



HAL
open science

Dynamic reconfiguration of visuomotor-related functional connectivity networks

Andrea Brovelli, Jean-Michel Badier, Francesca Bonini, Fabrice Bartolomei,
Olivier Coulon, Guillaume Auzias

► **To cite this version:**

Andrea Brovelli, Jean-Michel Badier, Francesca Bonini, Fabrice Bartolomei, Olivier Coulon, et al..
Dynamic reconfiguration of visuomotor-related functional connectivity networks. *Journal of Neuro-*
science, 2016, 37 (4), pp.839-853. 10.1523/JNEUROSCI.1672-16.2016 . hal-01464162

HAL Id: hal-01464162

<https://amu.hal.science/hal-01464162v1>

Submitted on 10 Feb 2017

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Research Articles: Behavioral/Cognitive

Dynamic reconfiguration of visuomotor-related functional connectivity networks

Andrea Brovelli¹, Jean-Michel Badier^{2,3}, Francesca Bonini^{2,3}, Fabrice Bartolomei^{2,3}, Olivier Coulon^{1,4,*} and Guillaume Auzias^{1,4,*}

¹Institut de Neurosciences de la Timone UMR 7289, Aix Marseille Université, CNRS, 13385, Marseille, France

²Aix Marseille Université, INS UMR_S 1106, 13005, Marseille, France

³Inserm, UMR_S 1106, 13005, Marseille, France

⁴Aix-Marseille Université, CNRS, LSIS UMR 7296, Marseille, France

DOI: 10.1523/JNEUROSCI.1672-16.2016

Received: 17 May 2016

Revised: 3 November 2016

Accepted: 12 November 2016

Published: 15 December 2016

Author contributions: A.B. designed research; A.B., B.J.-M., and F. Bonini performed research; A.B., F. Bartolomei, O.C., and G.A. contributed unpublished reagents/analytic tools; A.B. analyzed data; A.B., O.C., and G.A. wrote the paper.

*equal contribution

We are extremely thankful to Faical Isbaine and Sophie Chen for helping in the MEG experiments, and to Patrick Marquis and Catherine Liegeois-Chauvel for SEEG experiments. This work was partly supported by Projets exploratoires pluridisciplinaires (PEPS) from the CNRS/Inserm/Inria "Bio-math-Info" entitled "Computational and neurophysiological bases of goal-directed and habit learning". This work was performed on a MEG platform member of France Life Imaging network (grant ANR-11-INBS-0006).

Corresponding author: Andrea Brovelli, andrea.brovelli@univ-amu.fr, Institut de Neurosciences de la Timone (INT), UMR 7289 CNRS, Aix Marseille University, Campus de Santé Timone, 27 Bd. Jean Moulin, 13385 Marseille, France, Tel.: 0033 4 91 16 43 99, Fax: 0033 4 91 16 44 98

Cite as: J. Neurosci 2016; 10.1523/JNEUROSCI.1672-16.2016

Alerts: Sign up at www.jneurosci.org/cgi/alerts to receive customized email alerts when the fully formatted version of this article is published.

Accepted manuscripts are peer-reviewed but have not been through the copyediting, formatting, or proofreading process.

Copyright © 2016 the authors

1

2 **Dynamic reconfiguration of visuomotor-related**
3 **functional connectivity networks**

4

5 Andrea Brovelli¹, Jean-Michel Badier^{2, 3}, Francesca Bonini^{2, 3}, Fabrice Bartolomei^{2,3},
6 Olivier Coulon*^{1,4}, Guillaume Auzias*^{1,4}

7

8 ¹ Institut de Neurosciences de la Timone UMR 7289, Aix Marseille Université, CNRS, 13385,
9 Marseille, France

10 ² Aix Marseille Université, INS UMR_S 1106, 13005, Marseille, France

11 ³ Inserm, UMR_S 1106, 13005, Marseille, France

12 ⁴ Aix-Marseille Université, CNRS, LSIS UMR 7296, Marseille, France

13

14 *equal contribution

15

16 Corresponding author:

17 Andrea Brovelli
18 andrea.brovelli@univ-amu.fr
19 Institut de Neurosciences de la Timone (INT),
20 UMR 7289 CNRS, Aix Marseille University,
21 Campus de Santé Timone,
22 27 Bd. Jean Moulin,
23 13385 Marseille,
24 France
25 Tel.: 0033 4 91 16 43 99
26 Fax: 0033 4 91 16 44 98

27

28 Manuscript details:

29 Number of pages: 34

30 Number of figures: 8

31 Number of tables: 2

32 Number of words: 240 (abstract), 426 (introduction), 1650 (discussion)

33

34 Abbreviations

35 MEG: magnetoencephalography

36 EEG: electroencephalography

37

38 Keywords

39 High-gamma activity; functional connectivity dynamics; MEG; SEEG; executive
40 functions; dynamic reconfiguration

41

42

43 Acknowledgements

44

45 We are extremely thankful to Faical Isbaine and Sophie Chen for helping in the MEG
46 experiments, and to Patrick Marquis and Catherine Liegeois-Chauvel for SEEG
47 experiments. This work was partly supported by Projets exploratoires
48 pluridisciplinaires (PEPS) from the CNRS/Inserm/Inria “Bio-math-Info” entitled
49 “Computational and neurophysiological bases of goal-directed and habit learning”.
50 This work was performed on a MEG platform member of France Life Imaging network
51 (grant ANR-11-INBS-0006).

52 **ABSTRACT**

53 Cognitive functions arise from the coordination of large-scale brain networks. Yet, the
54 principles governing interareal functional connectivity dynamics (FCD) remain
55 elusive. Here, we test the hypothesis that human executive functions arise from the
56 dynamic interplay of multiple networks. To do so, we investigated FCD mediating a
57 key executing function, known as arbitrary visuomotor mapping, using brain
58 connectivity analyses of high-gamma activity recorded using
59 magnetoencephalography and intracranial electroencephalography. Visuomotor
60 mapping was found to arise from the dynamic interplay of three partly-overlapping
61 cortico-cortical and cortico-subcortical FC networks. First, visual and parietal regions
62 coordinated with sensorimotor and premotor areas. Second, the dorsal fronto-parietal
63 circuit together with the sensorimotor and associative fronto-striatal networks took the
64 lead. Finally, cortico-cortical interhemispheric coordination among bilateral
65 sensorimotor regions coupled with the left fronto-parietal network and visual areas.
66 We suggest that these networks reflect the processing of visual information, the
67 emergence of visuomotor plans and the processing of somatosensory reafference or
68 action's outcomes, respectively. We thus demonstrated that visuomotor integration
69 resides in the dynamic reconfiguration of multiple cortico-cortical and cortico-
70 subcortical FC networks. More generally, we showed that visuomotor-related FC is
71 non-stationary, and displays switching dynamics and areal flexibility over time scales
72 relevant for task performance. In addition, visuomotor-related FC is characterized by
73 sparse connectivity with density less than 10%. To conclude, our results elucidate the
74 relation between dynamic network reconfiguration and executive functions over short
75 time scales, and provide a candidate entry point towards a better understanding of
76 cognitive architectures.

77 SIGNIFICANCE STATEMENT

78 Executive functions are supported by the dynamic coordination of neural
79 activity over large-scale networks. The properties of large-scale brain coordination
80 processes, however, remain unclear. Using tools combining
81 magnetoencephalography and intracranial electroencephalography with brain
82 connectivity analyses, we provide evidence that visuomotor behaviors, a hallmark of
83 executive functions, are mediated by the interplay of multiple and spatially
84 overlapping sub-networks. These sub-networks span visuomotor-related areas,
85 whose cortico-cortical and cortico-subcortical interactions rapidly evolve and
86 reconfigure over time-scales relevant for behavior. Visuomotor-related Functional
87 Connectivity Dynamics (FCD) is characterized by sparse connections, non-
88 stationarity, switching dynamics and areal flexibility. We suggest that these properties
89 represent key aspects of large-scale functional networks and cognitive architectures.

90 **INTRODUCTION**

91 The dynamic coordination of neural activity over large-scale networks is
92 thought to support cognitive functions (Varela et al., 1999; von der Malsburg et al.,
93 2010; Bressler and Menon, 2010). Growing evidence from fMRI has shown that
94 spontaneous and task-related activity is composed of multiple and spatially
95 overlapping sub-networks that dynamically evolve over tens of seconds to minutes
96 (Hutchinson et al., 2013; Yeo et al., 2013; Allen et al., 2014; Calhoun et al., 2014;
97 Cole et al., 2014; Zalski et al., 2014; Hansen et al., 2015). Indeed, dynamic
98 network reconfiguration has been suggested to represent a fundamental
99 neurophysiological process supporting executive function (Bassett et al., 2011; Braun
100 et al., 2015).

101 A hallmark of executive function is the ability to rapidly associate arbitrary
102 actions to visual inputs and internal goals. This ability, known as arbitrary visuomotor
103 mapping, recruits a large-scale network comprising the sensorimotor and
104 frontoparietal circuits, in addition to medial prefrontal areas and basal ganglia (Wise
105 et al., 1996; Murray et al., 2000; Passingham et al., 2000; Wise and Murray, 2000;
106 Hadj-Bouziane et al., 2003; Petrides, 2005). In the current study, the goal was to
107 investigate whether visuomotor mapping results from the dynamic interplay of
108 multiple sub-networks. More precisely, we tested the hypothesis that multiple sub-
109 networks reconfigure in a dynamic fashion over time scales relevant for executive
110 behaviors.

111 To do so, we exploited the high-gamma activity (ranging from approximately
112 60 to 150Hz), which reflects population-level local neural activity (Ray et al., 2008;
113 Ray and Maunsell, 2011). In humans, power modulations in the high-gamma range
114 are commonly recorded using magnetoencephalography (MEG) and intracranial
115 electroencephalography to map task-related brain regions (Brovelli et al., 2005;
116 Crone et al., 2006; Vidal et al., 2006; Ball et al., 2008; Jerbi et al., 2009; Darvas et
117 al., 2010; Lachaux et al., 2012; Cheyne and Ferrari, 2013; Ko et al., 2013).
118 Additionally, high-gamma power modulations can be used to characterize functional
119 connectivity (FC) among brain regions supporting executive functions (Brovelli et al.,
120 2015).

121 Here, we predicted visuomotor mapping to reflect an initial activation of visual
122 circuits mediating the processing of sensory input, followed by fronto-parietal and

123 motor networks for visuomotor integration and motor planning. We tested these
124 hypotheses in a group of healthy participants during MEG recordings by combining
125 FC analysis of atlas-based HGA with methods from network science and graph
126 theory. In particular, we investigated the presence of multiple visuomotor-related
127 spatiotemporal patterns through the analysis of functional connectivity dynamics
128 (FCD). Intracranial assessment of HGA activations from MEG was also performed in
129 three epileptic patients performing the same task during stereo-
130 electroencephalographic (SEEG) recordings.

131 **MATERIALS & METHODS**

132 Experimental procedure and data acquisition

133 Experimental conditions and behavioral tasks

134 Eleven healthy participants and three epileptic patients accepted to take part
135 in our study. Healthy participants were right handed and the average age was
136 approximately 23 years (the standard deviation was 3.8 years), 4 were females and 7
137 males. All gave written informed consent according to established institutional
138 guidelines and local ethics committee, and received monetary compensation (€ 50).
139 Three patients (one right-handed female aged of 29, two right-handed males aged of
140 29 and 43) undergoing presurgical evaluation of drug-resistant epilepsy (Epilepsy
141 Unit, La Timone Hospital, Marseille, France) participated in this study. They all gave
142 their informed consent prior to their participation. The SEEG study was approved by
143 the Institutional Review Board of the French Institute of Health. Healthy participants
144 and patients performed the same behavioral task. We asked participants to perform
145 an associative visuomotor mapping task, where the relation between visual stimulus
146 and motor response is arbitrary and deterministic (Wise and Murray, 2000; Brovelli et
147 al., 2015). As shown in Figure 1A, the task required participants to perform a finger
148 movement associated to a digit number: digit “1” instructed the execution of the
149 thumb, “2” for the index finger, “3” for the middle finger and so on. Maximal reaction
150 time was 1s. After a fixed delay of 1 second following the disappearance of the digit
151 number, an outcome image was presented for 1 s and informed the subject whether
152 the response was correct, incorrect, or too late (if the reaction time exceeded 1 s).
153 Incorrect and late trials were excluded from the analysis, because they were either
154 absent or very rare (i.e., maximum 2 late trials per session). The next trial started
155 after a variable delay ranging from 2 to 3 s (randomly drawn from a uniform
156 distribution) with the presentation of another visual stimulus. Each participant
157 performed two sessions of 60 trials each (total of 120 trials). Each session included
158 three digits randomly presented in blocks of three trials. The average reaction time
159 was $0.504s \pm 0.004s$ (mean \pm s.e.m.).

160

161 Anatomical, functional and behavioral data acquisition in healthy participants

162 Anatomical MRI images were acquired for healthy participant using a 3-T
163 whole-body imager equipped with a circular polarized head coil. High-resolution

164 structural T1-weighted anatomical image (inversion-recovery sequence, $1 \times 0.75 \times 1.22$
165 mm) parallel to the anterior commissure-posterior commissure plane, covering the
166 whole brain, were acquired. Magnetoencephalographic (MEG) recordings were
167 performed using a 248 magnetometers system (4D Neuroimaging magnes 3600).
168 Visual stimuli were projected using a video projection and motor responses were
169 acquired using a LUMItouch® optical response keypad with five keys. Presentation®
170 software was used for stimulus delivery and experimental control during MEG
171 acquisition. Reaction times were computed as the time difference between stimulus
172 onset and motor response. Sampling rate was 2034.5 Hz. Location of the
173 participant's head with respect to the MEG sensors was recorded both at the
174 beginning and end of each session to potentially exclude sessions and/or participants
175 with large head movements. For each session and participant, we computed the
176 displacement between the beginning and end of a session. A supine position was
177 chosen to minimize head movements. This cut-off was decided by considering the
178 spatial distance between sources (5mm), as described in the following sections.
179 None of the participants moved more than 3 mm during all sessions. Thus, all
180 participants were considered for further analysis.

181

182 Anatomical, functional and behavioral data acquisition in epileptic patients

183 The surgical treatment of drug-resistant epilepsy may require direct
184 intracerebral recording of cortical activity IEEG in multiple brain areas in order to
185 localize the epileptic tissue to be removed. Before SEEG all patients had high
186 resolution MRI, performed with a 3T Siemens Magnetom scanner (Siemens AG,
187 Erlangen, Germany) including a three-dimensional T1-weighted acquisition.
188 Intracerebral multiple contacts electrodes (10 to 15 contacts, length: 2 mm, diameter:
189 0.8 mm, 1.5 mm apart) were implanted using a stereotactic method (Talairach et al,
190 1992). A post-operative computerized tomography (CT) scan without contrast was
191 used to verify the absence of bleeding and the location of each recording lead.
192 During this pre-surgical evaluation period, we asked patients to participate in our
193 behavioral protocol at the Timone Hospital. They were seated in a Faraday cage and
194 stimuli were presented on a display monitor at 70 cm to patient's eyes with an
195 angular size of 1.26° . Presentation® software was used for stimulus delivery and
196 experimental control during SEEG acquisition. Motor responses were acquired using
197 a 5-button response pad. SEEG signals were acquired on referential montage with a

198 sampling frequency of 1000 Hz and an acquisition band-pass filter between 0.1 and
199 200Hz.

200

201 Brain parcellation

202 In order to map brain activations and Functional Connectivity (FC) patterns to
203 specific anatomical brain networks, single-subject brain parcellation can be created
204 from macro-anatomical information, such as primary and secondary sulci, using
205 either volume-based (Lancaster et al., 2000; Tzourio-Mazoyer et al., 2002) or
206 surface-based (Fischl et al., 1999; Van Essen and Drury, 1997; Desikan et al., 2006)
207 algorithms. Recent developments now allow single-subject cortical parcellation
208 complying with a model of anatomo-functional gradients in the rostro-caudal and
209 dorso-ventral directions (Auzias et al., 2013) optimized for functional mapping using
210 HGA (Auzias et al., 2016). Such approach allows group-level analyses and
211 comparison between individual patients and healthy participants in control group. To
212 do so, we created a whole-brain parcellation including cortical (Figure 1B) and
213 subcortical (Figure 1C) regions based on macro-anatomical information. The
214 identification of the cortical regions requires several processing steps. After denoising
215 using a non-local means approach (Coupé et al., 2008), T1-weighted MR-images
216 were segmented using the FreeSurfer “recon-all” pipeline (<http://freesurfer.net>). Grey
217 and white matter segmentations of each hemisphere were imported into the
218 BrainVisa software and processed using the Morphologist pipeline procedure
219 (<http://brainvisa.info>). White matter and pial surfaces were reconstructed and
220 triangulated, and all sulci were detected and labelled automatically (Mangin et al.,
221 2004; Perrot et al., 2011). A parameterization of each hemisphere white matter mesh
222 was performed using the Cortical Surface toolbox ([http://www.meca-](http://www.meca-brain.org/software/)
223 [brain.org/software/](http://www.meca-brain.org/software/)). It resulted in a 2D orthogonal system defined on the white
224 matter mesh, constrained by a set of primary and secondary sulci (Auzias et al.,
225 2013). This parameterization naturally leads to a complete parcellation of the cortical
226 surface, the *MarsAtlas* model (Auzias et al., 2016).

227 *MarsAtlas* complies with the dorsoventral and rostrocaudal trends of cortical
228 organization (Régis et al., 2005; Pandya and Yeterian, 1985) and provides a good
229 level of both functional segregation and inter-subject matching for functional analysis
230 using single-trial MEG high-gamma activity (Auzias et al., 2016). The resulting

231 cortical surface parcellation was then propagated to the volume-based grey matter
232 segmentation, using a front propagation from the surface through the volumetric
233 cortex segmentation (Cachia et al., 2003), hence producing a volume-based
234 parcellation of the entire cortex. The parcels corresponding to the subcortical
235 structures were extracted using Freesurfer (Fischl et al, 2002). The subcortical
236 structures included in the brain parcellation were the caudate nucleus, putamen,
237 nucleus accumbens, globus pallidus, thalamus, amygdala and hippocampus. The
238 whole-brain parcellation therefore comprised 96 areas (41 cortical and 7 subcortical
239 areas per hemisphere) (Figure 1). All these processing steps can be performed using
240 the BrainVisa neuroimaging platform (<http://brainvisa.info/web/index.html>). *MarsAtlas*
241 is included in the cortical surface toolbox.

242

243 Single-trial high-gamma activity (HGA) in *MarsAtlas*

244 Preprocessing and spectral analysis of MEG and SEEG signals

245 The preprocessing and spectral analyses steps for MEG and SEEG signals
246 were identical. Concerning SEEG signals, electrode's contacts owing to the
247 epileptogenic zone were excluded from the analysis. SEEG contacts outside the
248 epileptogenic zone were chosen for analysis. In addition, epochs with signs of
249 epileptic activity were removed. MEG and SEEG signals were first down-sampled to
250 1 kHz, low-pass filtered to 250 Hz and then segmented into epochs aligned on finger
251 movement (i.e., button press). Epoch segmentation was also performed on stimulus
252 onset and the data from -0.5 and -0.1 s prior to stimulus presentation was taken as
253 baseline activity for the calculation of the single-trial high-gamma activity (HGA).
254 Artefact rejection was performed semi-automatically and by visual inspection. For
255 each movement-aligned epoch and channel, the signal variance and z-value were
256 computed over time and taken as relevant metrics for the identification of artefact
257 epochs. All trials with a variance greater than $1.5 \cdot 10^{-24}$ across channels were
258 excluded from further search of artefacts. Metrics such as the z-score, absolute z-
259 score, and range between the minimum and maximum values were also inspected to
260 detect artefacts. Channels and trials displaying outliers were removed. Two MEG
261 sensors were excluded from the analysis for all subjects.

262 Spectral density estimation was performed using multi-taper method based on
263 discrete prolate spheroidal (slepian) sequences (Percival and Walden, 1993; Mitra

264 and Pesaran, 1999). To extract high-gamma activity from 60 to 120, MEG time series
265 were multiplied by k orthogonal tapers ($k = 8$) (0.15s in duration and 60Hz of
266 frequency resolution, each stepped every 0.005s), centered at 90Hz and Fourier-
267 transformed. Complex-valued estimates of spectral measures $X_{sensor}^n(t, k)$, including
268 cross-spectral density matrices, were computed at the sensor level for each trial n ,
269 time t and taper k .

270

271 MEG source analysis and high-gamma activity

272 Source analysis requires a physical forward model or leadfield, which
273 describes the electromagnetic relation between sources and MEG sensors. The
274 leadfield combines the geometrical relation of sources (dipoles) and sensors with a
275 model of the conductive medium (i.e., the headmodel). For each participant, we
276 generated a headmodel using a single-shell model constructed from the
277 segmentation of the cortical tissue obtained from individual MRI scans as described
278 in section 3.2 (Nolte, 2003). Leadfields were not normalized. Sources were placed in
279 the single-subject volumetric parcellation regions. For each region, we computed the
280 number of sources nSP as the ratio of the volume and the volume of a sphere of
281 radius equal to 3 mm. The k-means algorithm (Tou & Gonzalez, 1974) was then used
282 to partition the 3D coordinates of the voxels within a given volumetric region into nS
283 clusters. The sources were placed at the center of each partition for each brain
284 region. The headmodel, source locations and the information about MEG sensor
285 position for both models were combined to derive single-participant leadfields. The
286 orientation of cortical sources was set perpendicular to the cortical surface, whereas
287 the orientation for subcortical sources was left unconstrained.

288 We used adaptive linear spatial filtering (Veen et al., 1997) to estimate the
289 power at the source level. In particular, we employed the Dynamical Imaging of
290 Coherent Sources (DICS) method, a beamforming algorithm for the tomographic
291 mapping in the frequency domain (Gross et al., 2001), which is a well suited for the
292 study of neural oscillatory responses based on single-trial source estimates of band-
293 limited MEG signals (for a series of review see, Hansen et al., 2010). At each source
294 location, DICS employs a spatial filter that passes activity from this location with unit
295 gain while maximally suppressing any other activity. The spatial filters were
296 computed on all trials for each time point and session, and then applied to single-trial
297 MEG data. DICS allows the estimate of complex-value spectral measures at the

298 source level, $X_{source}^n(t, k) = A(t)X_{sensor}^n(t, k)$, where $A(t)$ is the spatial filter that
299 transforms the data from the sensor to source level and $X_{sensor}^n(t, k)$ is the complex-
300 valued estimates of spectral measures, including cross-spectral density matrices,
301 computed at the sensor level for each trial n , time t and taper k (for a detailed
302 description of a similar approach see (Hipp et al., 2011)). The single-trial high-gamma
303 power at each source location was estimated by multiplying the complex spectral
304 estimates with their complex conjugate, and averaged over tapers k , $P_{source}^n(t) =$
305 $\langle X_{source}^n(t, k)X_{source}^n(t, k)^* \rangle_k$, where angle brackets refer to the average across tapers
306 and $*$ to the complex conjugate. Single-trial power estimates aligned on movement
307 and stimulus onset were log-transformed to make the data approximate Gaussian
308 and low-pass filtered at 50Hz to reduce noise. Single-trial mean power and standard
309 deviation in a time window from -0.5 and -0.1 s prior to stimulus onset was computed
310 for each source and trial, and used to z-transform single-trial movement-locked
311 power time courses. Similarly, single-trial stimulus-locked power time courses were
312 log-transformed and z-scored with respect to baseline period, so to produce HGAs
313 for the prestimulus period from -1.6 to -0.1 s with respect to stimulation for
314 subsequent functional connectivity analysis. Finally, single-trial HGA for each brain
315 region of *MarsAtlas* was computed as the mean z-transformed power values
316 averaged across all sources within the same region.

317

318 SEEG localization and high-gamma activity

319 Electrodes were localized using the CTMR toolbox (Hermes et al., 2010).
320 Briefly, post-implant CT scans were coregistered and re-sliced to the MRI coordinate
321 scans of each subject using SPM12. A manual procedure was then carried out to
322 mark the electrodes in the co-registered CT space using the CTMR toolbox. The
323 coordinates of each electrode were transformed to MRI space (1mm resolution).
324 Since we used bipolar derivations, we computed the coordinates of the mid-point
325 between pairs of adjacent electrodes. A cube of 5mm in size was placed at these
326 positions (i.e., at the position of the bipolar derivation) and each voxel of the cube
327 (1mm resolution) was labeled according to *MarsAtlas*. The location of each bipolar
328 derivation was then labelled according to the label associated to the largest number
329 of voxels within the cube. Bipolar derivations labelled in the white matter were
330 excluded from further analyses.

331 Similarly to MEG HGA estimation, single-trial power estimates in the high-
332 gamma range (60-120Hz) aligned on movement and stimulus onset were log-
333 transformed and low-pass filtered at 50Hz to reduce noise. Single-trial estimates of
334 high-gamma power were z-transformed with respect to baseline period from -0.5 and
335 -0.1 s prior to stimulus onset. Finally, single-trial HGA for each labelled brain region
336 of *MarsAtlas* was defined as the mean z-transformed power values averaged across
337 all electrodes within the same region.

338

339 Single-trial Functional Connectivity Dynamic (FCD) measures

340 Power modulations in the high-gamma range reflect the activity of local neural
341 populations (Ray et al., 2008; Ray and Maunsell, 2011). Here, we assume that
342 tracking statistical dependencies between HGA from different brain regions provides
343 information about how local processing units coordinate at the large-scale level
344 during cognitive tasks. The goal is not infer the mechanisms mediating inter-areal
345 communication. This would require complementary approaches based on the study
346 of role of neural oscillations and synchrony for inter-regional communication (e.g.,
347 Buzsáki & Schomburg, 2015; Fries, 2015). Rather, the aim was to map task-related
348 FCD onto anatomical circuits. Given the sparseness of brain regions sampled with
349 SEEG, FCD was exclusively performed for whole-brain MEG data.

350 We used linear correlation analysis to study the functional connectivity (FC)
351 between brain regions. To quantify the evolution of FC over time (i.e., FCD), we
352 computed the Pearson's correlation coefficient between pairs of HGA signals over
353 sliding windows of 500msec, stepped every 10 msec. The same procedure was
354 performed across all pairs of brain regions and for each trial. This resulted in a 4-
355 dimensional FCD matrix (i.e., regions x regions x time points x trials) representing the
356 evolution of linear correlation across all pairs of brain areas from -0.7 to 0.7s around
357 movement onset. The single-trial FCD matrix was also computed during the pre-
358 stimulus period, from -0.8 to -0.1s prior to stimulus onset for baseline. Statistical
359 analyses searched for significant modulations in movement-related FCD with respect
360 to those in the prestimulus interval.

361

362 Statistical analysis

363 Linear Mixed Effect (LME) model

364 Statistical inference of single-trial HGAs was performed using a linear mixed-
 365 effect (LME) model approach at the group level. We used a LME model, because
 366 they are particularly suited for the analysis of data collected from multiple subjects (or
 367 sessions) where it is important to take into account inter-individual variability. These
 368 models formalize the relation between a response variable and independent
 369 variables using both fixed and random effects. Fixed effects model the response
 370 variable in terms of explanatory variables as non-random quantities. For example,
 371 experimental conditions related to population mean may be considered as fixed
 372 effects. Random effects are associated with individual experimental units drawn at
 373 random from a population, which may correspond to different participants in the study
 374 (or experimental sessions). In other words, whereas fixed effects are constant,
 375 random effects are drawn from a prior known distribution. A LME model is generally
 376 expressed in matrix formulation as,

$$377 \quad y = X\beta + Zb + e \quad (1)$$

378 where y is the n -by-1 response vector and n is the number of observations. X is an n -
 379 by- p fixed-effects design matrix and β is the fixed-effect vector of p -by-1, where p is
 380 the number of fixed effects. Z is an n -by- q random-effects design matrix and b is a q -
 381 by-1 random-effects vector, where q is the number of random effects; e is the n -by-1
 382 observation error. The random-effects vector, b , and the error vector, e , were
 383 assumed to be drawn from independent normal distributions. Parameter estimation
 384 was performed using maximum likelihood method, using the *fitlme.m* function in the
 385 Statistical Toolbox of Matlab (The MathWorks, Inc.). In order to test for significant
 386 modulations in single-trial HGA and FCD measures around movement onset with
 387 respect to the baseline period, we used a random-intercept and random-slope LME
 388 model, which is described by,

$$389 \quad y(t) = \beta_0(t) + \beta_1(t)x_j + b_{0j}(t) + b_{1j}(t)z_j + \epsilon_j(t) \quad (2)$$

390 where $y(t) = [y_{bl}(1), y_{bl}(2), \dots, y_{bl}(np), y_{mv}(1, t), y_{mv}(2, t), \dots, y_{mv}(np, t)]$.

391 For MEG data analysis, $y_{bl}(j)$ was a vector containing the baseline neural
 392 activity (i.e., the HGA from single brain regions or FCD values for single pairs of
 393 regions) for all trials and sessions (i.e., data from both sessions were concatenated,
 394 because they were acquired in uninterrupted succession) for subject $j = 1, 2, \dots, np$,
 395 where np is the number of participants, at time instant t . Note that t does not refer to
 396 trials, but time within each trial. $y_{mv}(j, t)$ was a vector including brain activity across

397 all trials for subject j at time t with respect to movement onset.

398 For SEEG data analysis, statistical inference was performed at the single-
399 participant level, due to the limited number of patients and limited sampling of
400 *MarsAtlas* regions. However, given that the SEEG experiments were composed of
401 two sessions acquired at different times (approximately 1 hours interval), we modeled
402 sessions as random effects. $y_{bl}(j)$ was then a vector containing the baseline neural
403 activity (i.e., the HGA from single brain regions) for all trials for sessions $j = 1,2$, at
404 time instant t . As before, t did not refer to trials, but time within each trial. $y_{mv}(j, t)$
405 was a vector including brain activity across all trials for session j at time t with respect
406 to movement onset.

407 The following statistical analysis was similar for both MEG and SEEG data.
408 The design matrices contain two columns. The first column is a vector of ones to
409 model the intercept, and thus it was eliminated from eq. 2. The second column
410 contains negative ones for baseline trials and ones for event-related trials, therefore
411 modelling the change with respect to baseline, or slope, and it is referred as x_j and z_j
412 in eq. 2. Thus, the first and third terms in the right-hand-side of eq. 2 model the
413 intercepts, which correspond to the mean values between baseline and movement-
414 related activity. The second and fourth terms model the slopes, which are the
415 differences between baseline and movement-related activity. The $\beta_1(t)$ values are
416 fixed across subjects, whereas the $b_{1j}(t)$ values model the random variations across
417 subjects (for MEG) or sessions (for SEEG). In other words, the parameter $\beta_1(t)$
418 models the change in neural activity (e.g., HGA or FCD for MEG data) with respect to
419 baseline at each time point t at the group level; the parameter $b_{1j}(t)$ models the
420 change in neural activity with respect to baseline for each participant (or sessions) j
421 and therefore explains the across-subjects (or across-session) variability for MEG
422 and SEEG data, respectively. The across-subject and across-session variability was
423 considered of no interest for the scope of the current analyses. We thus analyzed
424 fixed-effects. Given the structure of the fixed-effect design matrix, significant
425 differences in movement-related neural activity with respect to baseline can thus be
426 inferred by testing whether β_1 coefficients are significantly greater than zero. More
427 formally, the significance of movement-related modulations was inferred using a t-test
428 by testing the null hypothesis $H_0: \beta_1 \leq 0$.

429 Statistical inference was performed for each time point t and each brain area

430 for the analysis of HGAs. To account for the multiple comparisons problem, we
431 controlled the false discovery rate (FDR) (Benjamini and Yosef, 1995). For mean
432 HGA statistical analyses, we corrected for the number of time points and brain
433 regions; for FCD analyses, we corrected for the number of time points and for the
434 number of pairs of brain regions. To further assess the validity of our results, we
435 quantified the minimum number of consecutive significant time points required to
436 reject a null hypothesis of absence of a cluster given a chance probability $p_0 = 0.5$
437 (two possible outcomes, significant or non-significant), and kept only those clusters
438 whose duration exceeded a given significance level. Details of the calculation are
439 given in the appendix of (Smith et al., 2004).

440 The statistical analyses of MEG HGA modulations resulted in a group-level
441 FCD matrix containing time-evolving t- and p-values for each brain region in
442 *MarsAtlas* (whole-brain analysis). For brain regions covered by the SEEG implants,
443 the analysis of HGA modulations produced intracranial validation at the single-
444 participant level. The analysis of FCD from MEG HGA produced t- and p-value time
445 courses for all pairs of brain regions.

446

447 Graph theoretical analysis

448 Strength of Functional Link (SFL)

449 To gain insight into the topology of the task-related functional network arising
450 from group-level MEG analyses, we performed graph theoretical analyses of the FCD
451 matrix containing the p-values associated with the LME analysis. The weight or
452 strength of the evidence of a functional link was defined as the minimum Bayes
453 Factor (BF) associated with such p-values (Goodman, 1999b). The rationale behind
454 the transformation of p-values to minimum Bayes Factors is an attempt to move
455 towards statistical measures that can be better interpreted (Goodman, 1999a). The
456 BF is a convenient measure of the strength of statistical evidence and it can be
457 computed from p-values as $BF_{up} < -1/(e p \ln(p))$, if p-values satisfy the relation $p <$
458 $1/e$, in which $e \approx 2.72$. This estimate provides an upper bound (BF_{up}) on the BF, and it
459 can be thought as providing an 'optimistic' limit of the BF for a given p-value
460 (Goodman, 2001; Stephens and Balding, 2009). We log-transformed the BFs so to
461 give a measure which quantifies the strength in the evidence of the presence of a
462 functional link between two brain regions, Strength of the Functional Link $SFL =$

463 $\log_{10} BF_{up}$. The *SFL* matrix has the same dimensions of group-level FCD matrix (i.e.,
464 regions x regions x time points). A value between 1 and 2 can be interpreted as
465 providing strong to very strong evidence of a functional link (i.e., increase in
466 correlation with respect to baseline), whereas a value higher than 2 is interpreted as
467 decisive.

468

469 Analysis of time-averaged and time-dependent SFL

470 A caveat of FC analysis is the dependence of functional links on the threshold
471 chosen for statistical significance. Thus, to explore how graph theoretical measures
472 vary according to significance levels, we multiplied the *SFL* matrix with different
473 binary masks obtained from the FDR-correction of the FCD matrix over a wide range
474 from highly significant values ($p_{FDR-corrected} = q < 0.001$) to non-significant ($q <$
475 0.99999). Note that a FDR adjusted p-value is denoted as q-value. This produced
476 several thresholded *SFL* matrices, each one associated with a given level of
477 significance.

478 As a first analysis, we computed the mean *SFL* matrices over time, thus giving
479 an adjacency matrix (regions x regions) representing the mean strength between
480 brain regions at different significance levels. We computed the density *D* (the ratio
481 between the number of functional links and the number of possible connections) as a
482 function of the q-value. In addition, to identify the most important brain regions in
483 average *SFL* graph, we computed the strength of each region (sum of functional links
484 of a region) and two indicators of centrality, such as the eigenvector centrality *EC*,
485 defined as the absolute value of the eigenvector associated with the largest
486 eigenvalue of the adjacency matrix *W* and it measures the importance of a region,
487 and the betweenness centrality *BC*, equal to the fraction of all shortest paths that pass
488 through a given region, so it measures the number of times a region acts as a
489 “bridge”. These measures were, however, computed only at $q < 0.05$. Finally, to
490 evaluate the evolution of density of the thresholded FCD, we computed it for each
491 time slice rather over the averaged FCD. Graph theoretical measures were computed
492 using the Brain Connectivity Toolbox (Rubinov & Sporns, 2010).

493

494 Detection of functional sub-networks

495 A critical step in the analysis of brain networks is the detection of communities,
496 which may correspond to functional subnetworks. Subnetworks, however, may

497 overlap spatially, such that a given brain region may belong to more than one group.
498 Link communities, defined as groups of links rather than nodes, provide an
499 appropriate framework for capturing the relationships between overlapping
500 communities while revealing hierarchical organization (Ahn et al., 2010). To detect
501 time-varying link communities, we used an approach based on the analysis of the
502 correlation of edge weights over time, rather than nodes, similarly to previous works
503 analyzing "cross-links" or "hyper-edges" (Bassett et al., 2014; Davison et al., 2015).

504 First, we computed the Pearson linear correlation between significant (at $q <$
505 0.05) pairs of *SFL* time courses. This produced an adjacency matrix (number of links
506 in size) representing the temporal correlation between functional links. Secondly, we
507 searched for the optimal subdivision of such graph into groups of links. To do so, we
508 used the Louvain method (Blondel et al., 2008) that attempts to optimize the
509 "modularity" of a partition of the network. The Louvain algorithm for modularity
510 maximization is a non-deterministic heuristic, and therefore needs to be initialized
511 with random seeds. In addition, it depends on the resolution parameter γ which
512 controls over the size and number of communities found (resolution equal to 1 leads
513 to the standard Louvain method, whereas higher and lower resolutions produce
514 larger and smaller number of clusters, respectively). We scanned different resolution
515 parameters from $\gamma = 0.5$ to $\gamma = 1.5$ in increments of 0.1. At each scale, we ran the
516 Louvain method 250 times to test whether the non-deterministic nature of the method
517 could produce non-robust results. For all pairs of partitions (250×249 in total), we
518 computed their similarity, defined as the z-score of the Rand index (Traub et al.,
519 2011) and we averaged them across all pairs of partitions. The optimal resolution
520 parameter γ was associated with the largest average similarity between partitions.
521 The largest similarity was observed at $\gamma = 1$. For $\gamma = 1$, we studied the consensus
522 partition to identify a single representative partition from a set of 250 partitions, based
523 on statistical testing in comparison to a null model. The representative partition is
524 obtained by using a generalized Louvain algorithm on the thresholded nodal
525 association matrix (Bassett et al., 2013). We found that for our FCD matrix at $\gamma = 1$,
526 the Louvain algorithm is extremely stable and the 250 partitions are all identical.
527 These graph theoretical analyses were performed using the "Consensus and
528 Comparison Methods" in the Network Community Toolbox
529 (<http://commdetect.weebly.com/>).

530 This approach provides a subdivision of non-overlapping communities by
531 maximizing the number of within-group edges and minimizing the number of
532 between-group edges. Given that community detection was performed on links, the
533 detected communities represent link communities where individual brain areas may
534 participate in multiple overlapping networks. Finally, we computed the mean time-
535 course of the SFL averaged across all links comprising each link community.

536 **RESULTS**537 **Visuomotor-related functional network**

538 The brain regions displaying a significant increase in movement-related HGA
539 with respect to the mean baseline (averaged from -0.5 to -0.1s prior to stimulus
540 onset) defined the arbitrary visuomotor-related network (Figure 2). For cortical
541 regions, the largest increase in HGA was observed over the left parietal lobe,
542 primarily over the dorsal (dorsal intraparietal cortex, IPCd, and the superior parietal
543 cortex, SPC) and medial (medial superior and medial parietal cortices, SPCm and
544 PCm, respectively) parietal regions, the dorsal somatosensory areas (Sdl and Sdm)
545 and the posterior cingulate cortex (PCC). The ventral regions, such as (IPCv and Sv),
546 displayed a smaller increase relative to the dorsal and medial territories in the left
547 hemisphere and were not significant in the right hemisphere. Over the motor,
548 premotor and prefrontal areas, the dorsolateral and dorsomedial regions (PFcdl,
549 PFcdm, PMdl, PMdm, Mdl and Mdm) showed the most significant increase. In
550 addition, the mid-cingulate cortex (MCC) showed significant response, bilaterally. The
551 ventral and ventromedial prefrontal and orbitofrontal cortices did not display a strong
552 increase in HGA, nor anterior temporal regions. These cortical modulations are
553 similar to those presented in a previous paper (Auzias et al., 2016), which we
554 replicate them here for completeness.

555 The novel finding, however, is the presence of significant HGA modulations in
556 subcortical areas. The strongest response was observed in the left hemisphere in the
557 dorsal striatum (caudate nucleus and putamen), globus pallidus (GP) and thalamus
558 (Thal). The thalamus and caudate nucleus displayed a clear bilateral activation,
559 whereas the GP and putamen showed primarily an activity in the hemisphere
560 contralateral to the motor response. A significant response was also observed in the
561 right thalamus and caudate nucleus. No significant increase was seen in other
562 subcortical areas examined such as the nucleus accumbens, amygdala and
563 hippocampus.

564

565 **Visuomotor-related functional connectivity dynamics**

566 The analysis of Functional Connectivity Dynamics (FCD) between all pairs of
567 brain regions of *MarsAtlas* was performed by estimating Pearson's correlation

568 coefficients between pairs of single-trial HGA values over sliding windows of 500
569 msec, stepped every 10 msec. For each participant, FCD analysis resulted in a 4-
570 dimensional matrix (i.e., regions x regions x time points x trials) representing the
571 evolution of linear correlation across all pairs of brain areas from -0.7 to 0.7s around
572 movement onset. Significant modulations in movement-related FCD with respect to
573 those in the baseline period from -0.8 to -0.1s prior to stimulus onset using a linear
574 mixed-effect (LME) approach. Figure 3A shows the connectivity matrix of the average
575 SFL (i.e., Strength of Functional Link) over time. Note that p-values were thresholded
576 at $q < 0.05$ (FDR-corrected) previous to SFL computation, which corresponds to a
577 threshold value of SFL equal to 2.43. All significant links shows decisive evidence in
578 FC averaged over time among occipital areas bilaterally with strong links with parietal
579 regions, in addition to the fronto-parietal network. Subcortical regions, especially in
580 the left hemisphere, showed a strong FC with the rest of the network. Regions in the
581 temporal lobes, however, were not found to play a key role in the FC patterns.

582 To better characterize the evolution of the SFL over time, we computed the
583 mean SFL across pairs of brain regions displaying a significant increase in linear
584 correlation (Fig. 3B). The mean time course displays two peaks of decisive and
585 strong evidence at approximately -0.4 and 0.2s around finger movement. The time
586 intervals around the two peaks represent moments when FC pattern is strongest,
587 which correspond to the largest increase in linear correlation between HGA time
588 courses. Given the shape of the group-level HGA responses shown in Figure 2, the
589 first peak at -0.4s reflects the positive covariation in HGA across the whole network
590 occurring after stimulus presentation and during movement planning (as early as -
591 0.55 in visual areas to approximately -0.25s before finger movement). Such common
592 increase in HGA produces an increase in linear correlation and it reflects the
593 emergence of the FC network. The second peak occurring at 0.2s reflects a common
594 return to baseline of the HGA across the whole network after finger movement (from
595 approximately 0.05s to 0.35s after finger movement). Such global decrease in HGA
596 from maximal activity produces an increase in linear correlation, but it reflects the
597 dissolution of the FC network. Thus, the two peaks correspond to the emergence and
598 dissolution of the FC pattern. The decrease in FC occurring approximately -0.12s to -
599 0.03s before finger movement corresponds to the positive peak of HGA (Fig. 2). Such
600 decrease in FC, therefore, does not reflect an absence of HGA, but rather a
601 maximum of HGA. However, it corresponds to the time interval when FC lacks any

602 significant covariation. Overall, the analysis of the FCD time course reveals two key
603 processes such as the creation and dissolution of FC network.

604

605 Graph theoretical analysis of FC network

606 To gain insight into the properties of the average FC pattern, we performed
607 graph theoretical analyses of the average SFL matrix shown in Fig. 4A. We
608 investigated graph theoretical measures of the mean SFL matrices averaged over
609 time at different thresholds ($q < 0.001$) to non-significant ($q < 0.99999$). Figure 4A
610 shows the FC network density D (the ratio between the number of functional links
611 and the number of possible connections) as a function of threshold q -values. The
612 density of the functional network trivially increase as a function of the threshold, i.e.,
613 the more functional links, the higher is the density. The density values for significant q
614 < 0.05 are less than 10%, meaning that the functional network is not dense, but
615 sparse. We then computed the density for each time slice of the FCD. Network
616 density is maximal (approximately 5%) approximately 0.4 s and then displays a
617 second peak 0.2 after finger movement (2% in density), as shown in Figure 4B.

618 Finally, to identify the most important brain regions in the average SFL graph,
619 we computed the strength S (sum of functional links of a region), the eigenvector
620 centrality EC and the betweenness centrality BC at $q < 0.05$. The strength of a brain
621 area is the simplest measure to estimate the importance of a node in a network. A
622 natural extension of strength centrality is eigenvector centrality EC , and it stands on
623 the notion that a node is important if it is linked to by other important nodes. In fact, a
624 node receiving many links (i.e., high strength) does not necessarily have a high
625 eigenvector centrality, because it may be linked to node with low strength. Thus, EC
626 provide additional information, because it computes the centrality of a node as a
627 function of the centralities of its neighbors. Finally, the betweenness centrality BC is
628 equal to the number of shortest paths that pass through a brain region. Thus, a
629 region with high BC has the potential to play a key role in the network. Convergence
630 of these three metrics provides information about the importance of different brain
631 regions in the network.

632 Table 1 shows the brain regions sorted in a descending order according to S ,
633 EC , and BC . The brain areas that commonly emerge as relevant across the three
634 measures are the dorsomedial and dorsolateral sensorimotor regions (Mdm, Mdl,

635 Sdm), in addition to dorsolateral premotor area (PMdl), superior parietal regions
636 (SPC, SPCm) and the caudomedial visual cortex (VCcm).

637

638 Dynamic reconfiguration of functional connectivity subnetworks

639 To search for functional subnetworks generating the observed dynamics, we
640 performed link community analysis. To do so, we first computed the Pearson linear
641 correlation between significant (at $q < 0.05$) pairs of *SFL* time courses. Then, we
642 found the optimal subdivision of such link graph into communities of links using an
643 algorithm that attempts to optimize the "modularity" of a partition of the network,
644 named the Louvain method (Blondel et al., 2008). This approach provides a
645 subdivision of non-overlapping communities by maximizing the number of within-
646 group edges and minimizing the number of between-group edges. Given that
647 community detection was performed on links, the detected sub-networks represent
648 link communities, where individual brain areas may participate in multiple overlapping
649 networks. The analysis revealed the presence of 3 link communities (Figure 5). The
650 first link community (LC1) primarily included the visual and superior and medial
651 parietal regions, bilaterally, in addition to the left dorsomedial and dorsolateral
652 sensorimotor regions (Fig. 5B). These brain regions form a FC subnetwork emerging
653 approximately 0.5s before finger movement, roughly corresponding to the processing
654 of the visual cue (Fig. 5A). The second link community (LC2) included the left
655 dorsolateral and dorsomedial sensorimotor regions and the dorsal fronto-parietal
656 network. Interestingly, it included the mid and anterior cingulate cortices, the
657 dorsomedial prefrontal cortex and the dorsal striatum, in the caudate nucleus (Fig.
658 5C). LC2 emerged later during the trial and its maximum of expansion occurred
659 approximately 100-150 msec after LC1, that is -0.35s before movement. LC3
660 involved a larger brain network involving the bilateral sensorimotor regions, the left
661 fronto-parietal network and visual areas (Fig. 5D). LC3 showed a strongest peak after
662 finger movement at 0.2s, but displays a peak at -0.4s. The only regions of the
663 temporal lobe showing significant FC were the superior and mid-temporal cortices in
664 the left hemisphere. However, these regions displayed a relative weak strength in the
665 observed networks (Figure 5B, C and D). Overall, the link community analyses
666 allowed us to identify multiple and spatially overlapping FC patterns that evolve
667 dynamically during the trial.

668 We can therefore depict the involvement of key brain regions in a given link
669 community, such as the motor and premotor areas. Figure 6 shows the contribution
670 of the dorsolateral motor and dorsal premotor areas, Mdl and PMdl, respectively, in
671 the three subnetworks as it unfolds over time. Around the presentation of the visual
672 stimulus, the Mdl primarily participates in the LC1, which gradually declines over time
673 (blue curve in Fig. 6A and B). Then, its involvement in LC2 and LC3 increases in
674 parallel, but peaks earlier for LC2 (red curve in Fig. 6A and B) rather than for LC3
675 (green curve). These curves depict the dynamic reconfiguration of the primary motor
676 area from stimulus onset to motor output. For what concerns the dorsolateral
677 premotor cortex, its contribution peaking for LC1, followed by LC3 and LC2 (Fig. 6C
678 and D) confirms that the dynamic engagement in different subnetworks occurs over a
679 short time scale.

680 Finally, to quantify the dynamics of reconfiguration among the three functional
681 subnetworks, we inferred the evolution of network “flexibility” (following the same
682 ideas developed in Braun and collaborators, 2015). We defined the flexibility of a
683 given brain region as the entropy associated to the probabilities of involvement in the
684 three LCs (shown in Fig. 6B and D, for Mdl and PMdl, respectively). Accordingly,
685 node flexibility is maximal for nodes participating with equal probability in the different
686 LCs and minimal for nodes participating in a single LC. Figure 7A shows the mean
687 dynamics of network flexibility averaged over nodes. Interestingly, its reconfiguration
688 shows a single peak occurring at approximately 0.4s before finger movement, which
689 corresponds to the moment when the three LCs overlap more strongly in time and
690 space. Figure 7B shows the mean flexibility averaged over time for the first five
691 strongest brain regions. The parietal regions (SPC, PCm and PPC) display the
692 largest flexibility together with the dorsal premotor cortex.

693

694 Control analyses and intracranial SEEG validation

695 The interpretation of FC measures from non-invasive techniques such as EEG
696 and MEG may suffer limitations, among which volume conduction and leakage are
697 potential confounds (Bastos & Schoffelen, 2016). We performed a series of control
698 analyses to assess the influence of such confounds.

699 First, we studied the relation between the mean SLF for two subcortical
700 regions displaying a significant increase in HGA and FC with cortical regions, as a

701 function of their respective distance to cortical regions. The rationale was to check
702 whether volume conduction and leakage effects could have produced the observed
703 HGA modulations in subcortical regions and the FC patterns between deep sources,
704 such as the thalamus and caudate nucleus, and cortical areas. Figure 8 shows that a
705 clear relation between distance and FC measures (as assessed through the mean
706 SFL) is lacking, neither for the thalamus (Fig., 8A) nor for the caudate nucleus (Fig.
707 8B).

708 Second, we investigated the dipole orientation of all sources within the
709 thalamus and caudate nucleus. The rationale was that differences in dipole
710 orientation of nearby regions may suggest that the estimated HGAs originate from
711 spatially-separable brain structures. To do so, we computed the average dipole
712 orientation both for the thalamus and caudate nucleus. Then, we compared the
713 average dipole orientations by means of the normalized inner product. This measure
714 equals one for identically-oriented dipoles, minus one for dipoles pointing in opposite
715 directions, and zero for orthogonal dipoles. The boxplot displayed in Figure 9A
716 depicts the distribution of normalized inner products between the thalamus and
717 caudate nucleus across participants. The values of normalized inner products span a
718 broad range from -0.45 to 0.85, with median value around 0.65. Extremely high
719 values of raw correlation coefficient between subcortical HGAs would also suggest
720 strong leakage effects. We thus plotted the Pearson correlation coefficient between
721 the HGA at the thalamus and caudate nucleus, averaged over sessions and
722 participants (Figure 9B). The value in the prestimulus interval (i.e., approximately
723 around -0.8s before finger movement) was 0.615. The corresponding coefficient of
724 determination R^2 was 37,8%, (i.e., $R^2 = 0.615 \times 0.615 = 0.3782$), and it equals the
725 proportion of the variance in HGA shared by the thalamus and caudate nucleus.

726 Finally, to assess the relevance of cortical HGA modulations, we asked three
727 patients candidate for surgical treatment of drug-resistant epilepsy to perform the
728 same visuomotor task while recording stereotactic electroencephalography (SEEG)
729 in multiple brain areas. In fact, high-gamma activity from intracranial recordings in
730 epileptic patients is largely exploited for cognitive mapping and it represents an
731 optimal opportunity to validate MEG results. Results from single-patient SEEG cannot
732 be taken as representative of the population, contrary to group-level MEG results. In
733 fact, we cannot exclude that across-subject variability is due to either physiological
734 and/or pathological factors. However, SEEG data provide direct measures of

735 intracranial HGA, free from alteration due to volume conduction or limitation of source
736 imaging tools. Thus, they provide important additional evidence to support the
737 significance of the MEG results.

738 Electrodes were localized by combing post-implant CT scans with pre-surgical
739 anatomical MRI scans, and they were labelled according to *MarsAtlas* (see methods
740 section). Single-trial HGA for each labelled brain region of *MarsAtlas* was defined as
741 the mean z-transformed power values averaged across all electrodes within the
742 same region. To increase the local specificity of SEEG recordings, bipolar derivations
743 were performed among adjacent contacts. Statistical analyses were performed
744 separately for each patient. Twelve brain areas across the three patients were found
745 to display a significant increase in HGA (Table 2) ($q < 0.05$). These included the
746 dorsomedial and dorsolateral motor cortex, the dorsolateral somatosensory region,
747 and the dorsal fronto-parietal network (SPC, SPCm, PMdl, PMdm). In patient 2, the
748 ventral portions of the motor and premotor areas were significantly active. Note that
749 the SEEG implant did not cover the entire brain, but selected regions in the fronto-
750 parietal network.

751 We then compared the average time course of single-patient HGA
752 modulations with those from the MEG group-level analyses (Fig. 10). Seven out of
753 twelve regions displayed a strong (larger than 0.65) linear correlation between the
754 group-level MEG results and the single-patient SEEG time courses. The most striking
755 similarity was observed for brain regions of the sensorimotor cortices and the dorsal
756 fronto-parietal network. Overall, these results confirm that the increase in HGA
757 observed in the MEG data over sensorimotor cortices and the dorsal fronto-parietal
758 network results from area-specific increases in HGA, rather than by leakage from
759 nearby regions displaying a strong response.

760 **DISCUSSION**

761

762 **Brain network and interactions of visuomotor mapping**

763 Previous analyses of arbitrary visuomotor-related functional connectivity have
764 shown that parietal areas play a driving role in the network, whereas premotor areas
765 act as relays from parietal to medial prefrontal cortices, which participate as receivers
766 (Brovelli et al., 2015). Such approach, however, neither considered the time-evolving
767 nature of FC patterns, nor analyzed the involvement of subcortical areas. Our whole-
768 brain and time-dependent brain connectivity analyses showed that visuomotor
769 mapping resides in three distinct and partly overlapping subnetworks with time-
770 evolving cortico-cortical and cortico-subcortical interactions. Approximately 0.5s
771 before finger movement, visual and parietal regions coordinate with sensorimotor and
772 premotor areas (LC 1 in Fig. 5B; blue curve in Fig. 5A). Subsequently, the
773 sensorimotor regions, the dorsal fronto-parietal circuit, the medial prefrontal regions,
774 the basal ganglia and the thalamus (LC 2 in Fig. 5C) dominated the FC pattern. The
775 dorsal fronto-parietal circuit, known to support visuomotor transformations and goal-
776 directed attentional processes (Wise et al., 1996; Wise and Murray, 2000; Corbetta
777 and Shulman, 2002; Culham and Valyear, 2006), is tightly coupled with the
778 sensorimotor and associative fronto-striatal circuit for a brief period around 0.35s
779 prior to action (red curve in Fig. 5A). This FC network includes medial prefrontal
780 areas, such as the dorso-medial prefrontal cortex (PFCdm), mid-cingulate cortex
781 (MCC), anterior cingulate cortex (ACC) and rostro-medial prefrontal (PFrm), with a
782 strongest increase in HGA in the MCC and PFCdm (Fig. 2). The involvement of
783 medial prefrontal areas may correspond to the activation of visuomotor-related neural
784 populations of the rostral cingulate zone (RCZ), a key node of the human motor
785 system (Picard and Strick, 1996; Amiez and Petrides, 2014). At the subcortical level,
786 the dorsal striatum (caudate nucleus and putamen), globus pallidus and thalamus
787 displayed the strongest HGA, in the hemisphere contralateral to the motor response
788 (Fig. 2). Indeed, intracranial recordings from patients with motor disorders have
789 described HGA in the subthalamic nucleus (Amirnovin et al., 2004; Alegre et al.,
790 2005; Androulidakis et al., 2007; Lalo et al., 2008), globus pallidus (Tsang et al.,
791 2012a) and thalamus (Brucke et al., 2013) during different types of motor behaviors.
792 High-gamma oscillatory activity in the sub-thalamic nucleus (STN) and globus

793 pallidus (GPi) has been found to be coherent with cortical activity during voluntary
794 movement (Cassidy et al., 2002; Brown, 2003). Granger causality analysis also
795 showed that STN drives activity in M1 (Litvak et al., 2012), thus suggesting that HGA
796 in motor areas is due to propagating activity from the basal ganglia through the
797 thalamus (Brucke et al., 2012). Our results showed that the caudate nucleus and
798 thalamus are coupled with the sensorimotor cortex and the dorsal fronto-parietal
799 networks (LC 2 in Fig. 5C), thus confirming a dynamic coordination between cortical
800 and subcortical regions also during visuomotor behaviors most prominently during
801 the planning phase prior to movement initiation.

802 Several lines of evidence suggest that the reported subcortical activations are
803 primarily local, rather than due to leakage from cortical areas. First, we observed that
804 the putamen significantly activated only in the left hemisphere, whereas the thalamus
805 was activated bilaterally (Fig. 2). If the bilateral activation in the thalamus were due to
806 leakage from cortical areas, we would have expected a bilateral activation also in the
807 putamen, given that the thalamus is deeper than the putamen. Second, no significant
808 correlation was found between the SFL and distance for the thalamus and caudate
809 nucleus (Fig. 8). Third, the average dipole orientation for the thalamus and caudate
810 nucleus are significantly different (i.e., the normalized inner product is less than one)
811 and the distribution of values covers a wide range from -0.45 to approximately 0.85.
812 This suggests that the thalamus and caudate nucleus lack a systematic similarity in
813 dipole orientation (Fig. 9A). Forth, the mean Pearson correlation values and the
814 corresponding coefficient of determination do not saturate at high values and show a
815 modulation similar to the average time course of FCD (Fig. 9B). This suggests a lack
816 of strong covariance, as it would be expected if leakage effects were dominating.

817 Nevertheless, we cannot *a priori* exclude that the observed subcortical
818 increases in HGA and FC patterns may be due to complex configurations of cortical
819 activations. Indeed, we suggest that HGA estimation at subcortical areas and FC
820 analysis should not be performed blindly. Rather, the analysis of raw correlations and
821 dipole orientations provide important insight into the origin of the results.
822 Experimentally, simultaneous MEG and subcortical measures of HGA from
823 intracranial recordings would be required to confirm or disprove the ability of MEG to
824 capture subcortical HGA and FC.

825 Overall, our result suggests that the basal ganglia form a dynamic functional
826 network, which may allow the coordination within and across different processing

827 streams in the basal ganglia (Brown, 2003) and facilitate motor output (Cheyne and
828 Ferrari, 2013). The involvement of sensorimotor and associative fronto-striatal
829 circuits, classically thought to be involved in habits (Yin and Knowlton, 2006;
830 Graybiel, 2008; Ashby et al., 2010), also suggests that performance of arbitrary
831 visuomotor mappings can be viewed as a form of acquainted instrumental behavior
832 (Brovelli et al., 2015), whose gradual consolidation would lead to the formation of
833 habitual responses (Dickinson, 1985; Dickinson and Balleine, 1993). We therefore
834 suggest that the FCD pattern observed for LC2 depicts how motor plans circulate in
835 the sensorimotor and associative cortico-striatal loop in coordination with fronto-
836 parietal circuits.

837 Finally, a last subnetwork (LC 3 in Fig. 5D) primarily emerging after motor
838 response peaking around 0.2s (green curve in Fig. 5A), involved the bilateral
839 sensorimotor regions, the left fronto-parietal network and visual areas. The
840 involvement of bilateral sensorimotor regions indicates that this network mediates
841 cortico-cortical interhemispheric coordination processes via the corpus callosum.
842 Such interhemispheric coupling may support the selective inhibition of inappropriate
843 responses occurring between motor and premotor cortices across hemispheres in
844 situations when multiple choices are available (Duque et al., 2013; Burle et al., 2016).
845 Alternatively, this network may be involved in the processing of the somatosensory
846 refference at the end of the movement and/or the processing action's outcome.

847 To exclude potential confounds due to volume conduction or limited spatial
848 resolution of MEG and beamforming technique (Bastos & Schoffelen, 2016), we
849 showed that local field potentials derived from SEEG recordings displayed significant
850 increase in HGA in these regions (Fig. 10, Table 2). We confirmed invasively that
851 brain regions of the dorsal fronto-parietal network and the sensorimotor and/or
852 associative fronto-striatal circuits display local increase in HGA, which do not result
853 from volume conduction effects.

854

855 Towards a better understanding of cognitive architectures

856 We computed the density of the thresholded FC and FCD graphs as a function
857 of significance threshold (Fig. 4) using the FDR-controlling procedure to estimate the
858 relevant range of q-values. For $q < 0.05$, the density of the visuomotor-related FC
859 network is less than 10% (approximately 5% for $q < 0.05$). This shows that

860 visuomotor-related FC is not dense, but sparse. Future work on the relation between
861 structural and functional connectivity may provide clues of how anatomical
862 connectivity between brain areas shapes how neural information flows and constrains
863 the dynamics of FC patterns.

864 A second characteristic of FC is its non-stationarity nature. Indeed, fMRI
865 investigations have shown that resting-state networks (RSNs) display non-stationarity
866 and dynamically evolve over tens of seconds to minutes (Hutchinson et al., 2013;
867 Yeo et al., 2013; Allen et al., 2014; Cole et al., 2014; Calhoun et al., 2014; Zalski et
868 al., 2014; Hansen et al., 2015). Inter-areal phase-synchronisation is known to display
869 non-stationarity, and to underlie perception and executive functions (e.g., Pesaran et
870 al., 2008; Hipp et al., 2011; Salazar et al., 2012). Our results further support the
871 notion that FC is non-stationary and evolves over time scales relevant for visuomotor
872 integration in the order of tens to hundreds of milliseconds (Fig. 3B and Fig. 5).
873 Modelling studies of resting-state activity suggest that non-stationarity arises from the
874 out-of-equilibrium sampling of alternative dynamical modes (Deco & Jirsa, 2012;
875 Hansen et al., 2015; Deco et al., 2015). Switching between collective dynamical
876 states have the potential to induce network-wide reorganization of information
877 sharing and routing patterns and, thus, provides an effective mechanism for flexible
878 inter-areal communication (Battaglia et al., 2012; Kirst et al., 2016). We suggest that
879 such underlying mechanisms mediating spontaneous large-scale dynamics may also
880 underlie task-related activity at shorter time scale. In addition, our results may provide
881 the basis for linking similar patterns of FCD that have been observed, albeit over
882 different time scales, during visuomotor learning (Bassett et al., 2011; Heitger et al.,
883 2012).

884 A third characteristic of FCD is the presence of multiple and spatially
885 overlapping sub-networks. Each brain area can participate in multiple sub-networks
886 depending of task demands. In analogy to the concept of cell assembly, where single
887 neurons can participate in multiple functional populations depending on context, a
888 sub-network may be viewed as a brain assembly. A brain assembly would constitute
889 a dynamic entity, whose constituents engage in multiple sub-networks in a time-
890 dependent manner (Fig. 6). Spatially, areal flexibility was larger for associative
891 parietal regions, such as the SPC, PCm and PPC together with the dorsal premotor
892 cortex, which represent the core cortical network for visuomotor transformation (Fig.
893 7B). Temporally, network flexibility showed a maximum around 0.4s before finger

894 movement, which corresponds to the moment when the three sub-networks interact
895 more strongly (Fig. 7A). We therefore suggest that visuomotor integration processes
896 occur in this time interval, when the level of interactions between multiple brain
897 assemblies is strongest.

898 To conclude, our study confirms that executive functions arise from the
899 dynamic coordination of neural activity over large-scale networks (Varela et al., 1999;
900 von der Malsburg et al., 2010; Bressler and Menon, 2010). More precisely, the results
901 supports the notion that functional specialization is due to the interplay of multiple
902 and spatially overlapping subnetworks, rather than properties of single brain regions
903 (Fedorenko and Thompson-Schill, 2014; Petersen and Sporns, 2015). Future work
904 investigating how subnetworks differently participate depending on tasks demands
905 may provide a better understanding of the cognitive architectures of executive
906 functions (Dehaene et al., 2015).

907 **REFERENCES**

- 908 Ahn Y-Y, Bagrow JP, Lehmann S (2010) Link communities reveal multiscale
909 complexity in networks. *Nature* 466:761–764
- 910 Alegre M, Alonso-Frech F, Rodriguez-Oroz MC, Guridi J, Zamarbide I, Valencia M,
911 Manrique M, Obeso JA, Artieda J (2005). Movement-related changes in
912 oscillatory activity in the human subthalamic nucleus: ipsilateral vs. contralateral
913 movements. *Eur. J. Neurosci.* 22, 2315–2324.
- 914 Androulidakis AG, Kuhn AA, Chen CC, Blomstedt P, Kempf F, Kupsch A, Kupsch A,
915 Schneider GH, Doyle L, Dowsey-Limousin P, Hariz MI, Brown P (2007).
916 Dopaminergic therapy promotes lateralized motor activity in the subthalamic
917 area in Parkinson's disease. *Brain* 130, 457–468.
- 918 Allen EA, Damaraju E, Plis SM, Erhardt EB, Eichele T, Calhoun VD (2014). Tracking
919 whole-brain connectivity dynamics in the resting state. *Cereb Cortex.* 24(3):663-
920 76.
- 921 Amiez C, Petrides M (2014) Neuroimaging evidence of the anatomo-functional
922 organization of the human cingulate motor areas. *Cereb Cortex* 24:563–578.
- 923 Amirnovin R, Williams ZM, Cosgrove GR, Eskandar EN (2004). Visually guided
924 movements suppress subthalamic oscillations in Parkinson's disease patients. *J.*
925 *Neurosci.* 24, 11302–11306.
- 926 Ashby FG, Turner BO, Horvitz JC (2010). Cortical and basal ganglia contributions to
927 habit learning and automaticity. *Trends Cogn Sci.* 2010 May;14(5):208-15.
- 928 Auzias G, Lefèvre J, Le Troter A, Fischer C, Perrot M, Régis J, Coulon O (2013).
929 Model-driven harmonic parameterization of the cortical surface: HIP-HOP. *IEEE*
930 *Trans Med Imaging.* 32(5):873-87.
- 931 Auzias G, Coulon O, Brovelli A (2016). MarsAtlas: A cortical parcellation atlas for
932 functional mapping. *Hum Brain Mapp.* 37(4):1573-92.
- 933 Ball T, Demandt E, Mutschler I, Neitzel E, Mehring C, Vogt K, Aertsen A, Schulze-
934 Bonhage A (2008) Movement related activity in the high gamma range of the
935 human EEG. *Neuroimage* 41:302–310.
- 936 Bassett DS, Wymbs NF, Porter MA, Mucha PJ, Carlson JM, Grafton ST (2011).
937 Dynamic reconfiguration of human brain networks during learning. *Proc Natl Acad*
938 *Sci U S A.* 108(18):7641-6.

- 939 Bassett DS, Porter MA, Wymbs NF, Grafton ST, Carlson JM, Mucha PJ (2013).
940 Robust detection of dynamic community structure in networks. *Chaos*, 23, 1.
- 941 Bassett DS, Wymbs NF, Porter MA, Mucha PJ, Grafton GT (2014). Cross-linked
942 structure of network evolution. *Chaos*, 24:013112.
- 943 Bastos AM, Schoffelen JM (2016). A Tutorial Review of Functional Connectivity
944 Analysis Methods and Their Interpretational Pitfalls. *Front Syst Neurosci*. 8;9:175.
- 945 Battaglia D, Witt A, Wolf F, Geisel T (2012) Dynamic Effective Connectivity of Inter-
946 Areal Brain Circuits. *PLoS Comp Biol* 8:e1002438.
- 947 Benjamini Y, Yosef H (1995) Controlling the False Discovery Rate : A Practical and
948 Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society.*
949 *Series B (Methodological)*, 57:289-3001.
- 950 Blondel VD, Guillaume JL, Lambiotte R, Lefebvre E (2008). Fast unfolding of
951 communities in large networks. *Journal of Statistical Mechanics: Theory and*
952 *Experiment* (10), P1000
- 953 Braun U, Schäfer A, Walter H, Erk S, Romanczuk-Seiferth N, Haddad L, Schweiger
954 JI, Grimm O, Heinz A, Tost H, Meyer-Lindenberg A, Bassett DS. Dynamic
955 reconfiguration of frontal brain networks during executive cognition in humans.
956 *Proc Natl Acad Sci U S A*. 112(37):11678-83.
- 957 Bressler SL, Menon V (2010) Large-scale brain networks in cognition : emerging
958 methods and principles. *Trends Cogn Sci* 14:277–290.
- 959 Brovelli, A., Lachaux, J., Kahane, P., Boussaoud, D. (2005) High gamma frequency
960 oscillatory activity dissociates attention from intention in the human premotor
961 cortex. *Neuroimage* 28:154–164.
- 962 Brovelli A, Chicharro D, Badier JM, Wang H, Jirsa V (2015). Characterization of
963 Cortical Networks and Corticocortical Functional Connectivity Mediating Arbitrary
964 Visuomotor Mapping. *J Neurosci*. 35(37):12643-58.
- 965 Brown P (2003). Oscillatory nature of human basal ganglia activity: relationship to the
966 pathophysiology of Parkinson's disease. *Mov Disord*. 18(4):357-63.
- 967 Brücke C, Bock A, Huebl J, Krauss JK, Schönecker T, Schneider GH, Brown P, Kühn
968 AA (2013). Thalamic gamma oscillations correlate with reaction time in a
969 Go/noGo task in patients with essential tremor. *Neuroimage* 75C, 36–45.
- 970 Burle B, van den Wildenberg WP, Spieser L, Ridderinkhof KR (2016). Preventing
971 (impulsive) errors: Electrophysiological evidence for online inhibitory control over
972 incorrect responses. *Psychophysiology*. Mar 23.

- 973 Buzsáki G, Schomburg EW (2015). What does gamma coherence tell us about inter-
974 regional neural communication? *Nat Neurosci*. 18(4):484-9.
- 975 Cachia A, Mangin JF, Rivière D, Papadopoulos-Orfanos D, Kherif F, Bloch I, Régis J
976 (2003). A generic framework for the parcellation of the cortical surface into gyri
977 using geodesic Voronoï diagrams. *Medical Image Analysis*, 7(4), 403–16.
- 978 Calhoun VD, Miller R, Pearlson G, Adalı T (2014) The Chronnectome: Time-Varying
979 Connectivity Networks as the Next Frontier in fMRI Data Discovery. *Neuron*
980 84:262–274.
- 981 Cassidy M, Mazzone P, Oliviero A, Insola A, Tonali P, Di Lazzaro V, Brown P (2002).
982 Movement-related changes in synchronization in the human basal ganglia. *Brain*.
983 125(Pt 6):1235-46.
- 984 Cheyne D, Ferrari P (2013) MEG studies of motor cortex gamma oscillations:
985 evidence for a gamma “fingerprint” in the brain? *Front Hum Neurosci* 7:575.
- 986 Cole MW, Bassett DS, Power JD, Braver TS, Petersen SE (2014). Intrinsic and task-
987 evoked network architectures of the human brain. *Neuron* 83(1):238-51.
- 988 Corbetta M, Shulman GL (2002). Control of goal-directed and stimulus-driven
989 attention in the brain. *Nat Rev Neurosci*. 3(3):201-15.
- 990 Coupe P, Yger P, Prima S, Hellier P, Kervrann C, Barillot C (2008). An optimized
991 blockwise nonlocal means denoising filter for 3-D magnetic resonance images.
992 *IEEE Trans Med Imaging*. 2008 Apr;27(4):425-41.
- 993 Crone NE, Sinai A, Korzeniewska A (2006) High-frequency gamma oscillations and
994 human brain mapping with electrocorticography. *Prog Brain Res* 159:275–295.
- 995 Culham JC, Valyear KF (2006). Human parietal cortex in action. *Curr Opin Neurobiol*.
996 16(2):205-12.
- 997 Davison EN, Schlesinger KJ, Bassett DS, Lynall ME, Miller MB, Grafton ST, Carlson
998 JM. Brain network adaptability across task states (2015). *PLoS Comput Biol*.
999 8;11(1):e1004029.
- 1000 Darvas F, Scherer R, Ojemann JG, Rao RP, Miller KJ, Sorensen LB (2010) High
1001 gamma mapping using EEG. *Neuroimage* 49:930–938.
- 1002 Dickinson A, Balleine B (1993) Actions and responses: The dual psychology of
1003 behaviour. In: Eilan, N.; McCarthy, R.A.; Brewer, B., Eds. *Spatial*
1004 *Representation: Problems in Philosophy and Psychology*. Malden, MA: Blackwell
1005 Publishers, pp. 277–293

- 1006 Deco G, Jirsa VK (2012) Ongoing cortical activity at rest: criticality, multistability, and
1007 ghost attractors. *Journal of Neuroscience* 32:3366–3375.
- 1008 Deco G, Tononi G, Boly M, Kringelbach ML (2015). Rethinking segregation and
1009 integration: contributions of whole-brain modelling. *Nat Rev Neurosci.* 16(7):430-9.
- 1010 Dehaene S, Dudai Y, Konen C (2015). Cognitive Architectures. *Neuron.* 88(1):1.
- 1011 Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL,
1012 Dale AM, Maguire RP, Hyman BT, Albert MS, Killiany RJ. (2006). An automated
1013 labeling system for subdividing the human cerebral cortex on MRI scans into gyral
1014 based regions of interest. *NeuroImage*, 31, 968–980.
- 1015 Dickinson AD (1985) Actions and habits: the development of behavioral autonomy.
1016 *Philos Trans R Soc Lond B Biol Sci* 308:67–78.
- 1017 Duque J, Olivier E, Rushworth M (2013). Top-down inhibitory control exerted by the
1018 medial frontal cortex during action selection under conflict. *J Cogn Neurosci.*
1019 25(10):1634-48.
- 1020 Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, van der Kouwe A,
1021 Killiany R, Kennedy D, Klaveness S, Montillo A, Makris N, Rosen B, Dale AM
1022 (2002). Whole brain segmentation: automated labeling of neuroanatomical
1023 structures in the human brain. *Neuron* 33, 341-355.
- 1024 Fedorenko E, Thompson-Schill SL (2014). Reworking the language network. *Trends*
1025 *Cogn Sci.* 18(3):120-6.
- 1026 Fries P (2015). Rhythms for Cognition: Communication through Coherence. *Neuron.*
1027 88(1):220-35.
- 1028 Goodman SN (1999a). Toward evidence-based medical statistics. 1: The P value
1029 fallacy. *Annals of Internal Medicine.* 130(12): 995–1004.
- 1030 Goodman SN (1999b). Toward evidence-based medical statistics. 2: The Bayes
1031 factor. *Annals of Internal Medicine.* 130(12):1005-13.
- 1032 Goodman SN (2001). Of P-values and Bayes: a modest proposal. *Epidemiology.* 12(3):295-
1033 7.
- 1034 Graybiel AM (2008) Habits, Rituals and the Evaluative Brain. *Annu Rev*
1035 *Neurosci*:359–387.
- 1036 Gross J, Kujala J, Hamalainen M, Timmermann L, Schnitzler A, Salmelin R (2001)
1037 Dynamic imaging of coherent sources: Studying neural interactions in the human
1038 brain. *Proc Natl Acad Sci USA* 98:694–699.
- 1039 Hadj-bouziane F, Meunier M, Boussaoud D (2003) Conditional visuo-motor learning

- 1040 in primates : a key role for the basal ganglia. *J Physiol Paris*. 97:567–579.
- 1041 Hansen EC, Battaglia D, Spiegler A, Deco G, Jirsa VK (2015). Functional connectivity
1042 dynamics: modeling the switching behavior of the resting state.
1043 *Neuroimage*.105:525-35.
- 1044 Heitger MH, Ronsse R, Dhollander T, Dupont P, Caeyenberghs K, Swinnen SP
1045 (2012). Motor learning-induced changes in functional brain connectivity as
1046 revealed by means of graph-theoretical network analysis. *Neuroimage*.
1047 2;61(3):633-50.
- 1048 Hermes D, Miller KJ, Noordmans HJ, Vansteensel MJ, Ramsey NF (2010).
1049 Automated electrocorticographic electrode localization on individually rendered
1050 brain surfaces. *Journal of neuroscience methods*.185:293–298.
- 1051 Hipp JF, Engel AK, Siegel M (2011) Oscillatory synchronization in large-scale cortical
1052 networks predicts perception. *Neuron* 69:387–396.
- 1053 Hutchison RM, Womelsdorf T, Allen EA, Bandettini PA, Calhoun VD, Corbetta M,
1054 Della Penna S, Duyn JH, Glover GH, Gonzalez-Castillo J, Handwerker DA,
1055 Keilholz S, Kiviniemi V, Leopold DA, de Pasquale F, Sporns O, Walter M, Chang
1056 C. (2013). Dynamic functional connectivity: Promise, issues, and interpretations.
1057 *Neuroimage* 80, 360–378.
- 1058 Jerbi K, Dalal SS, Jung J, Minotti L, Bertrand O, Berthoz A, Kahane P, Lachaux J,
1059 Bernard C (2009) Task-Related Gamma-Band Dynamics From an Intracerebral
1060 Perspective : Review and Implications for Surface EEG and MEG. 1771:1758–
1061 1771.
- 1062 Ko AL, Weaver KE, Hakimian S, Ojemann JG (2013) Identifying functional networks
1063 using endogenous connectivity in gamma band electrocorticography. *Brain*
1064 *Connect* 3:491–502.
- 1065 Lachaux J-P, Axmacher N, Mormann F, Halgren E, Crone NE (2012) High-frequency
1066 neural activity and human cognition: past, present and possible future of
1067 intracranial EEG research. *Prog Neurobiol* 98:279–301.
- 1068 Lalo E, Thobois S, Sharott A, Polo G, Mertens P, Pogosyan A, Brown P (2008).
1069 Patterns of bidirectional communication between cortex and basal ganglia during
1070 movement in patients with Parkinson disease. *J. Neurosci*. 28, 3008–3016.
- 1071 Lancaster JL, Woldorff MG, Parsons LM, Liotti M, Freitas CS, Rainey L, Kochunov
1072 PV, Nickerson D, Mikiten SA, Fox PT (2000). Automated Talairach atlas labels
1073 for functional brain mapping. *Hum Brain Mapp*, 10(3), 120–131.

- 1074 Litvak V, Eusebio A, Jha A, Oostenveld R, Barnes G, Foltynie T, Limousin P, Zrinzo
1075 L, Hariz MI, Friston K, Brown P (2012). Movement-related changes in local and
1076 long-range synchronization in Parkinson's disease revealed by simultaneous
1077 magnetoencephalography and intracranial recordings. *J Neurosci* 32, 10541–
1078 10553.
- 1079 Kirst C, Timme M, Battaglia D (2016) Dynamic information routing in complex
1080 networks. *Nat Comms* 7:11061.
- 1081 Mangin JF, Rivière D, Cachia A, Duchesnay E, Cointepas Y, Papadopoulos-Orfanos
1082 D, Scifo P, Ochiai T, Brunelle F, Régis J (2004). A framework to study the
1083 cortical folding patterns. *Neuroimage*. 23 Suppl 1:S129-38.
- 1084 Markov NT, Ercsey-Ravasz MM, Ribeiro Gomes AR, Lamy C, Magrou L, Vezoli J,
1085 Misery P, Falchier A, Quilodran R, Gariel MA, Sallet J, Gamanut R, Huissoud C,
1086 Clavagnier S, Giroud P, Sappey-Marinié D, Barone P, Dehay C, Toroczkai Z,
1087 Knoblauch K, Van Essen DC, Kennedy H (2014). A weighted and directed
1088 interareal connectivity matrix for macaque cerebral cortex. *Cereb Cortex*.
1089 24(1):17-36.
- 1090 Markov NT, Ercsey-Ravasz M, Van Essen DC, Knoblauch K, Toroczkai Z, Kennedy
1091 H (2013). Cortical high-density counterstream architectures. *Science*.
1092 1;342(6158):1238406.
- 1093 Mitra PP, Pesaran B (1999) Analysis of dynamic brain imaging data. *Biophys J*
1094 76:691–708.
- 1095 Murray E a, Bussey TJ, Wise SP (2000) Role of prefrontal cortex in a network for
1096 arbitrary visuomotor mapping. *Exp brain Res* 133:114–129.
- 1097 Nolte G (2003) The magnetic lead field theorem in the quasi-static approximation and
1098 its use for magnetoencephalography forward calculation in realistic volume
1099 conductors. *Phys Med Biol* 48:3637–3652.
- 1100 Passingham RE, Toni I, Rushworth MF (2000) Specialisation within the prefrontal
1101 cortex: the ventral prefrontal cortex and associative learning. *Exp brain Res*
1102 133:103–113.
- 1103 Picard N, Strick PL (1996) Motor areas of the medial wall: a review of their location
1104 and functional activation. *Cereb cortex* 6:342–353
- 1105 Onnela JP, Saramäki J, Kertész J, Kaski K (2005). Intensity and coherence of motifs
1106 in weighted complex networks. *Phys. Rev. E* 71:065103

- 1107 Pandya D.N., Yeterian E. (1985). Architecture and connections of cortical association
1108 areas, 1985. http://link.springer.com/chapter/10.1007/978-1-4757-9619-3_1
- 1109 Perrot M, Rivière D, Mangin JF (2011). Cortical sulci recognition and spatial
1110 normalization. *Med Image Anal.* 15(4):529-50.
- 1111 Percival DB, Walden AT (1993) *Spectral Analysis for Physical Applications.*
1112 Cambridge: Cambridge University Press
- 1113 Pesaran B, Nelson MJ, Andersen RA (2008). Free choice activates a decision circuit
1114 between frontal and parietal cortex. *Nature.* 453(7193):406-9.
- 1115 Petersen SE, Sporns O (2015). Brain Networks and Cognitive Architectures. *Neuron.*
1116 88(1):207-19.
- 1117 Petrides M (2005) Lateral prefrontal cortex : architectonic and functional organization.
1118 *Philos Trans R Soc Lond B Biol Sci.* 360:781-95.
- 1119 Ray S, Crone NE, Niebur E, Franaszczuk PJ, Hsiao SS. Neural correlates of high-
1120 gamma oscillations (60–200 Hz) in macaque local field potentials and their
1121 potential implications in electrocorticography (2008). *Journal of Neuroscience.*
1122 28:11526–11536
- 1123 Ray S, Maunsell JH (2011). Different origins of gamma rhythm and high-gamma
1124 activity in macaque visual cortex. *PLoS Biol* 9: e1000610.
- 1125 Régis J, Mangin J-F, Ochiai T, Frouin V, Rivière D, Cachia A, Samson Y (2005).
1126 “Sulcal Root” Generic Model: a Hypothesis to Overcome the Variability of the
1127 Human Cortex Folding Patterns. *Neurologia Medico-Chirurgica*, 45(1), 1–17
- 1128 Rubinov M, Sporns O (2010). Complex network measures of brain connectivity: Uses
1129 and interpretations. *NeuroImage* 52:1059-69.
- 1130 Salazar RF, Dotson NM, Bressler SL, Gray CM (2012). Content-specific fronto-
1131 parietal synchronization during visual working memory. *Science.* 338(6110):1097-
1132 100.
- 1133 Smith AC, Frank LM, Wirth S, Yanike M, Hu D, Kubota Y, Graybiel AM, Suzuki W a,
1134 Brown EN (2004) Dynamic analysis of learning in behavioral experiments. *J*
1135 *Neurosci* 24:447–461.
- 1136 Stephens M, Balding DJ (2009). Bayesian statistical methods for genetic
1137 association studies. *Nat Rev Genet.* 10(10):681-90.
- 1138 Tou JT, Gonzalez RC (1974). *Pattern Recognition Principles.* Reading,
1139 Massachusetts: Addison-Wesley Publishing Company.

- 1140 Traud AL, Kelsic ED, Mucha PJ and Porter MA (2011) Comparing community
1141 structure to characteristics in online collegiate social networks. *SIAM Review* 53,
1142 526-543.
- 1143 Tsang EW, Hamani C, Moro E, Mazzella F, Lozano AM, Hodaie M, Yeh IJ, Chen R
1144 (2012). Movement related potentials and oscillatory activities in the human internal
1145 globus pallidus during voluntary movements. *J. Neurol. Neurosurg. Psychiatry* 83,
1146 91–97.
- 1147 Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N,
1148 Mazoyer B, Joliot M. (2002). Automated anatomical labeling of activations in SPM
1149 using a macroscopic anatomical parcellation of the MNI MRI single-subject brain.
1150 *NeuroImage*, 15(1), 273–89.
- 1151 Van Essen DC, Drury HA (1997). Structural and Functional Analyses of Human
1152 Cerebral Cortex Using a Surface-Based Atlas. *J Neurosci*, 17(18), 7079–7102.
- 1153 Varela F, Lachaux JP, Rodriguez E, Martinerie J (2001). The brainweb: phase
1154 synchronization and large-scale integration. *Nat Rev Neurosci*. 2(4):229-39.
- 1155 Veen BD Van, Drongelen W Van, Yuchtman M, Suzuki A (1997) Localization of Brain
1156 Electrical Activity via Linearly Constrained Minimum Variance Spatial Filtering.
1157 *IEEE Trans Biomed Eng.* 44:867-80
- 1158 Vidal JR, Chaumon M, O'Regan JK, Tallon-Baudry C (2006) Visual grouping and the
1159 focusing of attention induce gamma-band oscillations at different frequencies in
1160 human magnetoencephalogram signals. *J Cogn Neurosci* 18:1850–1862.
- 1161 Von der Malsburg C, Phillips PEM, Singer W (2010). *Dynamic Coordination in the*
1162 *Brain* (MIT Press)
- 1163 Wise SP, Pellegrino G, Boussaoud D (1996) The premotor cortex and nonstandard
1164 sensorimotor mapping. *Can J Physiol Pharmacol* 482:469–482.
- 1165 Wise SP, Murray EA (2000) Arbitrary associations between antecedents and actions.
1166 *Trends Neurosci* 23:271–276.
- 1167 Yeo BT, Krienen FM, Chee MW, Buckner RL (2013). Estimates of segregation and
1168 overlap of functional connectivity networks in the human cerebral cortex.
1169 *Neuroimage*. 88C:212-227.
- 1170 Yin HH, Knowlton BJ (2006) The role of the basal ganglia in habit formation. *Nature*
1171 *Reviews Neurosci* 7:464–476.
- 1172 Zalesky A, Fornito A, Cocchi L, Gollo LL, Breakspear M (2014). Time-resolved
1173 resting-state brain networks. *Proc. Natl Acad. Sci. USA* 111, 10341–10346.

1174 **FIGURE and TABLE LEGENDS**

1175

1176 **Figure 1.** (A) Arbitrary visuomotor mapping task. (B) *MarsAtlas*: cortical parcellation
1177 displaying the anatomical gradients both in the rostro-caudal and dorso-ventral directions; for
1178 a detailed description see Auzias and collaborators (2016). (C) *MarsAtlas*: single-subject
1179 exemplar volumetric representation displaying subcortical regions included in the atlas:
1180 nucleus accumbens, amygdala, hippocampus, globus pallidus, putamen, caudate nucleus
1181 and thalamus.

1182

1183 **Figure 2.** Statistical map displaying the brain areas associated with a significant increases in
1184 HGA with respect to baseline (time-point and cluster-level threshold were set to $q < 0.001$
1185 FDR-corrected). The anatomical labels of subcortical areas are NAc (nucleus accumbens),
1186 Amyg (amygdala), Hipp (hippocampus), GP (globus pallidus), Put (putamen), Cd (caudate
1187 nucleus), Thal (thalamus).

1188

1189 **Figure 3.** Strength of the Functional Link (SFL). (A) Mean SFL connectivity matrix averaged
1190 over time. (B) SFL time course averaged over pairs of areas. The threshold for significant
1191 SFL was equal to 2.43. Error bars correspond to 95% confidence interval.

1192

1193 **Figure 4.** Graph theoretical measures. (A) Dependence between threshold values (q-values)
1194 and FC density. (B) Temporal evolution of density D at $q = 0.05$.

1195

1196 **Figure 5.** Functional Connectivity Dynamics (FCD). (A) Time course of the average SFL
1197 (Strength of Functional Link) for the three identified Link Communities (LC). Error bars
1198 correspond to 95% confidence interval. Spatial patterns for the three LCs are displayed in
1199 (B), (C) and (D). The thickness of the green links is proportional to the time-averaged SFL
1200 between areas, whereas the colour and size of nodes is proportional to the mean SFL
1201 between each area and the rest of the network (i.e., the weight).

1202

1203 **Figure 6.** Exemplar evolution for the dorsolateral motor (A, C) and premotor (B, D) areas. (A)
1204 and (B) show the involvement of Mdl and PMdl in the three LCs, respectively. (C) and (D)
1205 depict the involvement in percentage value.

1206

1207 **Figure 7.** Flexibility analysis. (A) Mean evolution of network flexibility (shaded area represent
1208 standard deviation). (B) Areal flexibility for the five most representative brain regions.

1209

1210 **Figure 8.** Relation between mean FC and distance for the thalamus (A) and caudate nucleus
1211 (B). Each dot corresponds to a brain area displaying significant FC with the seed regions.

1212

1213 **Figure 9.** Distribution of normalized inner products between the average dipole orientations
1214 of the left thalamus and caudate nucleus across participants (A). The boxplot depicts
1215 extreme values (whiskers), first and third quartile (box) and median (red line). (B) Time
1216 course of mean correlation coefficient.

1217

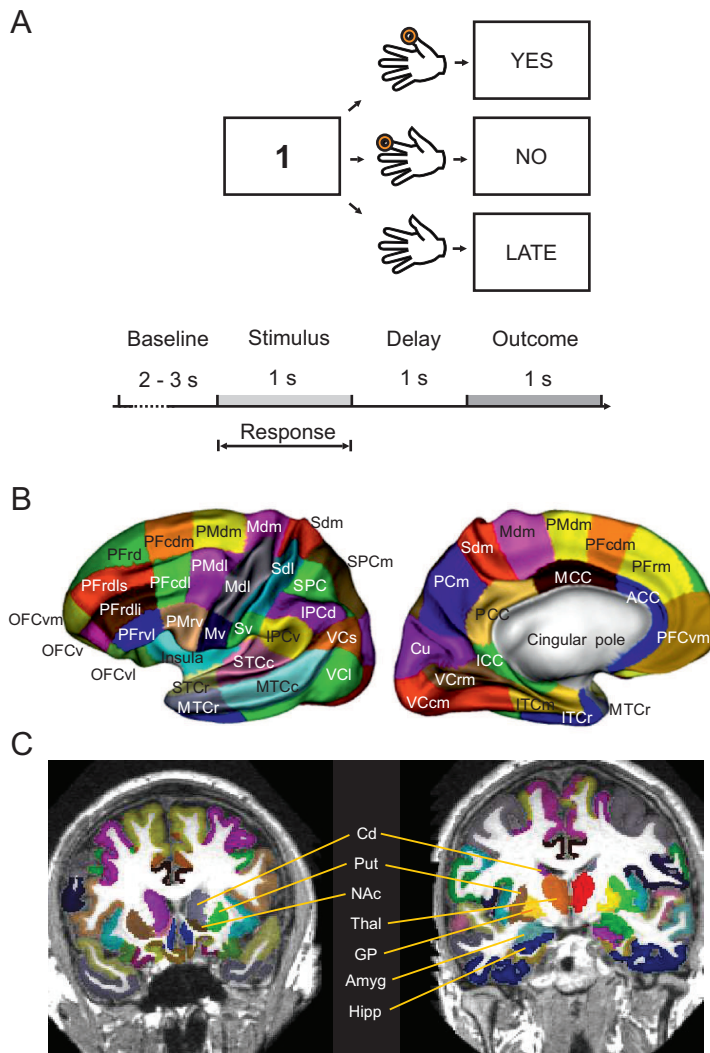
1218 **Figure 10.** SEEG validation of HGA modulations. Comparison between SEEG single-
1219 subjects t-value for HGA (blue) and group-level MEG results (red curves). Subject number,
1220 brain areas and the correlation coefficient between the curves is indicated on the top of each
1221 panel.

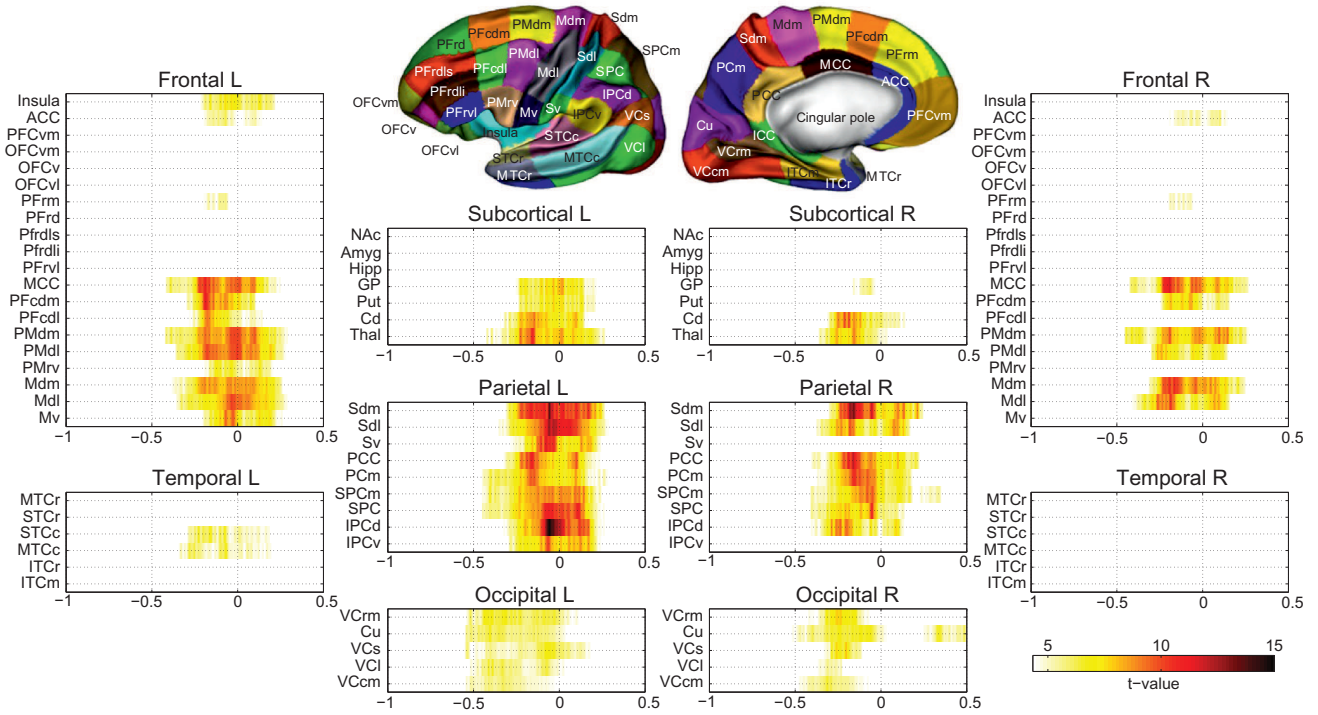
1222

1223 **Table 1.** Graph theoretical measures.

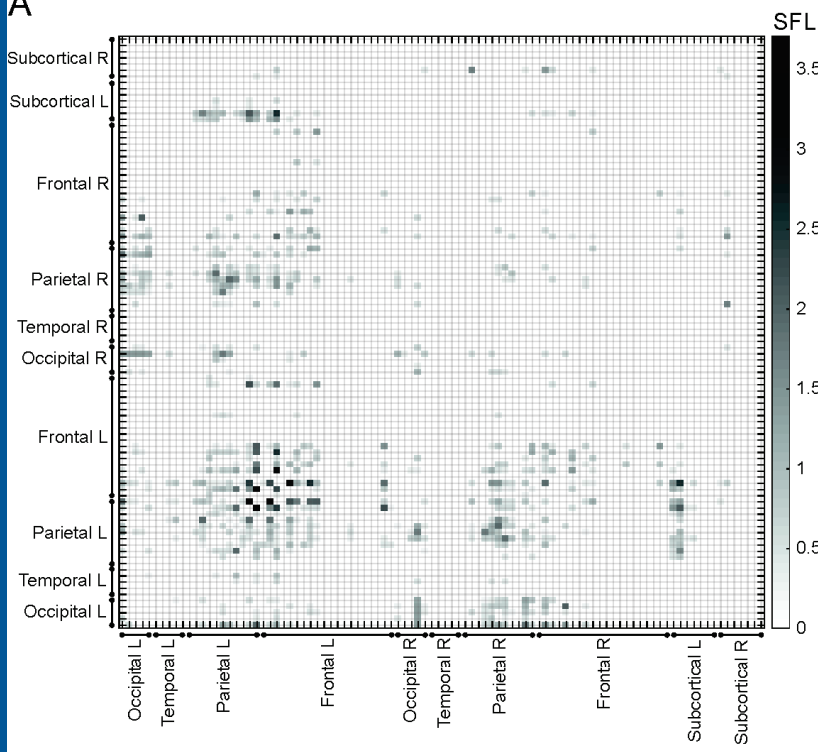
1224

1225 **Table 2.** SEEG activations

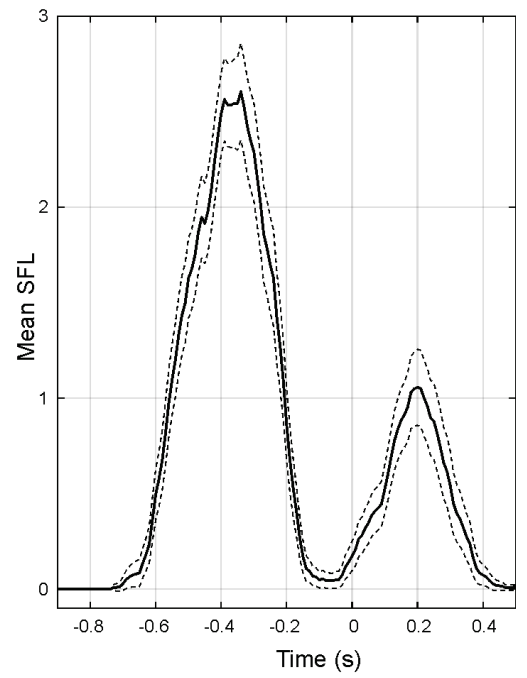


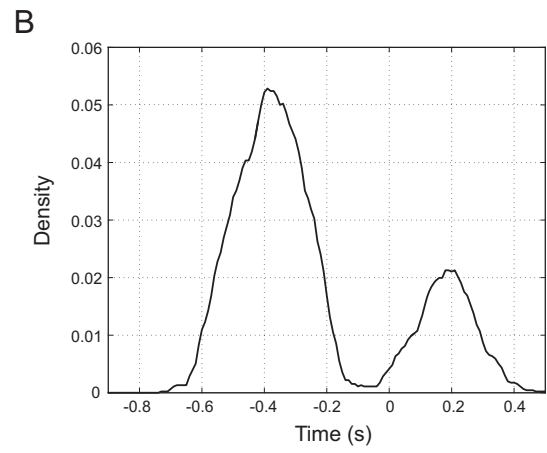
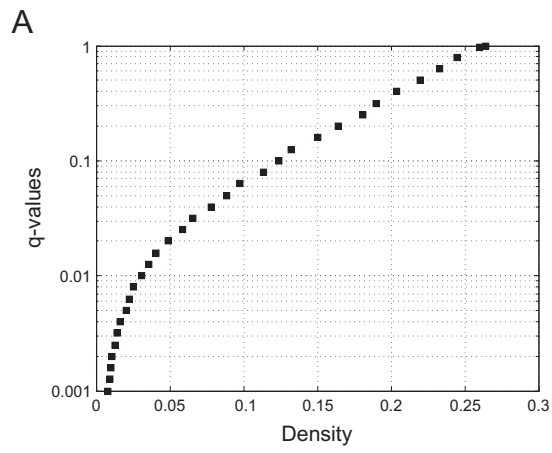


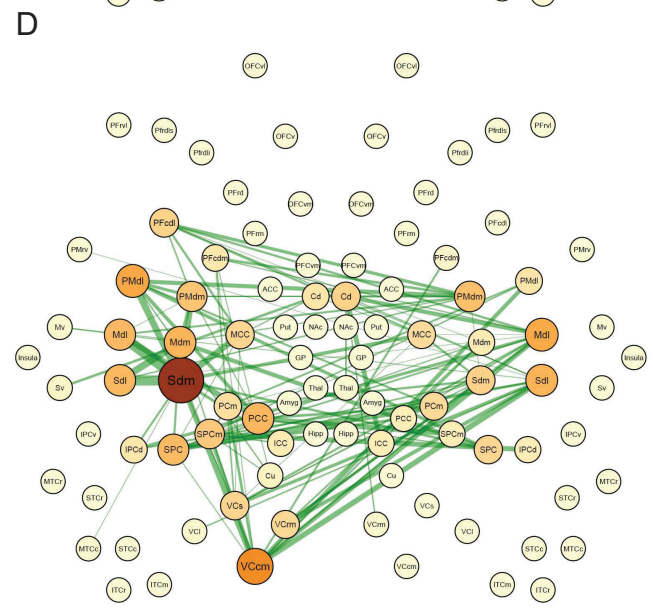
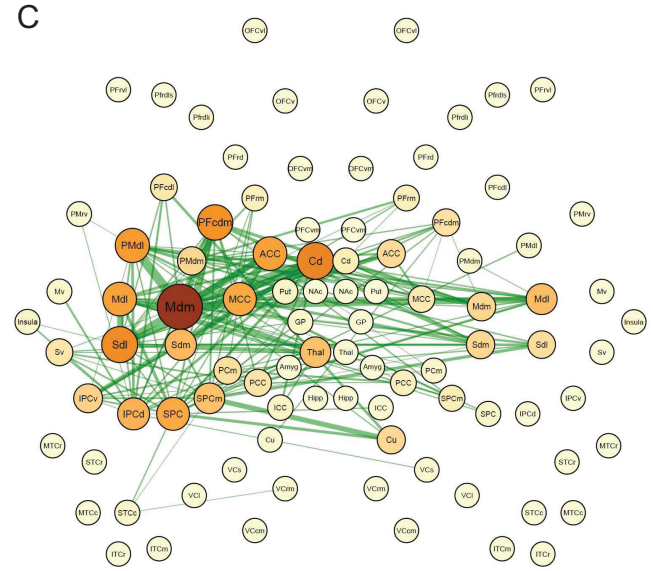
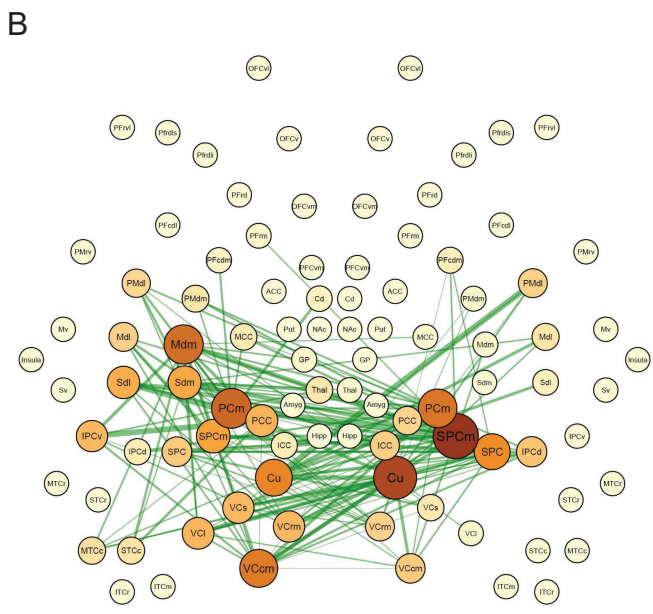
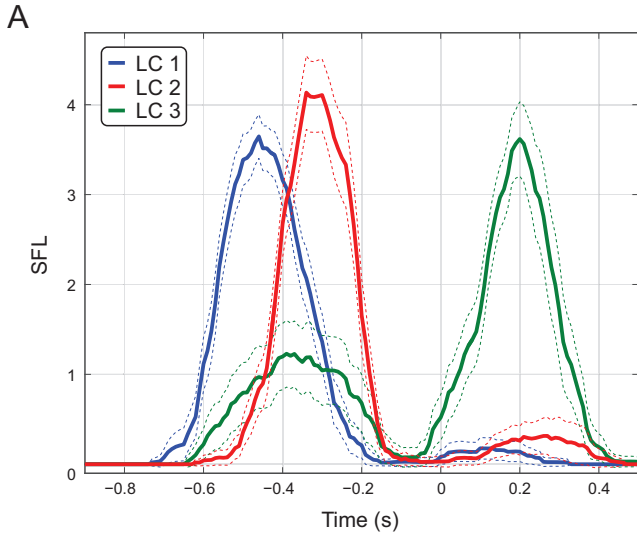
A

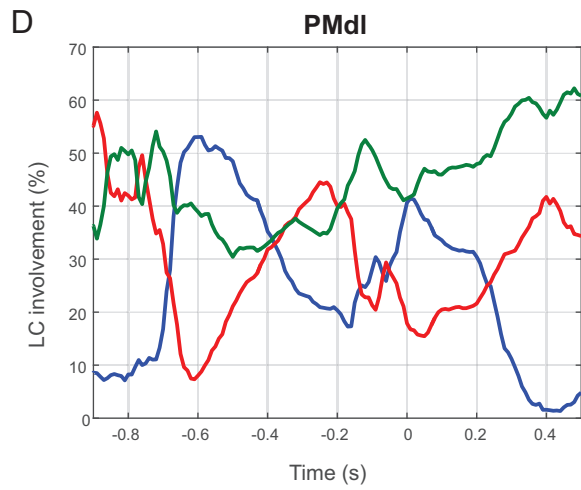
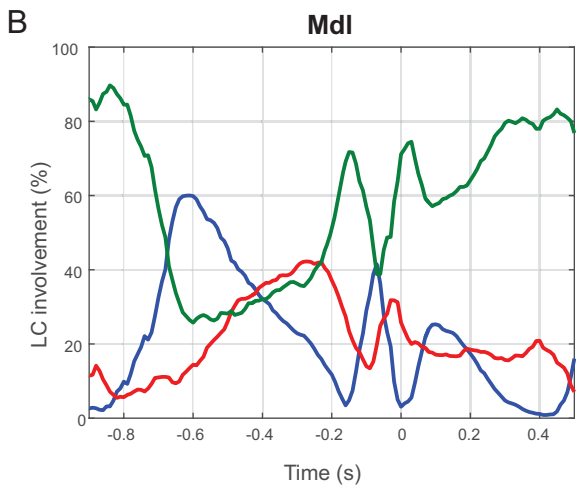
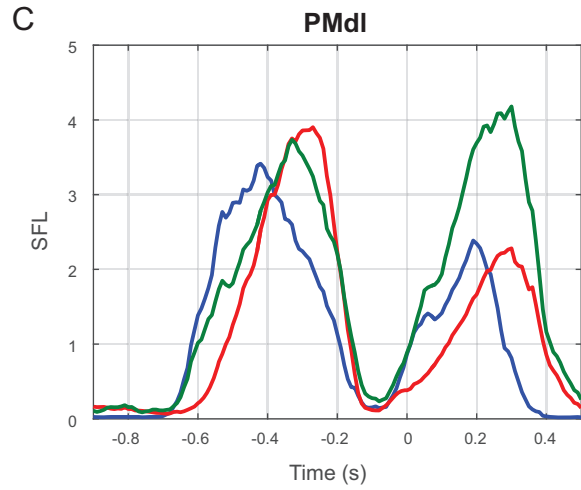
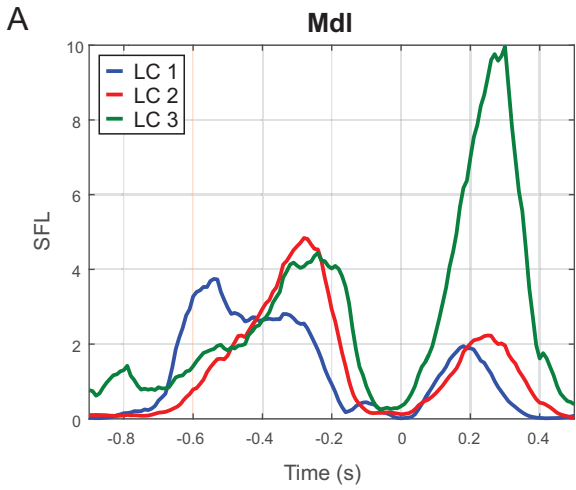


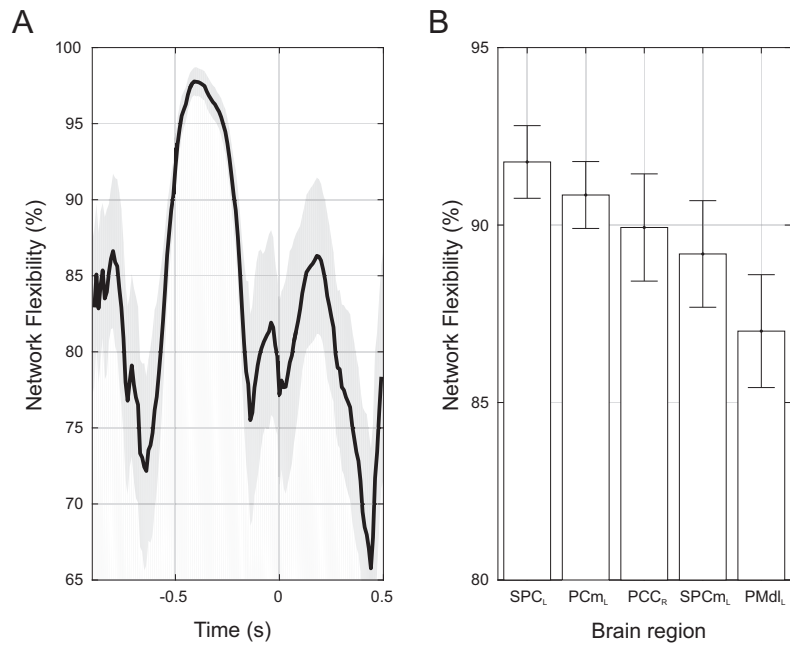
B

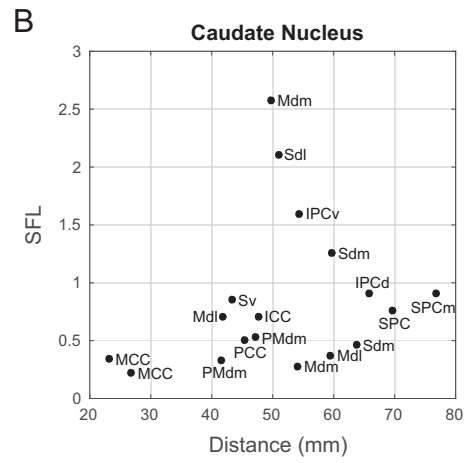
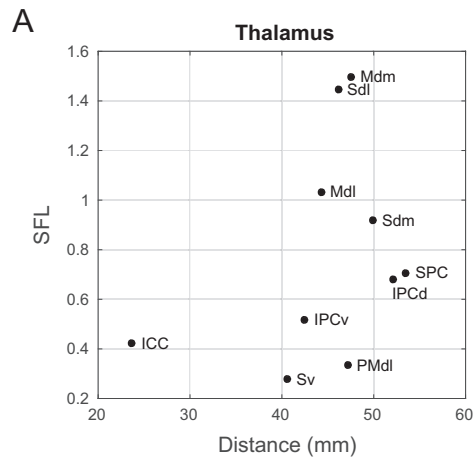


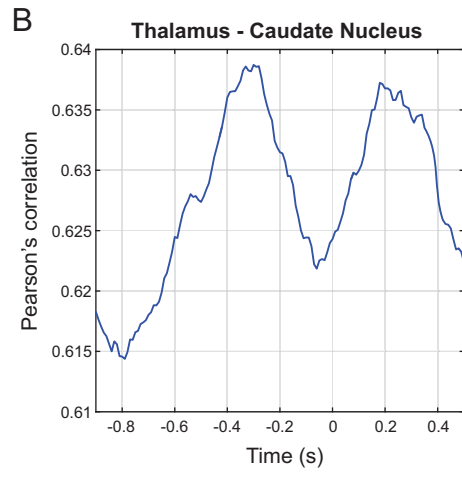
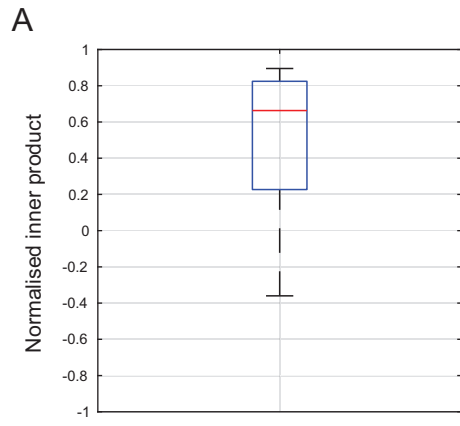


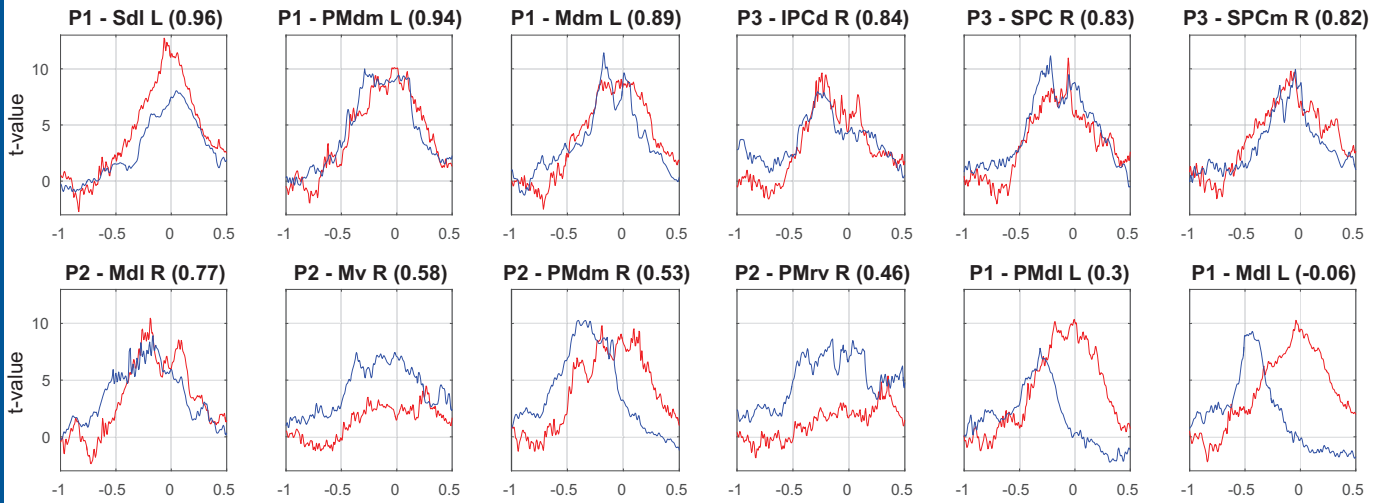












Strength (S)		Eigen Centrality (EC)		Betweenness Centrality (BC)	
<i>Value</i>	<i>Region</i>	<i>Value</i>	<i>Region</i>	<i>Value</i>	<i>Region</i>
7,39	Mdm	6,84	Mdm	16,25	Sdm
6,28	Sdm	6,42	Sdm	13,68	Mdm
4,64	Sdl	5,73	Sdl	9,98	Cu
3,88	PMdl	4,98	Mdl	9,52	VCcm
3,75	VCcm	4,37	PMdl	6,19	Sdl
3,70	Mdl	3,82	Cd	5,81	Mdl
3,34	SPC	3,56	VCcm	4,80	PMdl
3,25	SPCm	3,37	SPCm	4,46	IPCd
3,20	Cu	3,20	PFcdm	3,83	SPC
3,13	Cd	3,05	PCC	3,41	SPCm

Parcel name	Peak <i>p</i> -value	Peak <i>t</i> -value	Peak time (s)	Time interval (s)		Patient number
L Mdm	3,42E-20	11,43	-0,175	-0,28	0,125	1
R SPC	8,76E-20	11,15	-0,22	-0,44	0,2	3
R PMdm	1,41E-17	10,27	-0,34	-0,62	-0,06	2
L PMdm	5,65E-17	10	-0,29	-0,455	0,155	1
R SPCm	4,85E-17	9,96	-0,045	-0,275	0,05	3
L Mdl	2,21E-15	9,29	-0,435	-0,555	-0,315	1
R Mdl	1,52E-14	8,92	-0,165	-0,39	0,055	2
R PMrv	6,70E-14	8,63	-0,145	-0,5	0,155	2
L Sdl	1,29E-12	8,05	0,045	-0,225	0,26	1
R IPCd	1,69E-12	7,96	-0,28	-0,415	-0,135	3
L PMdl	4,22E-12	7,82	-0,315	-0,45	-0,185	1
R Mv	2,78E-11	7,44	-0,02	-0,44	0,18	2
R Mdl	9,89E-08	5,72	-0,475	-0,51	-0,4	2