained undetermined in another case. Of note, seven out of nine patients also reported pleasant sensations during their usual seizures. However, no one patient had a history of mood disorder or any other psychiatric comorbidity.

3.3. EBS characteristics and anatomical location

EBS evoking pleasant sensations were applied at 50 Hz with an average intensity of $1.4 \pm .55$ mA (range .5–2 mA). Among the twelve EBS that induced positive emotional responses in 9 participants, seven induced an after-discharge. Electrode contacts where a pleasant sensation could be evoked were mostly located in the anterior insula (AI, a total of six stimulation; right AI: $n = 3$, left AI: $n = 3$) and in the amygdala (five stimulation; right amygdala: $n = 4$, left amygdala: $n = 1$) (Fig. 1). One stimulation of the right anterior cingulate cortex and another of the right temporal pole also induced a feeling of well-being (Table 1). Overall, most EBS that evoked pleasant sensations were applied to the right cerebral hemisphere ($n = 9$), whereas only four were applied to the left hemisphere. In two patients (P4 and P8), the same sensation could be elicited from two different brain structures, i.e., a feeling of well-being by EBS in the right temporal pole and the amygdala (P4) and a positive emotion and well-being by EBS in the right AI and the amygdala (P8). Interestingly, patient P8 also reported bliss induced by the stimulation of the left AI. All but one of the positive stimulations were performed outside the MRI-visible

lesion. In two patients, the stimulation site was located outside the epileptogenic zone (anterior cingulate and anterior insula).

4. Discussion

To our knowledge, our study is the first to focus specifically on the generation of pleasant sensations, in the broad meaning of the term, from a large collection of EBS obtained during SEEG recordings (10 106 stimulations in 329 patients). We found that pleasant sensations were exceptional events during EBS, much rarer than negative sensations, as we observed only 13 positives sensations (.55%, versus 5.13% for negative feelings). This is possibly a particularity of the mammalian brain, which is more likely to generate negative emotions for rapid adaptive reactions favoring survival of species, e.g. when facing a danger (Phan et al., 2002). Another explanation lies in the largely subcortical and brainstem location of reward networks (Liu et al., 2011; Wise, 2002) when compared to the focus of EBS on cortical structures during SEEG for presurgical evaluation of epilepsy (see limitations).

4.1. Amygdala and anterior insula: two core regions for pleasant sensations

Our results identified two brain regions more frequently involved in pleasant sensations: the anterior insula (AI) and the amygdala. The AI is the source of heterogeneous clinical manifestations when it is involved in seizure or stimulated electrically as it can evoke gustatory, olfactory, auditory, somatosensitive, vestibular, viscerosensitive, visceromotor, experiential or emotional sensations (Mazzola et al., 2006, 2014, 2017, 2019). Functional neuroimaging highlighted the role played by the insula in the integration of information from our environment and the genesis of adapted emotions, showing the notable role of the AI (Kurth et al., 2010). Our data

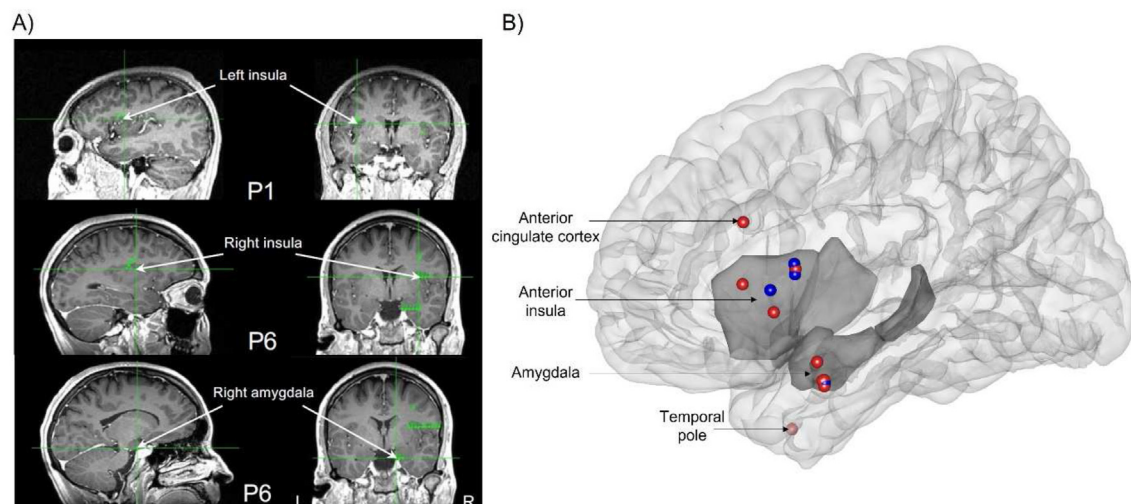


Fig. 1 – A) Example of localization and projection on patient's MRI of stimulated contacts inducing positive emotional sensations in some patients (GARDEL software. B) EBS sites are summarized by projection on the right hemisphere of the 3D mesh of the MNI normalized brain appended with meshes of amygdala and insula for better visualization. Colours indicate the lateralization these sites (blue = left side, red = right side).

are congruent with previous EBS studies showing the involvement of AI in pleasant emotions and particularly ecstatic sensations (Bartolomei et al., 2019; Nencha et al., 2022a; Ostrowsky et al., 2000). Gschwind and Picard (2016), in a meta-analysis of ecstatic aura, defined ecstatic sensations as the association of “intense positive emotion (bliss)”, “improved physical well-being”, “increased self-awareness or increased perception of the external world (clarity)”. According to a recent neurocognitive theory, the brain would operate on a prediction model (Clark, 2013), comparing real internal and external stimuli with reference theoretical patterns. The insula would be the key structure for processing the internal states of the body through interoceptive signals. Disruption of the predictive role of AI has been proposed as an explanation of the ecstatic auras (Picard et al., 2021). Recently a feeling of time dilation with a sense of pleasant eternity has been reported during AI stimulation (Sheikh et al., 2022).

The role of amygdala in generating negative emotions, especially fear, is well known both from animal and human studies (Davis & Whalen, 2001; LeDoux, 2003). However, the amygdala has also been involved in brain circuits related to happiness and pleasant sensations (Garavan et al., 2001; Hamann & Mao, 2002; Lanteaume et al., 2007; Sabatinelli et al., 2011). Animal studies showed that amygdala neurons respond to conditioning stimuli that have been associated with either appetitive or aversive outcomes (reviewed in Fernando et al., 2013). The activation of the amygdala in response to pleasant stimuli is suggested by human fMRI studies, notably when observing a pleasant image, face, word or scene (Garavan et al., 2001; Hamann & Mao, 2002; Sabatinelli et al., 2011), or during mental imagery of pleasant situations (Costa et al., 2010). On the other hand, only few publications reported pleasant sensations during EBS in the amygdala (see (Guillory & Bujarski, 2014) for review). Lanteaume et al. (2007) reported sensations of “joy” or “happiness” during left amygdala stimulation in a minority of patients, as most EBS resulted in negative sensations. This study quantified subjective responses using a basic emotion scale (Izard scale). A more recent study found that only one out of 150 amygdala stimulation resulted in a subjective feeling of joy (Inman et al., 2020).

Our study also shows that the anterior cingulate gyrus and the temporal pole may also contribute to pleasant sensations. These observations are consistent with some data from EBS of the temporal pole. Analyzing the semiological aspects of temporal pole stimulation, Ostrowsky et al. (2000) reported a sensation of happiness in 4 out of 150 temporal pole stimulation. Meletti et al. (2006) also described a pleasant and relaxing sensation during EBS in the temporal pole. Similarly, experiments involving recollection of positive autobiographical memories and positive emotions revealed the activation of hippocampus and temporo-polar regions (Markowitsch et al., 2003; Zotev et al., 2011). Concerning the anterior cingulate gyrus, in his work on the lateralization of affect, Smith et al. (2006a) described an euphoric sensation after its stimulation. Some functional imaging studies highlighted also the role of the anterior cingulate gyrus in the emotional mechanisms of happiness. Studies reported that when participants were asked to recall and attempt to re-experience and re-enact intense personal emotional episodes, there was an activation of the right insula, right somatosensory cortex,

bilateral anterior cingulate cortex and right posterior cingulate cortex (Damasio et al., 2000; Suardi, Sotgiu, Costa, Cauda, & Rusconi, 2016).

While our study highlights the predominant role in the conscious expression of positive affect of the AI and amygdala, these structures are likely embedded in a network of neural structures and probably do not act in isolation. There is evidence that direct high-frequency EBS activates a network of regions depending on the stimulation site and the effect produced (Bartolomei et al., 2019; Perrone-Bertolotti et al., 2020). As such, a recent study on a manic state induced by EBS of the right lateral prefrontal cortex demonstrated significant increase of functional coupling between the right hemispheric limbic nodes, the temporal pole and the claustrum (Scholly et al., 2022). There is evidence that the genesis of emotions requires the interaction between several brain networks, widely distributed, although none of them seems to be specific to the “emotion function” (Morawetz et al., 2020; Pessoa, 2018). Among these networks, the “salience network”, which has been widely studied, would be involved in a larger scale network leading to the generation of emotions. The salience network involves, among others, connections between the anterior cingulate gyrus, the AI, the amygdala and the hypothalamus (Kober et al., 2008; Lindquist, Satpute, Wager, Weber, & Barrett, 2016; Pessoa, 2018). The relative contribution of each of these regions in positive emotion networks remains to be determined.

A network of brain areas underpinning the experience of positive emotions and pleasant sensations could explain why, in two patients, stimulating different structures evoked the same sensations, with for patient P4, stimulation of the right amygdala and temporal pole evoking a feeling of well-being and for patient P8, stimulation of the right amygdala and AI evoking a feeling of well-being and positive emotion. The dense bidirectional connections between the anterior ventral part of the insula and the amygdala (Jakab et al., 2012; Mesulam & Mufson, 1982) and between the AI and the anterior cingulate gyrus (Ghaziri et al., 2017) can account for similar sensations evoked by EBS in distant areas within the same functional network.

4.2. Effect of hemispheric laterality and sex

Our study revealed a right-sided predominance of pleasant sensations. A right-side predominance of negative emotional valence induction for right side stimulations has been reported in previous EBS studies (review in (Guillory & Bujarski, 2014)). A left lateralization of positive emotion during amygdala stimulation has been previously suggested (Lanteaume et al., 2007). This apparent contradiction could be linked to the underrepresentation in the previous studies of the anterior insula stimulation which is the prominent site in our experience for pleasant evoked sensations. Smith et al. (2006b) also reported dysphoric responses primarily during right stimulation, but no lateralization for pleasant emotional responses. No clear lateralization effect was found as a function of emotional valence in amygdala activation in a large neuroimaging meta-analysis (Baas et al., 2004).

There was a predominance of pleasant sensations in men in our study. No previous study using EBS has reported such a

predominance of positive emotions, which could be related to the small number of patients in most EBS studies when compared to the large sample investigated here. However, regarding negative emotions Meletti et al. (2006) reported that the feeling of fear occurred significantly more in women than in men.

Data in the literature on gender differences in emotion are often inconsistent (Brody & Hall, 2000; Wester et al., 2002). There is evidence, primarily from self-report data, that women experience emotions with greater intensity than men (Whittle et al., 2011). Women have been found to be more reactive to emotional stimuli, and particularly to unpleasant, threatening, or traumatic stimuli. Research has also suggested that gender differences in self-report are greater for negative emotions such as fear and jealousy, and some neuroimaging studies support greater brain activation in women for negative stimuli (review in (Whittle et al., 2011)). There is also evidence that males may be physiologically more reactive to certain pleasurable stimuli, particularly erotic ones (Allen et al., 2007). A study reported that males exhibited greater activity than females in the frontal lobe and amygdala during exposure to photo stimuli with positive valence (Wrase et al., 2003).

Further studies are needed to better define the effects of these two factors in the genesis of pleasant sensations.

4.3. Limitations of the study

The first limitation of our study is its retrospective nature. Responses were systematically collected, but subjective reports may not have been exhaustive. Patients may have described their symptoms in a simplified way because of difficulties in expressing their feelings (Cirignotta et al., 1980). Moreover, how to perceive and express these sensations may depend on education, culture, information given to the patients, context of occurrence, the patients ability to introspection, their vocabulary and therefore vary between patients but also within the same patient (Williams, 1956). To overcome these difficulties, quantification by self-administered questionnaires (Lanteaume et al., 2007) is interesting but was not carried out in the majority of patients in the study. Prospective studies using standardized questionnaires will be particularly useful, especially if coupled with objective measures of the autonomic response, such as the electrodermal response (Inman et al., 2020; Lanteaume et al., 2007).

The second limitation is related to the spatial sampling of SEEG as it has been estimated that about 10 000 electrode contacts would be necessary to explore the brain volume covered by functional MRI (Lachaux et al., 2003). This limitation is partially counterbalanced by the large cohort of patients included and the large number of EBS considered in our analysis (the highest in the literature to date) that allow a large spatial sampling. In addition, the included patients cover a large temporal period with variations in the number of implanted electrodes and implanted sites. Insular implantations with orthogonal and especially oblique electrodes became more common from 2010 in our center. We

can also note that, for feasibility and safety reasons, some regions cannot be explored, in particular the brainstem whose role in emotional processing is important (Venkatraman et al., 2017).

Third, SEEG was performed in patients with epilepsy, and seven of them reported positive sensations belonging to the subjective symptoms of their usual seizures. Moreover, the stimulated sites were part of the epileptogenic zone in 8 out of 13 cases. Indeed, the organization of brain networks and the excitability of the brain of patients with epilepsy may be different from a non-epileptic subject. Nevertheless, direct brain stimulation in the history of neuroscience has allowed progress in the knowledge of the role of certain regions in subjective phenomena generated by the human brain, such as psychosensory or emotional phenomena (reviewed (Trébuchon & Chauvel, 2016)). Moreover, these phenomena can be obtained outside the usual clinical semiology of the patients (patients P1 and P7 in the present study) (Nencha et al., 2022b).

5. Conclusions

This study is the largest to date collecting positive emotional responses evoked by EBS. This study confirms that these are rare manifestations and mainly evoked by the stimulation of the amygdala or/and the anterior insula.

CRedit author statement

Cecile Villard: Investigation (data collection and analysis), writing original draft; Zoé Dary: Investigation (data collection and analysis), reviewing and editing draft; Jacques Léonard: Investigation (data collection); Samuel Medina Villalon: Data curation, Software development, visualization/data presentation; Romain Carron: investigation, reviewing and editing draft; Julia Makhalova: investigation, reviewing and editing draft; Stanislas Lagarde: investigation, reviewing and editing draft; Christophe Lopez: Conceptualization, Methodology, reviewing and editing, funding acquisition; Fabrice Bartolomei: Conceptualization, Methodology, supervision of the study, funding acquisition.

Data availability

Coregistration process (MRI/CT scan with electrode) is based on the automatic SEEG electrode localization, segmentation and reconstruction GUI GARDEL freely available at <https://meg.univ-amu.fr/wiki/GARDEL:presentation>. The participant data cannot be placed in an open archive because it is not permitted under the study's institutional review board of the Assistance Publique Hopitaux de Marseille due to the sensitive nature of patients' data. Qualified researchers wishing to access the data should contact the corresponding author (FB). Data may be shared after a data sharing agreement has been signed and approved by the institutional review board of the Assistance Publique Hopitaux de Marseille.

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Annexe 2

Le soi corporel en neurosciences : l'exemple de la localisation du soi

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Sous la direction de
Giuseppe Di Liberti et Pierre Léger



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ZOÉ DARY ET ESTELLE NAKUL

LE SOI CORPOREL EN NEUROSCIENCES L'exemple de la localisation du soi

Introduction

Nous pouvons distinguer deux façons différentes d'aborder le corps : en tant qu'objet ou en tant que sujet. Le corps-objet correspond aux aspects objectifs du soi, c'est-à-dire au corps physique et matériel. Le corps-sujet correspond quant à lui aux aspects subjectifs du soi, c'est-à-dire à l'expérience d'être un corps. Les neurosciences cognitives se sont longtemps concentrées uniquement sur le corps-objet. Elles reniaient la part subjective du corps afin de rester objectives : leurs paradigmes et leurs méthodes d'expérimentation ne permettaient pas d'inclure le corps-sujet dans leur champ de recherche. Or, dans le cadre de la cognition incarnée, les aspects subjectifs du corps apparaissent primordiaux pour comprendre le soi¹. L'objectif est de réconcilier le corps-sujet avec le corps-objet. Les neurosciences cognitives se sont ainsi emparées de cette question de recherche, conduisant à des approches diverses du corps-sujet. Certaines approches s'intéressent davantage aux aspects conceptuels et sémantiques du soi (langage, mémoire, etc.), d'autres aux aspects moteurs et sensoriels. La démarche décrite dans cet article s'inscrit dans cette seconde approche : elle s'articule autour du soi corporel². Ce dernier correspond aux aspects préreflexifs du soi, c'est-à-dire à la « représentation non-conceptuelle et

- 1 Shaun Gallagher, *How the Body Shapes the Mind*. 2005, Oxford University Press, 2006 ; Olaf Blanke et Thomas Metzinger, « Full-Body Illusions and Minimal Phenomenal Selfhood », *Trends in Cognitive Sciences*, n° 13, 2009, pp. 7-13.
- 2 Dorothée Legrand, « Le soi corporel », *L'Évolution Psychiatrique* 70, 2005, n° 4, pp. 709-19 ; Olaf Blanke et Thomas Metzinger. *art. cit.* ; Karl Schaller, Rita G. Iannotti, Pavo Orepic, Sophie Betka, Jullien Haemmerli, Colette Boex, Sixto Alcoba-Banqueri, et al. « The Perspectives of Mapping and Monitoring of the Sense of Self in Neurosurgical Patients », *Acta Neurochirurgica*, 163, 2021, n° 5, pp. 1213-26.



préréflexive des informations relatives au corps³ ». Le concept de soi corporel en neurosciences cognitives attribue au corps-objet des aspects subjectifs qui permettent ainsi d'étudier le corps-sujet à travers le corps-objet. Cette approche tente d'objectiver un phénomène reconnu comme subjectif, en le plaçant dans le champ des neurosciences cognitives et en l'assimilant à des phénomènes mieux maîtrisés, à savoir les mécanismes multisensoriels et cérébraux.

Dans ce cadre, le soi corporel repose principalement sur quatre expériences corporelles⁴ : la localisation du soi, le sentiment d'appartenance du corps, la perspective en première personne et le sentiment d'agentivité. La localisation du soi peut être définie comme le sentiment d'occuper un espace donné à un moment donné, généralement dans les limites physiques du corps. Le sentiment d'appartenance est le sentiment que notre corps et ses parties nous appartiennent. La perspective en première personne est la perspective spatiale du soi sur le monde. Enfin, l'agentivité fait référence au sentiment d'être à l'origine de nos actions et pensées. Ces différents aspects du soi corporel ont notamment été identifiés grâce aux rapports de patients présentant des atteintes neurologiques (épilepsie, migraine, tumeur, etc.), psychiatriques (dépersonnalisation, schizophrénie, dépression, etc.) ou sensorielles (atteintes du système vestibulaire ou somesthésique, désafférentation proprioceptive, etc.). Des illusions ont également été développées pour manipuler le soi corporel et en étudier la phénoménologie de façon plus contrôlée. Ces illusions ont pour but de mettre en évidence les mécanismes sensoriels et cérébraux à l'origine du soi corporel. Cette démarche s'appuie sur l'étude de l'*intégration multisensorielle*, qui correspond aux mécanismes par lesquels le cerveau unit les différentes informations sensorielles qui lui parviennent en une perception unique.

Dans cet article, nous illustrerons l'étude du soi corporel à travers l'exemple de la localisation du soi. Nous montrerons d'abord en quoi les études cliniques ont fourni de premiers indices sur cet aspect du soi corporel. Puis nous présenterons un paradigme devenu classique dans l'étude de la localisation du soi : l'illusion du corps entier et les mesures qui lui sont associées. Cela nous permettra d'illustrer puis de discuter les apports et les limites de la méthode neuroscientifique dans l'étude de la dimension subjective du soi.

3 Estelle Palluel, Jane E. Aspell, Olaf Blanke, « Leg muscle vibration modulates bodily self-consciousness : integration of proprioceptive, visual, et tactile signals », *Journal of Neurophysiology*, n°105, 2011, pp. 2239-2247.

4 Olaf Blanke et Thomas Metzinger, *art. cit.*, pp. 713.

1. Approches cliniques et expérimentales du soi corporel

1.1 Études phénoménologiques et cliniques

L'étude empirique de la localisation du soi bénéficie largement d'observations cliniques. Diverses pathologies neurologiques et psychiatriques se manifestent par des distorsions du soi corporel⁵. Parmi les plus spectaculaires, les expériences de sortie du corps se caractérisent par un sentiment de dissociation spatiale entre le soi et le corps⁶ : le soi est perçu comme localisé en dehors de l'espace corporel, dans un espace surélevé par exemple (Fig. 1). Cela peut s'accompagner d'un changement de perspective en première personne : le sujet semble observer son corps de ce nouveau point de vue.



Figure 1. Une expérience de sortie du corps. Pendant une expérience de sortie du corps, le patient rapporte être localisé en dehors de son corps (en noir) et observer ce dernier à partir de ce nouvel emplacement (en gris).

- 5 Christophe Lopez, Pär Halje et Olaf Blanke, « Body ownership and embodiment : Vestibular and multisensory mechanisms », *Neurophysiologie Clinique/Clinical Neurophysiology*, vol. 38, n° 3, 2008, pp. 149-161 ; Sebastian Dieguez et Olaf Blanke, « Altered states of bodily consciousness », dans *Altering consciousness : Multidisciplinary perspectives : History, culture, and the humanities ; Biological and psychological perspectives*, Vols. 1 and 2, Santa Barbara, CA, US, Praeger/ABC-CLIO, 2011, pp. 237-262.
- 6 Olaf Blanke et Christine Mohr, « Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness », *Brain Research Reviews*, vol. 50, n° 1, 2005, pp. 184-199.

Chez des sujets sains, de telles hallucinations peuvent survenir dans le cadre d'une anesthésie générale, de privations sensorielles, de migraines, d'utilisation de drogues, d'une peur extrême ou de la paralysie du sommeil⁷. Les expériences de sortie du corps peuvent également être déclenchées par des crises d'épilepsie ou des stimulations électriques intracrâniennes au niveau de la jonction temporo-pariétale, ce qui permet d'obtenir des descriptions de ces phénomènes pendant que les patients les expérimentent⁸. Une patiente déclarait par exemple « je me vois allongée dans mon lit, d'en haut, mais je ne vois que mes jambes et le bas du tronc⁹ », tandis qu'une autre rapportait que c'était « comme si elle flottait juste en dessous du plafond et qu'elle voyait son propre corps allongé sur la table d'opération¹⁰ ».

Les rapports phénoménologiques et l'étude des bases cérébrales de ces phénomènes suggèrent une origine multisensorielle des distorsions du soi corporel. Ces hallucinations font appel à plusieurs sens : elles peuvent être visuelles mais aussi somesthésiques et vestibulaires. En effet, les sujets rapportent souvent des déformations et des positions corporelles illusoire, ainsi que des sensations de mouvement et de flottement. Les distorsions du soi corporel sont également associées au dysfonctionnement de régions cérébrales impliquées dans l'intégration multisensorielle. Une étude clinique récente montre que les expériences de sortie du corps sont associées à une modification de l'activité cérébrale au niveau de la jonction temporo-pariétale, région cérébrale essentielle pour l'intégration des signaux multisensoriels (visuels, somesthésiques et vestibulaires)¹¹.

L'étude de cas cliniques ou de sujets sains dans des conditions extraordinaires apporte de précieux indices sur l'origine multisensorielle et cérébrale de la localisation du soi. Ces cas ne suffisent cependant pas pour décrire le fonctionnement et les bases cérébrales de ces phénomènes. Les

- 7 Silvia Bünning et Olaf Blanke, « The out-of body experience : precipitating factors and neural correlates », dans S. Laureys (dir.), *Progress in Brain Research*, s. l., Elsevier, n° 150, 2005, pp. 331-606.
- 8 Estelle Nakul et Christophe Lopez, « Commentary : Out-of-Body Experience during Awake Craniotomy », *Frontiers in Human Neuroscience*, vol. 11, n° 417, 2017.
- 9 Olaf Blanke, Stéphanie Ortigue, Theodor Landis, Margitta Seeck, « Stimulating illusory own-body perceptions », *Nature*, n° 419, 2002, pp. 269-270.
- 10 Eelke M. Bos, Jochem K. H. Spoor, Marion Smits, Joost W. Schouten, et Arnaud J. P. E. Vincent. « Out-of-Body Experience During Awake Craniotomy », *World Neurosurgery*, n° 92, 2016, pp. 586.e9-586.e13.
- 11 Eva Blondiaux, Lukas Heydrich, et Olaf Blanke, « Common and Distinct Brain Networks of Autoscopic Phenomena », *NeuroImage : Clinical*, n° 30, 2021, article 102612.

sujets pertinents sont trop rares et leurs caractéristiques trop hétérogènes (localisation des lésions, stimulations, étiologies, descriptions phénoménologiques). Les conclusions qui en sont tirées ne se généralisent pas facilement au fonctionnement d'un cerveau sain dans des conditions normales. Les neurosciences se sont donc tournées vers des études plus maîtrisées, avec des participants plus nombreux et sans pathologie qui pourrait affecter les processus étudiés. Pour cela, il a fallu inventer des paradigmes expérimentaux permettant d'étudier le soi corporel chez des participants sains.

1.2 Illusions pour l'étude expérimentale du soi corporel

Plusieurs illusions ont été développées pour manipuler les différents aspects du soi corporel, dont la localisation du soi. Ces paradigmes expérimentaux ont largement bénéficié du développement de technologies telles que les visiocasques et la réalité virtuelle, qui apportent de nouveaux moyens de manipuler les sens de façon contrôlée. Philosophes¹² comme neuroscientifiques¹³ se sont rapidement emparés de ces possibilités afin de manipuler et d'étudier le soi corporel. L'illusion du corps entier¹⁴ est l'un des paradigmes les plus connus et exploités pour analyser différents aspects du soi corporel. Cette illusion consiste à caresser le dos d'un participant pendant que celui-ci observe, à travers un visiocasque, une image de son corps ou un avatar virtuel. Ce corps virtuel est également touché dans le dos de façon synchrone ou asynchrone avec le toucher réalisé dans le dos du participant. Dans la condition synchrone, les mouvements de la manette de l'expérimentateur sur le dos du participant sont reproduits au même moment et au même endroit sur celui du corps virtuel. Dans la condition asynchrone, un délai est introduit entre le toucher dans le dos du participant et sa retransmission à travers le visiocasque. L'illusion du corps entier permet de comparer les effets des stimulations synchrones et asynchrones. Il s'agit de mesurer les différents aspects du soi corporel avant, pendant et après chaque condition et de comparer les résultats obtenus. Plusieurs techniques peuvent être utilisées pour cela.

12 Masaharu Mizumoto et Masato Ishikawa, « Immunity to Error through Misidentification and the Bodily Illusion Experiment », *Journal of Consciousness Studies*, vol 12, n° 7, 2005, pp. 3-19.

13 Bigna Lenggenhager *et al.*, « Video ergo sum : manipulating bodily self-consciousness », *Science (New York, N.Y.)*, vol. 317, n° 5841, 2007, pp. 1096-1099.

14 *Ibidem*.

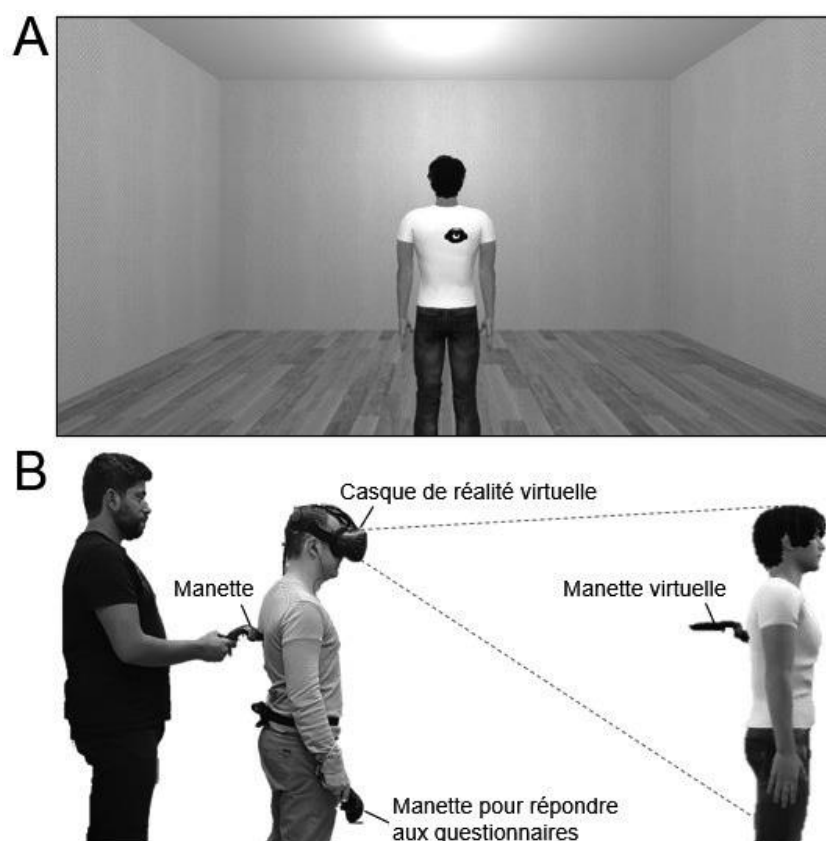


Figure 2. L'illusion du corps entier. A. Le participant est immergé en réalité virtuelle grâce à un casque de réalité virtuelle. Il observe le corps d'un avatar placé 2 m en face de lui. B. Pendant la stimulation visuo-tactile, l'expérimentateur caresse le dos du participant avec une manette de réalité virtuelle. Ce mouvement est reproduit par une manette virtuelle sur le dos de l'avatar, de façon synchrone ou asynchrone (avec un délai temporel). Le participant tient une manette qui lui permettra d'effectuer des tâches de localisation du soi et de remplir des questionnaires tout en restant immergé en réalité virtuelle¹⁵.

Des questionnaires permettent aux participants de rapporter leurs sensations. Ils doivent souvent répondre sur des échelles indiquant à quel point ils sont d'accord ou pas avec certaines propositions ou bien avec quelle intensité ils ont ressenti telle ou telle expérience. Les participants peuvent par exemple donner leur ressenti vis-à-vis de propositions telles que « Il m'a semblé que je sentais le toucher à l'endroit où je voyais le corps virtuel (donc sur le corps virtuel) », « J'ai eu l'impression que le corps virtuel

¹⁵ Estelle Nakul *et al.*, « Measuring perceived self-location in virtual reality », *Scientific Reports*, vol. 10, n° 1, 2020, article number 6802.



était mon propre corps » ou « Il m’a semblé être à deux endroits en même temps. » Ce type de questionnaires, largement utilisé, révèle que les participants rapportent plus de modifications de leur soi corporel à la suite d’une stimulation visuo-tactile synchrone, par rapport à une stimulation asynchrone¹⁶. Ces modifications comprennent notamment une relocalisation de la sensation de toucher et du soi vers le corps de l’avatar, et la possibilité de se sentir à la fois dans son propre corps et en dehors de lui. Ainsi, dans l’illusion du corps entier, la nouvelle relation spatio-temporelle entre les informations visuelles et tactiles modifierait le soi corporel et relocaliserait le soi. Le cerveau localiserait donc le soi en fonction de la congruence spatiale des informations sensorielles dont il dispose.

Des mesures comportementales peuvent également être utilisées pour mesurer la localisation du soi. Une tâche classique consiste à reculer les participants de quelques mètres à petits pas, les yeux fermés, guidés par l’expérimentateur¹⁷. Il leur est ensuite demandé de retourner à la position où ils estiment avoir été pendant la stimulation visuo-tactile. La différence entre leur position initiale et la position à laquelle ils retournent permet de calculer la déviation de la localisation du soi pendant l’expérience. Cette mesure révèle classiquement une relocalisation du soi vers l’avant, c’est-à-dire vers l’avatar, plus importante après une stimulation synchrone qu’asynchrone¹⁸.

D’autres tâches reposent sur l’imagerie mentale. Elles consistent à estimer le temps pour qu’un objet parcoure une certaine distance. Ce type de tâches peut être utilisé dans l’axe vertical lorsque les participants sont allongés, notamment dans le cadre d’illusions du corps entier compatibles avec des enregistrements en imagerie par résonance magnétique fonctionnelle¹⁹. Dans ce cas, les participants tiennent une balle et doivent indiquer successivement quand ils imaginent la lâcher et quand celle-ci atteint le sol, en pressant un bouton. La variation, entre la condition synchrone et asynchrone, du temps évalué pour que la balle touche le sol est interprétée comme une relocalisation du soi le long de l’axe gravitaire. Les travaux

16 Bigna Lenggenhager *et al.*, *art. cit.* pp. 1096-1099 ; Hsu-Chia Huang *et al.*, « The Sense of 1PP-Location Contributes to Shaping the Perceived Self-location Together with the Sense of Body-Location », *Frontiers in Psychology*, vol. 8, 2017, p. 370 ; Estelle Nakul *et al.*, *art. cit.*

17 Bigna Lenggenhager *et al.*, *art. cit.* pp. 1096-1099.

18 *Ibidem.*

19 Silvio Ionta *et al.*, « The brain network reflecting bodily self-consciousness : a functional connectivity study », *Social Cognitive and Affective Neuroscience*, vol. 9, n° 12, 2014, pp. 1904-1913.



ayant adapté l'illusion du corps entier à la neuroimagerie grâce à la tâche de lâcher de balle associent les changements de localisation du soi à l'activité de la jonction temporo-pariétale (gyrus angulaire et gyrus temporal supérieur) et de l'insula postérieure²⁰. Par ailleurs, l'utilisation de la réalité virtuelle a permis d'adapter la tâche de lâcher de balle à l'axe horizontal antéro-postérieur. Dans ce cas, une balle apparaît dans l'environnement virtuel après la fin de la stimulation visuo-tactile et commence à rouler en direction du participant. Après quelques secondes, l'écran devient totalement noir. Le participant doit imaginer que la balle poursuit son mouvement dans la même direction et à la même vitesse et indiquer quand elle atteint sa position. Cette tâche a révélé que les participants évaluent le temps nécessaire pour que la balle les atteigne comme significativement plus court à la suite d'une stimulation visuo-tactile synchrone par rapport à une stimulation asynchrone²¹. Cette différence est interprétée comme une relocalisation de soi vers l'avant, vers l'avatar auquel les participants s'identifient, induite par la stimulation visuo-tactile synchrone. Notons que ce type de tâche, tout comme la tâche décrite précédemment qui implique un déplacement réel du participant, ne montre pas une relocalisation totale du soi vers l'avatar : le résultat de l'estimation est situé entre le corps réel et celui de l'avatar virtuel. Cela pourrait s'expliquer par une mise à jour des informations sensorielles impliquées dans la localisation du soi²². Entre la stimulation visuo-tactile et la réalisation de la tâche, le soi corporel reviendrait à l'état dans lequel il était avant l'illusion, ce qui influencerait la réponse aux tâches de mesure de localisation du soi réalisées à ce moment-là.

Enfin, plusieurs études se sont employées à rechercher des marqueurs biologiques, considérés comme plus objectifs, afin de mesurer des différences entre les conditions synchrone et asynchrone. Il s'agit d'associer les différences observées avec les questionnaires et les tâches comportementales à des modifications physiologiques. Ces mesures pourraient remplacer les questionnaires et les tâches comportementales afin de mesurer l'expérience du sujet. Certains ont par exemple enregistré des variations de température cutanée²³ qui n'ont pas été par la suite reproduits²⁴.

20 Silvio Ionta *et al.*, « Multisensory Mechanisms in Temporo-Parietal Cortex Support Self-Location and First-Person Perspective », *Neuron*, vol. 70, n° 2, 2011, pp. 363-374.

21 Estelle Nakul *et al.*, *art. cit.*

22 *Ibidem.*

23 Roy Salomon *et al.*, « Full body illusion is associated with widespread skin temperature reduction », *Frontiers in Behavioral Neuroscience*, vol. 7, 2013.

24 Estelle Nakul *et al.*, *art. cit.*

Les questionnaires et les tâches comportementales montrent que manipuler la synchronisation des informations visuelles et tactiles modifie le soi corporel. De tels résultats ont été reproduits avec d'autres modalités sensorielles, en manipulant la congruence visuo-cardiaque²⁵ par exemple. Ensemble, les études à ce sujet soulignent que le soi corporel dépend de l'intégration des informations provenant à la fois de l'extérieur et de l'intérieur du corps (visuelles, tactiles, intéroceptives, mais aussi somesthésiques et vestibulaires).

2. Discussion

2.1 L'apport des neurosciences cognitives dans la conceptualisation du soi corporel

L'approche empirique montre que le soi corporel repose sur les sens. Elle justifie l'incarnation du soi et explique les mécanismes sous-jacents. Il s'agit notamment de déterminer la contribution relative de chacun des sens et les bases cérébrales de ce phénomène. Les recherches se fondent sur des modèles pathologiques dans lesquels le traitement des informations sensorielles dysfonctionne ainsi que sur des paradigmes expérimentaux qui manipulent l'intégration multisensorielle, tels que l'illusion du corps entier. L'ensemble de ces études met en évidence l'importance des informations sensorielles en provenance à la fois de l'extérieur et de l'intérieur du corps pour la construction du soi corporel. Elles révèlent aussi des régions cérébrales clefs pour sa construction, telles que la jonction temporo-pariétale.

L'approche empirique du soi corporel et de ses différents aspects permet également de les redéfinir et de mieux les caractériser. Ainsi, la localisation du soi a d'abord été définie comme le sentiment d'occuper un espace donné à un moment donné, généralement dans les limites physiques du corps. Les résultats obtenus par les neurosciences cognitives permettent d'ajuster et de compléter cette définition aux faits observés, en attribuant de nouvelles caractéristiques à la localisation du soi. Les neurosciences cognitives révèlent par exemple la plasticité de la localisation du soi : celle-ci évolue et s'adapte au cours du temps en fonction de paramètres tels que la relation spatio-temporelle entre les informations sensorielles disponibles.

25 Lukas Heydrich *et al.*, « Cardio-visual full body illusion alters bodily self-consciousness and tactile processing in somatosensory cortex », *Scientific Reports*, vol. 8, n° 1, 2018, article number 9230.

Les expériences de sortie du corps et la possibilité de modifier le soi corporel par des manipulations telles que l'illusion du corps entier en sont un exemple. Les neurosciences cognitives mettent également en évidence l'origine multisensorielle de la localisation du soi et plus généralement du soi corporel.

2.2 Les limites de l'étude empirique du soi corporel

La polysémie des concepts de soi corporel et de ses différents aspects, dont la localisation du soi, limite leur étude empirique. La pluralité de définitions selon les auteurs et les disciplines, rend ces concepts difficilement comparables d'une étude à l'autre. Une même tâche comportementale, avec une balle qui s'approche du participant, peut, par exemple, être utilisée pour mesurer la localisation du soi ou l'espace péripersonnel, c'est-à-dire l'espace d'action entourant le corps.

Des limites proviennent aussi des mesures et des méthodes utilisées. D'une part, les données obtenues ne permettent parfois pas de trancher entre différentes interprétations. Dans le cas de la relocalisation du soi dans l'illusion du corps entier, il peut être difficile d'interpréter la relocalisation du soi lorsque celle-ci est à mi-chemin entre le corps réel et l'avatar virtuel. Ce phénomène pourrait être dû à une mise à jour de l'intégration multisensorielle ou révéler une relocalisation seulement partielle du soi, voire une alternance de localisation du soi entre le corps réel et celui de l'avatar virtuel. Les mesures utilisées ne capturent donc pas exactement la phénoménologie de l'expérience vécue et laissent place à diverses interprétations.

D'autre part, les neurosciences cognitives cherchent à obtenir des mesures objectives et répliquables. Les tentatives de recueillir des marqueurs électrophysiologiques des changements phénoménologiques rapportés lors de l'illusion du corps entier en témoignent. Les neurosciences cognitives cherchent à objectiver un phénomène qu'elles reconnaissent comme subjectif, notamment en le réduisant à des phénomènes qu'elles maîtrisent mieux dans l'étude du corps-objet, à savoir les mécanismes multisensoriels et cérébraux. Pour cela, elles emploient des techniques d'étude du corps-objet afin d'aborder le corps-sujet. Ces mesures, nous l'avons vu, peuvent être des scores de réponse à des questionnaires, des réponses comportementales ou des réponses physiologiques. Les questionnaires proposés sont explicites et par conséquent réflexifs. Il en va de même pour les tâches comportementales : ces mesures sont plus ou moins explicites et nécessitent que le participant engage des processus réflexifs, ne serait-ce que pour comprendre l'instruction et apporter une réponse, même si celle-ci ne



mentionne pas clairement le soi corporel. Cette méthodologie, considérée comme nécessaire et adaptée pour l'étude du corps-objet, pourrait s'avérer trop limitée, voire inadaptée à l'étude du corps-sujet. Elle est cependant employée par les neurosciences de façon plus ou moins assumée. Utiliser d'autres méthodes, telles que l'introspection, des entretiens phénoménologiques ou des expériences de pensée, sortirait d'ailleurs l'étude du cadre disciplinaire des neurosciences cognitives.

Conclusion et perspectives

Cet article illustre la manière dont les neurosciences cognitives s'emparent d'outils conceptuels développés par la philosophie, tels que le « corps-vécu » et le « corps-objet », pour les intégrer dans leurs propres investigations. Cela passe notamment par la création d'un nouveau concept sensé effacer la distinction entre corps-vécu et corps-objet : le soi corporel. Les études cliniques et les travaux expérimentaux permettent d'approfondir et de nuancer les différentes expériences liées au soi corporel. Les neurosciences cognitives apportent ainsi un fondement empirique aux théories philosophiques. En retour, la philosophie dispose des méthodes conceptuelles qui relèveraient d'éventuels sauts conceptuels ou défauts théoriques rencontrés dans les conceptions neuroscientifiques du soi. Elle pourrait également proposer une homogénéisation des concepts. Pour relever le défi de l'étude du soi corporel, un travail commun interdisciplinaire semble donc nécessaire.

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