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Interoception and embodiment in patients with bilateral vestibulopathy

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Abstract

There are tight functional and anatomical links between the vestibular and interoceptive systems, and both systems have shown to fundamentally underlie emotional processes and our sense of a bodily self. Yet, nothing is known about how long-term bilateral vestibulopathy (BVP) influences interoception and its relation to embodiment and the sense of self. We thus compared cardiac interoceptive accuracy, confidence in the performance, and general body awareness in 25 BVP patients and healthy controls using a heartbeat tracking task, self-reports about interoceptive awareness, as well as measures of self-localization and of self-body closeness. Results showed no difference between patients and controls regarding interoceptive accuracy, confidence and body awareness, suggesting that long-term BVP does not influence cardiac interoception. Patients and controls did not differ either regarding self-location and self-body closeness. However, in our overall sample of patients and controls, we found that interoceptive accuracy increased with perceived self-body closeness, suggesting that anchoring the self to the body is generally linked with better cardiac interoception. This result is in line with previous suggestions of an important contribution of interoception to the sense of embodiment.

Introduction

Vestibular disorders are typically associated with deficits in balance and eye movements control. In addition to these deficits in reflexes, higher-level functions are often affected [1]. While most research has focused on spatial cognition, recent evidence in healthy participants suggests a vestibular contribution to cognitive and emotional functions, such as own-body perception, mood, empathy, and decision making [2]. In line with this, clinical studies showed that patients with **mainly unilateral peripheral vestibular disorders** report increased separation of the self from the body, symptoms of depersonalization and derealization (**reviewed in [3]**), **as well as** higher anxiety and depression (**reviewed in [4]**). Yet, the mechanisms underlying such deficits remain poorly understood, and it has been emphasized that further investigations are needed to better understand the full spectrum of high-level disorders associated with **peripheral** vestibular deficits, in particular with bilateral **vestibulopathy (BVP)** [5].

One way through which vestibular disorders may affect own-body and self-perception as well as emotional processes might be a change in the ability to perceive the internal states of the body. Interoception is the sense of the internal physiological condition [6, 7], originating from receptors in the gastrointestinal tract, kidneys, heart, blood vessels, etc. Interoception underpins emotional processes [7], and like the vestibular system, it is fundamental to the multisensory mechanisms underlying own-body and self perception [8–10]. Importantly, the vestibular and interoceptive systems are strongly interconnected at both anatomical and functional levels. **Studies in animals showed that** vestibular signals project to areas processing interoceptive signals in the brainstem, such as in the parabrachial nuclei, and project to the insular cortex [11]. **Conversely, interoceptive signals – such as those generated by mechanical stimulation of visceral receptors – can modulate the spontaneous firing rate of vestibular nuclei neurons** [12]. At a functional level, both vestibular and interoceptive systems inform about self-motion and gravity [11] and **they** interact to adapt blood pressure [13] **and respiratory pattern [14] to own body movement and** orientation. **However,** direct studies investigating the link between vestibular and interoceptive processes are to our knowledge lacking in the field of self-perception. It remains **especially** unclear to what degree **BVP** influences interoception and its relation to embodiment and the sense of self.

The present study primarily aims at evaluating the influence of long-term **BVP** on interoception. We measured the ability to perceive interoceptive signals using the heartbeat tracking task (HBTT), **during which participants estimated the number of heartbeats felt during a given time interval [15, 16]. The hypothesis about how BVP influences cardiac interoception is two-fold in that there is evidence to suggest either an increase in interoceptive sensitivity or a decrease in interoceptive sensitivity. On the one hand, considering that both vestibular and interoceptive signals contribute to own-body perception, BVP may result in a higher reliance on interoceptive signals to maintain stable the perceived anchoring of the self to the body, thus resulting in enhanced interoceptive sensitivity. Cross-modal plasticity and higher awareness for intact sensory systems have been observed in many instances of sensory deprivation (reviewed in [17]), such as in individuals with congenital blindness, showing higher odor awareness and lower odor detection**

threshold [18]. This mechanism might be prominent in the perception of gravity, shown to be crucial for the experienced self-location: BVP patients missing head-centered vestibular organs may rely more on information from trunk-centered inner organs typically linked to interoception [19]. On the other hand, the loss of vestibular signals may alter the processing of interoceptive signals in multisensory brainstem and cortical regions, thus decreasing interoceptive sensitivity. In line with this hypothesis is evidence of poorer cardiac interoception in patients with olfactory deficits [20] and in patients with spinal cord injury [21] when compared to healthy participants.

The secondary aim of the study is to evaluate the relation between the vestibular system, cardiac interoception and the sense of embodiment. We measured interoceptive awareness using the Body Perception Questionnaire (BPQ) [22]. BPQ scores have been positively correlated with gray matter volume in the right anterior insula, a core region for interoception [23]. Furthermore, we tested two aspects of self-location and analyzed them in relation to interoceptive abilities: (1) *Where* in the body is the self perceived, and (2) *How strong* is the anchoring of the self to the body. Self-location can be measured by asking participants to point on a human silhouette [24, 25]. Studies showed that most participants locate their self either in their head or trunk. Head-locators and trunk-locators may differ on their interoceptive abilities and personality traits [26, 27]. How strong the self is perceived to be anchored to the body can be measured by pictorial descriptions of self-body closeness [28]. We hypothesized that patients with BVP may report self-location differently than controls, potentially more around the trunk, a major egocentric reference frame whose importance might be further increased through higher reliance on somatosensory [29] and interoceptive signals.

Methods

Participants

We tested 25 patients with a BVP and 25 healthy controls matched for sex, age, education and body-mass index (Table 1). All patients had weak responses to a bithermal caloric test with water at 44°C and 30°C (mean slow phase eye velocity < 5°/s; left ear (mean ± SD): 44°C: 1.4 ± 2.3°/s, 30°C: 2.0 ± 2.6°/s; right ear: 44°C: 1.8 ± 2.7°/s, 30°C: 2.5 ± 5.3°/s) and reduced responses to the video head impulse test (gain < 0.7; horizontal canals: 0.33 ± 0.27; anterior canals: 0.26 ± 0.23; posterior canals: 0.27 ± 0.24). Otolithic functions were evaluated by cervical vestibular-evoked myogenic potentials (cVEMPs) over the sternocleidomastoid muscles and ocular vestibular-evoked myogenic potentials (oVEMPs) over the inferior oblique muscles. cVEMPs were present in the left ear for 9 patients (p13-n23 amplitude: 104 ± 36 µV) and in the right ear for 13 patients (75 ± 47 µV). oVEMPs were present in the left ear for 5 patients (2.3 ± 1.4 µV) and in the right ear for 6 patients (3.4 ± 1.0 µV). Controls had no history of vestibular, neurological, or psychiatric disease. All patients were right-handed (Edinburgh Handedness inventory: 97 ± 6%), 23 controls were right-handed (89 ± 13 %) and 2 were left-handed (-100%). All participants had normal or corrected-to-normal vision. Anxiety and depression measured with the Hospital Anxiety and

Depression scale [30] did not differ between patients and controls (**Table 1**). All participants were informed about the study and gave written informed consent. Procedures were approved by the Ethics Committee and followed the Declaration of Helsinki.

Heartbeat tracking task: procedures and analyses

Participants performed the HBTT following established procedures [16]. They sat comfortably on a stool with their arms dangling and counted the heartbeats they felt between two identical sounds, defining six time intervals of 25, 30, 35, 40, 45 and 50 s. They were instructed to count silently, without checking their heartbeat manually by pressing a body part on the floor or against their seat. The experimenter controlled that they followed the instructions. After each second sound, participants verbally indicated how many heartbeats they perceived. The six time intervals were presented once in a randomized order using Superlab 4.5 (Cedrus, San Pedro, USA). Participants could take a break for as long as they wanted between trials. Heartbeats were simultaneously recorded using FLAT Active electrodes (Biosemi, Amsterdam, The Netherlands) placed on their sternum and left chest. For each time interval, an interoceptive accuracy score was calculated using the following formula [16]:

$$1 - \frac{| \text{Recorded Heart Beats} - \text{Counted Heart Beats} |}{(\text{Counted Heart Beats} + \text{Recorded Heart Beats})/2}$$

Interoceptive accuracy scores can range from -1 to 1, indicating very poor to perfect performance. A mean interoceptive accuracy score was calculated for each participant by averaging the accuracy scores over the six time intervals.

Immediately after each trial, participants rated the confidence in their judgment on a vertical, continuous visual analogue scale, using pencil and paper. The upper part of the scale referred to “*Completely confident (perfect perception of my heartbeats)*” and the bottom part to “*Random answer (no awareness of my heartbeats)*”. For each time interval, confidence ratings were measured in mm and converted in percentage (Random answer: 0%; Completely confident: 100%). A mean confidence score was calculated for each participant by averaging the accuracy scores over the six time intervals.

Body awareness

Participants rated 45 items from the body awareness subscale of the BPQ [22]. They rated how aware they are of their bodily processes using a five-point scale ranging from “never” to “always”. One patient did not answer the questionnaire.

Self-location

Self-location was measured by a pointing task [31] on a computer screen (1366 × 768 pixels). After they read the instructions “*Where do you locate your ‘self’? On this picture representing a body, indicate the location (a single point) which according to you best represents the location of the self*”, participants were shown a human silhouette of their own sex, once from the front, once from the back, and once from the profile (**Figure 2A**), in a randomized order. With a computer mouse in their dominant hand they clicked on a point of the silhouette that best described the location of their self. Instructions and pictures were

presented with PsychoPy [32], which also recorded the coordinates of pointing. One control did not complete the task.

Self-body closeness

Participants reported the perceived closeness between self-body, self-immediate body environment, body-immediate body environment, and self-others using simple pictorial descriptions [28] adapted from the Inclusion of Other in the Self scale [33] (**Figure 3**). They reported the average perception over the last year. Participants selected 1 out of 7 pictorial descriptions of the closeness between, e.g., their self and body, whereby two distinct circles represent clear separation between their self and body (score = 1) and two overlapping circles represent maximal closeness between their self and body (score = 7).

Organization of a session

Participants completed the HBTT, BPQ, self-location and self-body closeness tasks in a random order.

Statistical analyses

As most of the dependent variables were not normally distributed (Shapiro-Wilk test), we used non-parametric procedures (SPSS 25, IBM, USA): inter-group differences were analyzed using Mann-Whitney U tests and Spearman correlations were used to analyze links between self-body closeness and cardiac interoception. Differences were considered significant for $p < 0.05$.

Results

Interoceptive accuracy, confidence and body awareness

We found no significant difference between patients and controls regarding their interoceptive accuracy ($U = 261.5$, $Z = -0.99$, $p = 0.32$) and confidence in their judgment ($U = 287.0$, $Z = -0.50$, $p = 0.62$; **Fig. 1A**). Similarly, body awareness as measured by BPQ scores did not differ significantly between patients and controls ($U = 287.0$, $Z = -0.02$, $p = 0.98$; **Fig. 1B**).

Self-location and its relation to cardiac interoception

Results from the pointing task revealed no significant difference in the coordinates of self-location between patients and controls for the front (x : $U = 246.0$, $Z = -1.49$, $p = 0.14$; y : $U = 273.0$, $Z = -0.98$, $p = 0.33$), back (x : $U = 290.0$, $Z = -0.66$, $p = 0.51$; y : $U = 308.0$, $Z = -0.32$, $p = 0.75$) and side (x : $U = 257.0$, $Z = -1.28$, $p = 0.20$; y : $U = 296.0$, $Z = -0.55$, $p = 0.59$) views of the body (**Fig. 2A**).

In a second step, patients and controls were allocated to the *head-locator* and *trunk-locator* groups, corresponding to any self-location above or below the neck, respectively: 12 patients and 13 controls were head-locators; 13 patients and 11 controls were trunk-locators (**Fig. 2B**). The proportion of head- and trunk-locators was similar in both groups ($\chi^2 = 0.19$, $p = 0.78$). Head- and trunk-locators did not differ regarding their interoceptive accuracy (patients: $U = 69.5$, $Z = -0.46$, $p = 0.64$; controls: $U = 67.0$, $Z = -0.26$, $p = 0.79$), confidence judgment (patients: $U = 66.0$, $Z = -0.65$, $p = 0.51$; controls: $U = 47.5$, $Z = 1.39$,

p = 0.16) and body awareness (patients: $U = 60.5$, $Z = -0.64$, $p = 0.52$; controls: $U = 51.5$, $Z = -0.89$, $p = 0.37$) (**Fig. 2C**). In addition, there was no difference between patients and controls from the head-location group (interoceptive accuracy: $U = 54.5$, $Z = -1.28$, $p = 0.20$; confidence: $U = 68.5$, $Z = -0.52$, $p = 0.60$; body awareness: $U = 76.0$, $Z = -0.05$, $p = 0.96$) and no difference between patients and controls from the trunk-location group (interoceptive accuracy: $U = 69.0$, $Z = -0.14$, $p = 0.88$; confidence: $U = 53.0$, $Z = -1.07$, $p = 0.28$; body awareness: $U = 72.0$, $Z = -0.27$, $p = 0.78$).

Perceived self-body closeness and its relation to cardiac interoception

Fig. 3 shows that patients and controls did not differ significantly regarding the perceived strength of closeness between their self and body ($U = 250.0$, $Z = -0.83$, $p = 0.41$), self and immediate body environment ($U = 285.5$, $Z = -0.05$, $p = 0.96$), body and immediate body environment ($U = 262.0$, $Z = -0.54$, $p = 0.59$), or self and others ($U = 282.0$, $Z = -0.13$, $p = 0.90$). However, we note large interindividual variability in these judgments, which were explored in correlation analyzes.

Our exploratory analyzes significantly related self-body closeness and cardiac interoception. In the overall population, interoceptive accuracy correlated positively with self-body closeness ($\rho = 0.31$, $p = 0.03$), indicating that stronger anchoring of the self to the body was associated with better cardiac interoception (**Fig. 4A**). Conversely, interoceptive accuracy negatively correlated with self-environment closeness ($\rho = -0.29$, $p = 0.04$), showing that lower anchoring of the self to the body was linked to lower cardiac interoception (**Fig. 4B**). Yet, when considering each group separately, interoceptive accuracy did not correlate with self-body closeness (patients: $\rho = 0.28$, $p = 0.18$; controls: $\rho = 0.37$, $p = 0.07$) and self-environment closeness (patients: $\rho = -0.35$, $p = 0.08$; controls: $\rho = -0.23$, $p = 0.26$).

In the overall population, body awareness (BPQ scores) was also positively correlated with self-body closeness ($\rho = 0.31$, $p = 0.03$; **Fig. 4C**), pointing to a link between interoceptive awareness and embodiment. BPQ scores did not correlate with self-body closeness in the patients ($\rho = 0.28$, $p = 0.19$) and in the controls ($\rho = 0.38$, $p = 0.07$) when considered separately. Finally, in the whole population, self-body closeness did not correlate with anxiety ($\rho = -0.23$, $p = 0.11$) and depression ($\rho = -0.20$, $p = 0.16$). However, self-body closeness was negatively correlated with anxiety ($\rho = -0.41$, $p = 0.04$) and depression ($\rho = -0.54$, $p = 0.005$) in the patients, but not in controls (anxiety: $\rho = -0.16$, $p = 0.44$; depression: $\rho = 0.02$, $p = 0.93$).

Discussion

The tasks used here revealed no difference between **BVP** patients and a carefully matched control group regarding their interoceptive accuracy, body awareness, self-location, and self-body closeness. Such negative findings are difficult to interpret and it cannot be excluded that differences could be found with other measures of interoception (see [34] for a critical account of the HBTT), or with larger samples. Nevertheless, our results help to better delineate the range of perceptual and cognitive deficits associated with **BVP**. The general trend to publish only positive results might bias the understanding of the patients'

symptomatology. Negative findings should thus be reported more systematically in clinical neuroscience to avoid such bias. Furthermore, explorative correlative analyses revealed a relation between interoception and self-body closeness, which might be important to consider in future studies.

No evidence for a change in cardiac interoception in bilateral vestibulopathy

Our results show no significant difference between BVP patients and controls in the tasks we used, suggesting that a long-lasting BVP does not change cardiac sensitivity or interoceptive awareness [35]. The results do not support the hypothesis of increased interoceptive sensitivity, suggesting that BVP does not involve higher focus on interoception through higher reliance on signals from trunk-centered inner organs. Likewise, the results do not support the hypothesis of decreased cardiac interoceptive sensitivity in BVP that may arise from altered interoceptive information processing in multisensory brainstem and cortical regions. Our findings contrast with alterations of cardiac interoception also measured with the HBTT in patients with olfactory [20] and sensorimotor deficits [21].

The lack of significant difference found in our study might be explained by several factors. First, the absence of effect of BVP on cardiac interoception may reflect a lack of relevance of vestibular signals for cardiac interoception or the poor interactions between these systems. This seems in contrast with the wealth of data on the anatomical and functional interplay between the vestibular and interoceptive systems, including the cardiovascular system [12–14, 36]. There is, for example, evidence that stimulation of the semi-circular canals can change the respiratory frequency in healthy participants, whereas this effect is not consistent in patients with BVP [14]. Similarly, caloric vestibular stimulation changed heart rate variability and blood pressure variability in healthy participant, an effect which was absent in a patient with BVP [36]. Second, the absence of effect of BVP on cardiac interoception may be related to the fact that BVP patients were tested years after the onset of the disease. Future studies should test whether a similar result is found in the acute phase of the BVP. Third, we only assessed cardiac interoception, while other aspects of interoception, e.g. related to graviceptors in the viscera, have not been measured. It is still an open debate to what extent a common interoceptive ability exists and how much from cardiac interoception can be generalized to other interoceptive systems [37]. Future studies should therefore investigate the link between vestibular information processing and other interoceptive signals, such as respiratory or gastric signals. Although graviceptors in the viscera contribute to encode own-body orientation in healthy participants [38], it remains to be established whether this information is used differently in BVP patients and if it also contributes significantly to an embodied sense of self.

No difference in perceived self-location and self-body closeness in bilateral vestibulopathy

Self-reports showed no difference between patients and controls regarding *where* in their body the self was perceived and *how strong* the self was perceived as anchored to the body. The vestibular system has been described as crucially involved in *perceiving* self-location within the bodily borders (reviewed in [8]). A higher occurrence of sensations of detachment of the self from the body has been reported in a

sample of 60 patients with mainly unilateral peripheral vestibular disorders than in sex- and age-matched healthy participants [39]. A prospective study in 210 patients suffering from vertigo and dizziness showed that full-blown out-of-body experiences were also more frequent in patients with documented unilateral peripheral vestibular disorders than in sex- and age-matched healthy participants [40]. Second, there is evidence that galvanic vestibular stimulation in healthy participants can modulate the anchoring of the self to the body as measured by tactile perception tasks [41]. Thus, while the vestibular system might be important for an embodied self-location, self-reports used in our study showed no effect of BVP on self-location and on the perceived self-body closeness.

In acute peripheral vestibular disorders (and during artificial vestibular stimulation in healthy participants), the central nervous system receives signals from the inner ear about self-motion and self-orientation that are incongruent with visual and somatosensory signals, thereby creating sensory mismatch and perceptual incoherence. By contrast, as vestibular information is missing in BVP patients, it does not conflict with (or confirm) visual and somatosensory encoding of self-motion. We argue that the absence of sensory mismatch in BVP may account for normal self-location and self-body closeness in the present study. In line with this idea, patients with a long history of BVP show similar abilities than controls to take another person's viewpoint, thus to mentally detached oneself from an embodied self-location [28]. By contrast, this perspective-taking task is influenced by vestibular stimulation on a rotatory chair in healthy participants [42], and is impaired in patients with unilateral vestibular failure (benign paroxysmal positional vertigo and acute vestibular neuritis) [43].

The self-localization task and the measure of self-body closeness yielded congruent results with previous studies in younger participants. As in previous studies, both groups localized their self either in their head or trunk [24, 25], and presented a similar degree of self-body closeness using an adaptation of the Inclusion of Other in the Self scale [28]. We also found a similar proportion of head- and trunk-locators. These interindividual differences in the perceived self-location have been related to cultural factors and personality traits [26]. Pioneering studies [e.g. 44] related self-location in the head to the origin of the multimodal, but mainly visual, first-person perspective. Self-location in the trunk, especially near the heart, was found in participants characterizing themselves as emotional, feminine and interpersonally warm [26]. Finally, we found no relation between head/trunk-location and interoceptive accuracy or body awareness, and could therefore not support the hypothesis that trunk-locators used cardiac interoceptive information differently.

Higher self-body closeness is associated with better interoceptive accuracy

Independent of the group, we found in an exploratory analysis, that interoceptive accuracy was positively correlated to self-body closeness and negatively correlated with self-environment closeness. This suggests that stronger anchoring of the self to the body, i.e. embodiment, is linked to better capacity to perceive and report cardiac interoceptive signals. In line with this finding, there is evidence that cardiac interoceptive accuracy can predict the malleability of body representations as measured by a multisensory illusion in

healthy participants (i.e. the rubber hand illusion [45]). Furthermore, body awareness (BPQ scores) also increased with self-body closeness, supporting the idea that a stronger sense of embodiment co-occurs with higher awareness of signals from internal organs. Finally, we found that self-body closeness decreased with increasing anxiety and depression in BFV patients, but not in controls, despite the fact that controls and patients do not differ in their anxiety and depression score. A recent prospective study reported that anxiety was a predictor of out-of-body experiences in patients suffering from dizziness and vertigo, but not in healthy controls [40]. Altogether, these results highlight the interplay between anxiety, depression and depersonalization-derealization symptoms in patients with vestibular disorders [40, 46, 47].

Limitations of the study and perspectives

Here, self-location was reduced to the coordinates of a single point in space, although self-location has also been defined as a volume occupied by the self in space [8], and has even been linked to peripersonal space [48]. Future studies should endeavor to measure self-location in BVP patients using tasks allowing 3D measures of self-location, e.g. using virtual reality [49], or measures of the peripersonal space boundaries. We also note that our negative findings may also be due to the fact that we used only self-reports to measure the *perceived* self-body closeness, rather than objective measures. Other measures have been proposed where participants explicitly evaluate their self-location and self-identification with an avatar shown in a head-mounted display in virtual reality. For example, when participants received a tactile stimulation on their back and observed an avatar being stroked at the same time on the same body region, they self-identified with the avatar and localized themselves closer to it (i.e., disembodied self-location) [49]. It will be important in future studies to investigate how BVP patients experience self-body closeness during experimentally-induced sensations of disembodied self-location.

Conclusions

The present study should help understand the complex symptomatology of patients with BVP, who present with deficits reaching far beyond the well-known imbalance and oscillopsia, including alterations of the most fundamental aspects of the self.

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Figure Legends

Figure 1. Cardiac interoception. (A) Interoceptive accuracy and confidence in the judgment for **BVP** patients (*red*) and healthy controls (*green*). (B) Score to the body awareness scale of the Body Perception Questionnaire for **BVP** patients (*red*) and controls (*green*). Box and whiskers plots show medians and interquartile ranges (10–90). Means are shown as + and dots are outliers.

Figure 2. Self-location and its relation to cardiac interoception. (A) Self-location indicated by patients (*red dots*) and controls (*green squares*) on a human silhouette seen from the back, profile and front. (B) Histograms show the number of participants according to the y coordinates of self-location. (C) Interoceptive accuracy compared in head- and trunk-locators for the patients (*red*) and controls (*green*). Box and whiskers plots show medians and interquartile ranges (10–90). Means are shown as + and dots are outliers.

Figure 3. Reported self–body closeness. Seven pairs of circles at the bottom of the figure were presented to participants, who had to indicate which one better represented the perceived degree of closeness between two items, such as their self and body. Box and whiskers plots show medians and interquartile ranges (10–90). Means are shown as + and dots are outliers.

Figure 4. Relation between self–body closeness, cardiac interoception and body awareness. Correlation between interoceptive accuracy and self–body closeness (A), between interoceptive accuracy and self–environment closeness (B) and between body awareness (BPQ score) and self–body closeness (C).

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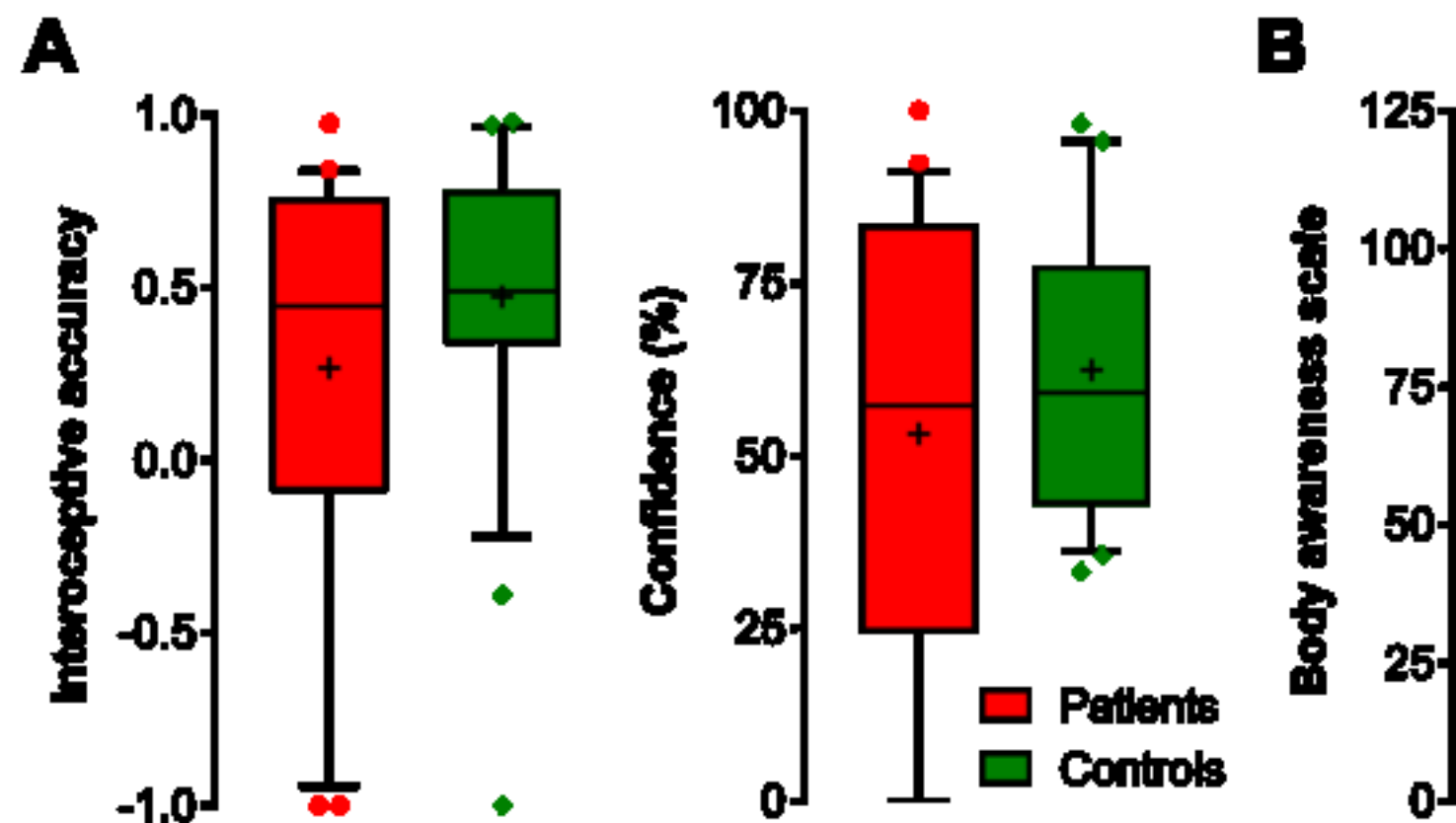


Figure 2

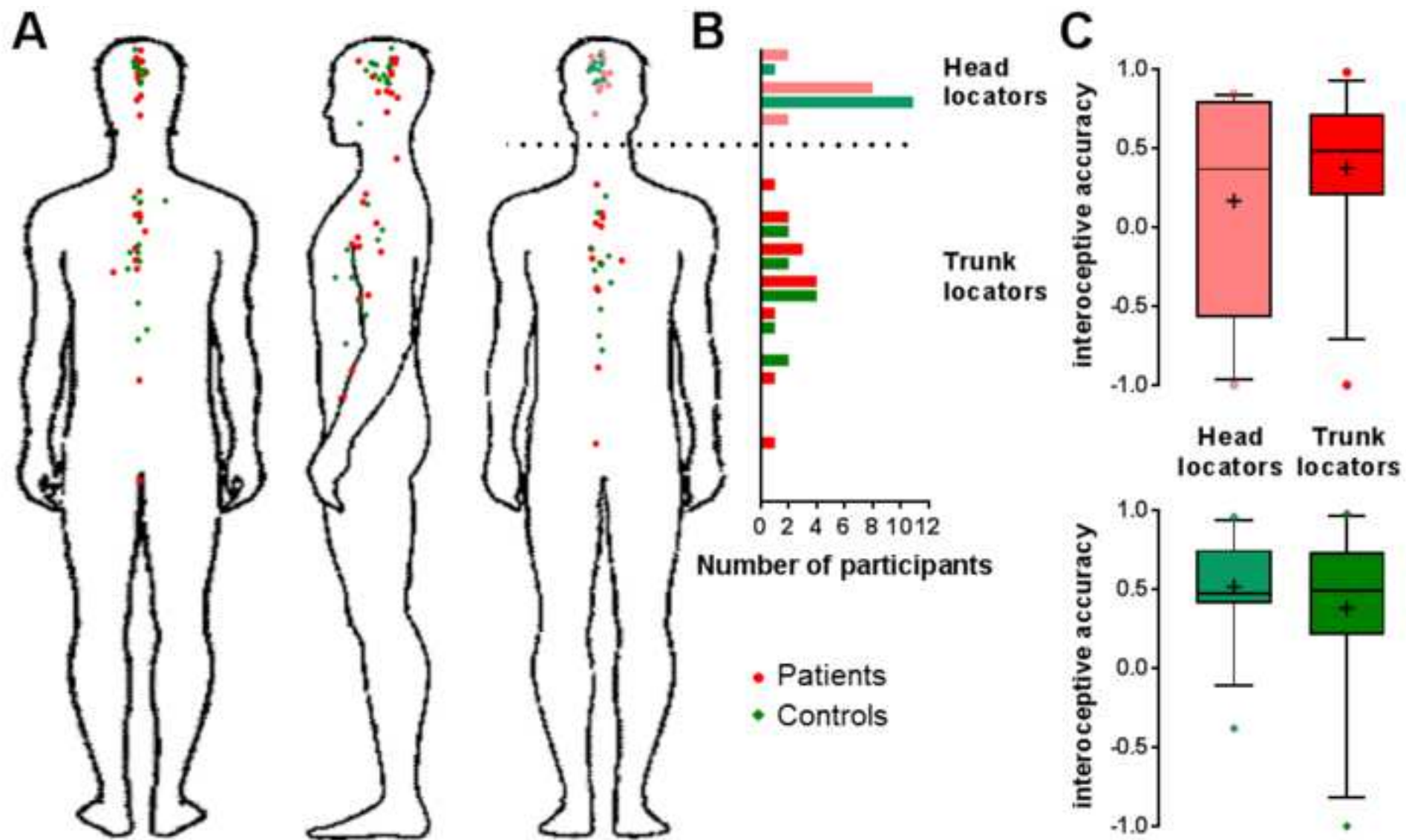


Figure 3

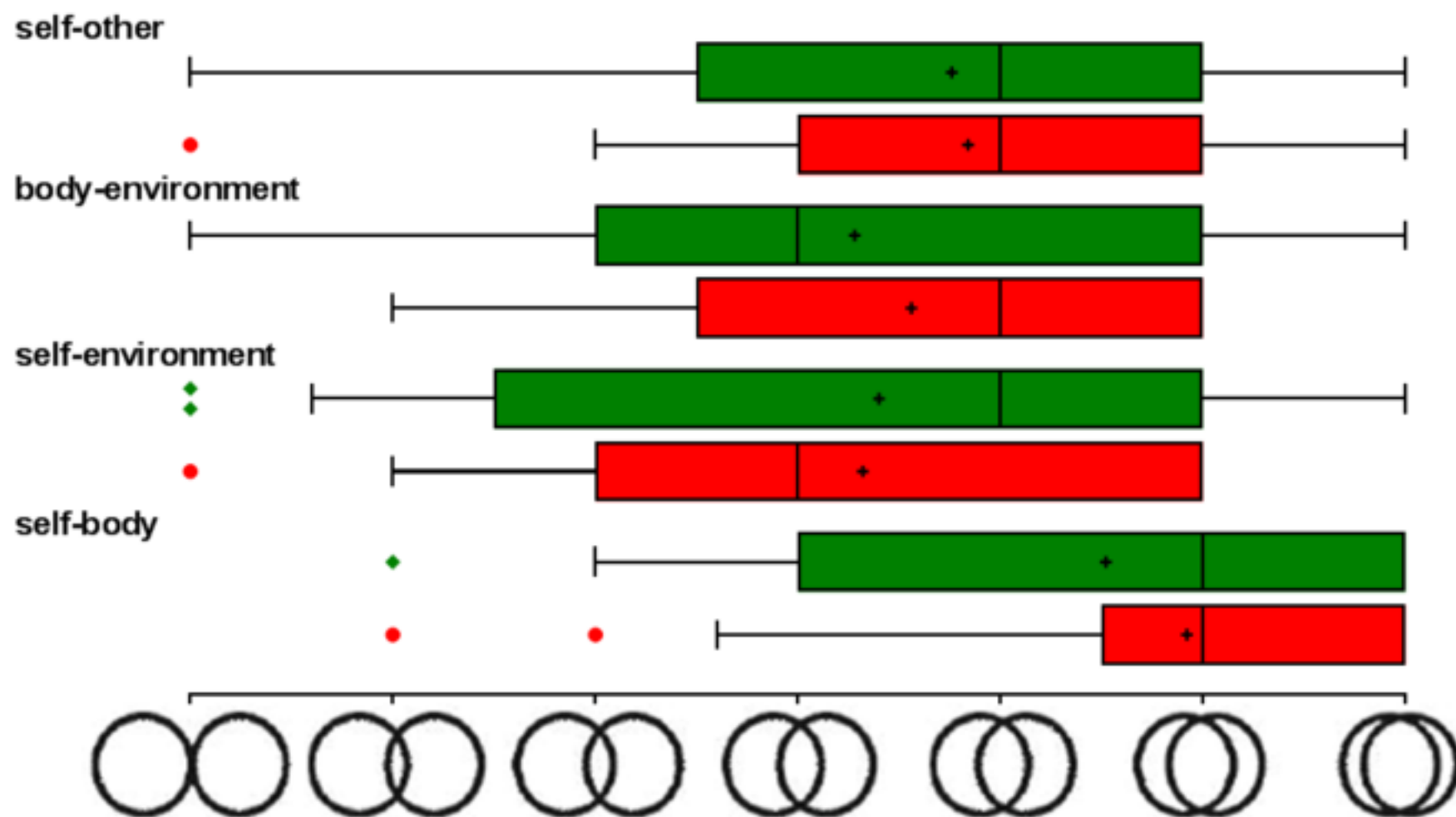


Figure 4

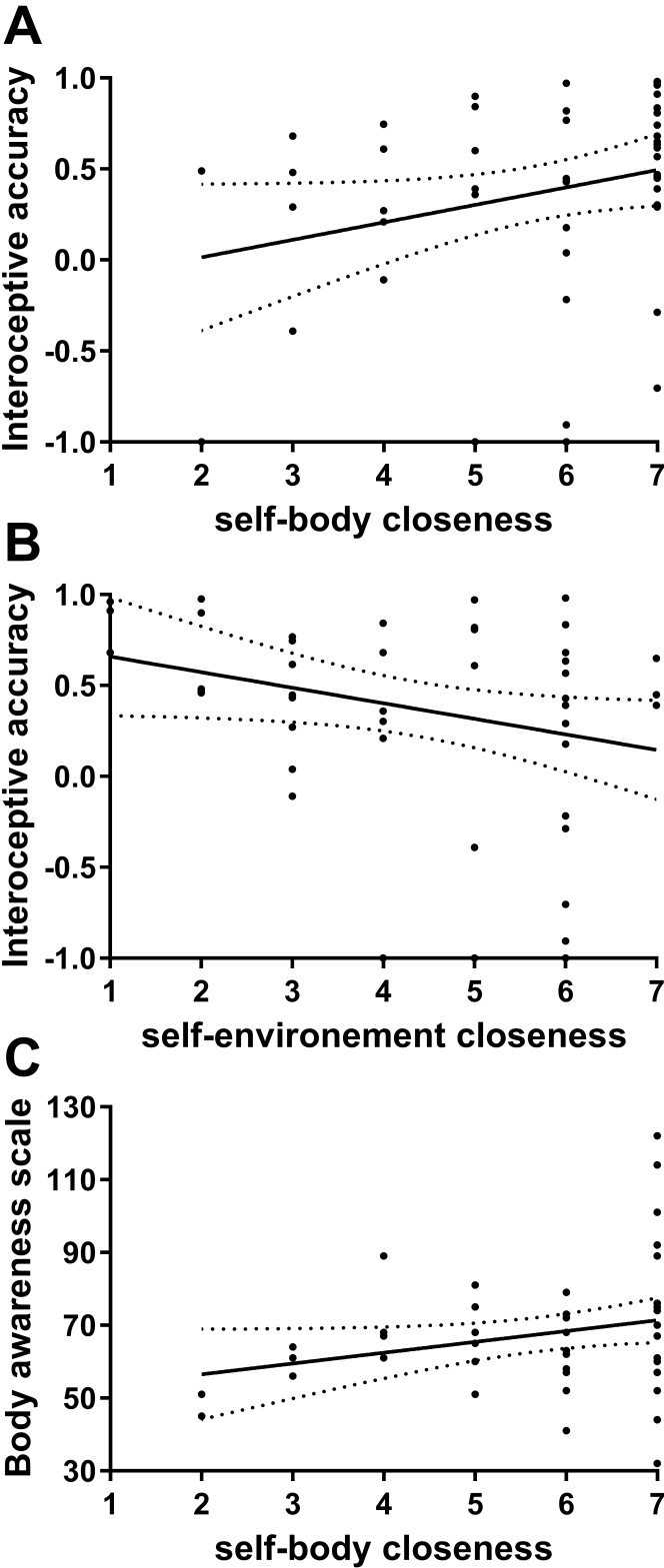


Table1

	Patient	Controls	Statistics
Males/Females (n)	11/14	11/14	–
Age (years)	60 ± 13	61 ± 11	t = −0.43, p = 0.67
Education (%)			
Level 1	8	4	χ = 3.72, p = 0.45
Level 2	4	8	
Level 3	16	20	
Level 4	32	12	
Level 5	40	56	
Body-mass index	24 ± 4	24 ± 3	t = −0.10, p = 0.92
Anxiety score	8.3 ± 2.5	7.1 ± 3.1	t = −0.63, p = 0.53
Depression score	4.0 ± 2.4	3.7 ± 2.6	t = 0.34, p = 0.74

Table 1. Demographic and clinical characteristics of **BVP patients and healthy controls.** Highest education level according to 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. Mean ± SD. Anxiety and depression scores were measured with the Hospital Anxiety and Depression scale.