The Prospective Sense of Agency is Rooted in Local and Global Properties of Intrinsic Functional Brain Networks

Simone Di Plinio, Mauro Gianni Perrucci, and Sjoerd J. H. Ebisch

Abstract

The sense of agency (SoA) refers to a constitutional aspect of the self describing the extent to which individuals feel in control over their actions and consequences thereof. Although the SoA has been associated with mental health and well-being, it is still unknown how interindividual variability in the SoA is embedded in the intrinsic brain organization. We hypothesized that the prospective component of an implicit SoA is associated with brain networks related to SoA and sensorimotor predictions on multiple spatial scales. We replicated previous findings by showing a significant prospective SoA as indicated by intentional binding effects. Then, using task-free fMRI and graph analysis, we analyzed associations between intentional binding effects and the intrinsic brain organization at regional, modular, and whole-brain scales. The results showed that intermodular connections of a frontoparietal module including the premotor cortex, supramarginal gyrus, and dorsal precuneus are associated with individual differences in prospective intentional binding. Notably, prospective intentional binding effects were also related to global brain modularity within a specific structural resolution range. These findings suggest that an implicit SoA generated through sensorimotor predictions relies on the intrinsic organization of the brain connectome on both local and global scales.

INTRODUCTION

The sense of agency (SoA) concerns the experience of oneself as the source of one’s actions and their consequences. This phenomenon is often investigated as a state- or event-related subjective experience from which researchers can extrapolate the extent to which an individual feels in control over his or her behavior, thoughts, and the environment. Acquiring a SoA is considered a fundamental step in cognitive development (Ruvolo, Messinger, & Movellan, 2015) as well as in human evolutionary adaptation (Taylor et al., 2014). The experience of a lower SoA can impair behavioral performances on cognitive tasks (Schooler et al., 2014), cause a loss of awareness (Berberian, Sarrazin, Le Blaye, & Haggard, 2012), and negatively impact the quality of everyday life (Renes & Aarts, 2018; Bandura, 2006) and mental health (de Bézenac, Swindells, & Corcoran, 2018; Moore & Fletcher, 2012).

The implicit SoA can be measured by intentional binding, that is, the shift of the subjectively perceived timing of a performed action toward the consequences of that action (Moore & Obhi, 2012; Haggard, Clark, & Kalogerou, 2002). Intentional binding can rely on two mechanisms (Moore & Haggard, 2008): First, prospective intentional binding is based on the probabilistic and context-dependent coding of action consequences supported by internal predictive models, and second, outcome-dependent, a posteriori inferences about action consequences support retrospective intentional binding.

Studies on intentional binding have highlighted many substantial interindividual differences in the SoA and their implications for mental health. For instance, although healthy individuals show a significant prospective component of the SoA as measured through intentional binding (Moore & Haggard, 2008), increased schizotypal traits and schizophrenia have been associated with weakened prospective and increased retrospective intentional binding effects (Moore, Dickinson, & Fletcher, 2011). It has also been shown that psychosis-related and positive social personality traits may predict decreases or increases in the prospective intentional binding depending on individual environmental control (Di Plinio, Arnò, Perrucci, & Ebisch, 2019). Furthermore, intentional binding differs between high- and low-hypnotizable individuals (Lush et al., 2019) and correlates with narcissistic personality traits (Hascalovitz & Obhi, 2015). These studies consistently demonstrate interindividual differences in the tendency to experience an enhanced or reduced SoA.

Increasing evidence from analyses based on graph theory (Rubinov & Sporns, 2010; Bullmore & Sporns, 2009) suggests that the intrinsic organization of brain networks contributes to the predisposition of an individual’s typical behavioral patterns (Gallen & D’Esposito, 2019). Intriguingly, many brain regions implicated in agency, including the premotor cortex (PMC), the inferior parietal lobule (IPL), the anterior insula, the cerebellum, and the precuneus (Haggard, 2017; Króliczak, Piper, & Frey, 2016; Chambon, Moore, & Haggard, 2015; Rae, Hughes, Weaver, Anderson, & Rowe, 2014; Chambon, Wenke, Fleming, Prinz, & Haggard, 2013;
Desmurget et al., 2009; Farrer et al., 2003), have been described as information hubs in the human brain (Power et al., 2014; Buckner et al., 2009). Hence, these regions could act as local multimodal integrators of sensorimotor information (van den Heuvel & Sporns, 2013) within motor control networks to support the SoA.

Besides, the potential link between agency and the intrinsic brain architecture may concern not only local elements of the brain (i.e., specific regions/nodes or networks/modules) but also whole-brain parameters (Mišić & Sporns, 2016). For example, it has been proposed that complex neurocognitive processes may also arise from the brain’s global modular structure, that is, to the degree of integration and segregation among brain subsystems (Ito, Hearme, Mill, Cocuzza, & Cole, 2019). This view is supported by recent studies that linked the brain’s intrinsic organization to the predisposition of individual behavioral patterns (Gupta, Bhushan, & Behera, 2018; Hilger, Ekman, Fiebach, & Basten, 2017; Godwin, Barry, & Marois, 2015). Specifically, the prospective SoA reflects a constitutional aspect of self-awareness (Prinz, 2012; Gallagher, 2000) that emerges from sensorimotor prediction models (Haggard, 2017; Clark, 2013; Wolpert, Diedrichsen, & Flanagan, 2011). Predictive coding, putatively grounded in the integration of actions and their outcomes (Kilner, Friston, & Frith, 2007), is a general property of the brain that is fundamental for both its development (Wolpert, 1997) and its adaptability (Sato & Yasuda, 2005). Indeed, better contextual predictions mean smaller prediction errors (Friston & Kiebel, 2009) and increased adaptability of the brain to external demands.

Whether the intrinsic functional connectivity patterns of regions associated with the SoA and sensorimotor predictions predispose individual propensities regarding the SoA is still unknown. Given these studies, the quality of these mechanisms likely depends on both local and global features of the brain system, whereas a high efficiency of the brain in generating accurate predictive schemes may be necessary for a healthy SoA.

The purpose of this fMRI study was to investigate if and how an implicit SoA, reflected by intentional binding, is associated with the brain’s intrinsic modular organization. To that end, we first assessed the prospective and retrospective components of the SoA following previous studies (Di Plinio et al., 2019; Voss et al., 2010; Haggard et al., 2002) in a sample of healthy individuals (n = 39). Then, we studied the associations between implicit measures of the SoA (prospective and retrospective intentional binding) and intrinsic functional network features during a task-free (i.e., resting) state on three different, complementary spatial scales: nodal (brain regions), modular (brain networks), and global (whole brain).

We hypothesized that the neural processing of the individual SoA may be specifically modulated according to individual patterns of intrinsic brain connectivity. Given that predictive mechanisms are more likely to be embedded in the intrinsic brain organization (Apps & Tsakiris, 2014; Kannape & Blanke, 2012; Kording, Tenenbaum, & Shadmehr, 2007), whereas retrospective mechanisms are more likely related to task-evoked signals, we mainly expected that the prospective SoA could be related with task-free fMRI measures. On the one hand, we supposed that the segregation of functional brain subsystems (i.e., modules) as indexed by global modularity may favor an efficient general organization of information processing in the brain, allowing higher adaptability of sensorimotor predictions and, consequently, a higher SoA indexed by the prospective component. On the other hand, we also hypothesized that topological features of specific regions or subsystems of the brain may be involved in the transfer and integration of sensorimotor information across brain subsystems/networks. Specifically, on the nodal and modular levels, we expected that prospective intentional binding may be associated with enhanced nodal efficiency (van den Heuvel & Sporns, 2013) or participation coefficients (Guimerà & Nunes Amaral, 2005) for regions such as the IPL, precuneus, PMC, insula, and cerebellum.

METHODS

Participants

Thirty-nine healthy Italian adults (19 women and 20 men, aged 23 ± 2 years; 35 right-handed and 4 left-handed) without a history of psychiatric or neurological disease and contraindications for MRI scanning participated in the experiment. The experiment was approved by the local ethics committee. All participants had normal or corrected-to-normal vision and provided written informed consent before taking part in the study in accordance with the Declaration of Helsinki (2013). Each participant performed the behavioral SoA task 1–3 days before the MRI acquisition.

Behavioral Procedure

All participants performed a well-established SoA paradigm (Di Plinio et al., 2019; Voss et al., 2010; Haggard et al., 2002). On each trial, the participants performed voluntary, self-initiated keypresses with the right index finger, while watching a clock hand rotating on a screen. The clock was labeled using a circular scale with numbers positioned at 5-min intervals. The participants’ task was to judge the timing of the keypress, that is, the clock time indicated by the clock hand when they pressed the key. The participants started each trial by voluntarily pressing a button with the left index finger. The clock hand rotation began at a random position in each trial and performed a full rotation every 2560 msec. The intertrial interval was jittered between 2 and 3 sec.

Two experimental conditions of action timing were used in the SoA task. In the 50% probability condition, participants heard a tone after the keypress in 50% of the trials. In the 75% probability condition, the keypress was followed by a tone presentation in 75% of the trials. The tone consisted of a single pulse at 1000 Hz and lasting 200 msec.
The tone was presented binaurally 250 msec after the keypress. The task was performed using E-Prime software (Schneider, Eschman, & Zuccolotto, 2002), while participants were sitting approximately 60 cm from the 20-in. monitor. Two blocks for each condition (50%, 75%) of the SoA task were performed by each participant. Each block consisted of 32 trials. The participants also performed a fifth, baseline block composed of 32 trials in which no tones occurred. Block order was pseudorandomized across participants. The whole procedure lasted approximately 45 min for each participant.

The variable measured in each trial of the SoA task was the perceptual shift (\(\Delta\)). The perceptual shift is defined as the time difference between the real keypress and the perceived keypress indicated by the participant in each trial, and it is expressed in milliseconds. Note that, although the perceptual shift and the phenomenon of the intentional binding are related, they should not be confused: Whereas the former represents the divergence between real and perceived keypresses, the second is a phenomenon that concerns the shift of the perceived timing of action toward the action consequences (sound).

The participants were instructed (i) to avoid the planning of their keypresses, (ii) to avoid answering in a stereotyped way, and (iii) to avoid answering before the end of the first full clock rotation. A brief training session was performed by each participant before the experiment. The task is illustrated in Figure 1.

**Data Acquisition**

Each participant performed two consecutive task-free fMRI runs, each consisting of 376 volumes. The participants were instructed to watch a white fixation cross on a black screen without performing a cognitive task. Each run lasted approximately 7.5 min. Functional images were acquired using a Philips Achieva 3-T scanner installed at the Institute for Advanced Biomedical Technologies (Gabriele d’Annunzio University). Whole-brain functional images were acquired with a gradient echo-planar sequence using the following parameters: repetition time = 1.2 sec, echo time = 30 msec, field of view = 256 × 256 × 180 mm, flip angle = 65°, in-plane voxel size = 2.5 mm², and slice thickness = 2.5 mm. A high-resolution T1-weighted whole-brain image was also acquired after functional sessions using the following parameters: repetition time = 8 msec, echo time = 3.7, field of view = 256 × 256 × 2180 mm, flip angle = 8°, in-plane voxel size = 1 mm², and slice thickness = 1 mm.

**Preprocessing of MRI Data**

The preprocessing steps and the analysis of functional images were implemented in AFNI (Cox, 1996). A slice-timing correction was applied to remove differences in acquisition times between the slices. The obtained functional images were deobliqued, despiked, corrected for time-shifted acquisition, and motion-corrected using a six-parameter rigid body realignment before being aligned to the Montreal Neurological Institute standard brain using nonlinear warping. During the preprocessing steps, motion parameters for each participant were collected. The functional images were scaled to have voxels with an average value of 100 to translate the unitless BOLD signal acquired by scanners to the “BOLD percent signal change” as a more interpretable index (Chen, Taylor, & Cox, 2017). A Gaussian filter of 5-mm FWHM was applied to spatially smooth the functional images.

Finally, the time series were censored (volumes with 10% or more outliers across voxels and volumes with Euclidean norm of the motion derivative exceeding 0.2 mm were excluded as suggested in Power et al., 2014) and band-pass filtered (frequency interval: 0.01–0.10 Hz) in a single regression step (Caballero-Gaudes & Reynolds, 2017) in which the motion parameters were also included as noise regressors together with white matter and cerebrospinal fluid signals. The mean framewise displacement was also added as an additional covariate of no interest (Ciric et al., 2018; Power et al., 2014). We did not regress out the global signal

![Figure 1. Behavioral task. Participants performed voluntary, self-paced keypresses with the right index finger while watching a clock hand rotating on a screen. Participants started each trial by themselves pressing a button with the left index finger, and they were instructed to judge the clock “time” indicated by the clock hand when they pressed the key. After the keypress, depending on the trial and on the experimental condition, auditory feedback (or nothing, contingent on the current trial) was binaurally presented through headphones. ITI = intertrial interval.](image-url)
because it is a controversial approach (Saad et al., 2012) and potentially introduces spurious negative correlations (Weissenbacher et al., 2009).

**Behavioral Data Analysis**

The average baseline perceptual shift ($\Delta_{b}$) was subtracted from the average perceptual shift in each experimental condition and each participant (Di Plinio et al., 2019; Voss et al., 2010). Linear mixed-effects analyses were implemented using tone probability (levels: 50% and 75%) and trial type (levels: action and tone, action only) as fixed effects, whereas a random intercept was added at the participant level. The dependent variable was the average perceptual shift minus the baseline perceptual shift ($\Delta - \Delta_{b}$). To identify the significance of prospective/retrospective components, we performed multiple comparisons using Tukey’s honestly significant difference test. The homogeneity of residuals was assessed using the D’Agostino–Pearson test.

We also implemented a bootstrap procedure to estimate the distributions of the effect sizes and to investigate the modulation of the prospective and retrospective components (Kirby & Gerlanc, 2013). The prospective component was estimated by contrasting the perceptual shifts during “action-only” trials in the 75% probability condition versus perceptual shifts during “action-only” trials in the 50% probability condition, thus reflecting the contextual effect of tone probability on perception. The retrospective component was estimated by contrasting the perceptual shifts between “action + tone” and “action-only” trials within the 50% probability condition, thus reflecting the outcome-dependent effect on perception. The effect size (Hedges’ $g$) was estimated in 10,000 bootstrap cycles with replacement for both the prospective and retrospective components.

**Connectomics**

The two task-free runs were concatenated, and whole-brain functional connectomes were formed using a set of 418 nodes derived from the cortical (346 parcels) and subcortical (40 gray nuclei) atlases from Joliot et al. (2015) plus the cerebellar (32 nodes) atlas from Diedrichsen, Balsters, Flavell, Cussans, and Ramnani (2009). Functional connectivity was calculated using the z Fisher transform of the Pearson correlation among average time series extracted from the voxels within each node. Connectomes were used to build binary undirected graphs after thresholding (the 10% strongest connections were retained). Graph analyses were performed within MATLAB (The MathWorks) using the Brain Connectivity Toolbox (Rubinov & Sporns, 2010). Modular subdivisions of the brain were visualized using the software BrainNet Viewer (www.nitrc.org/projects/bnv; Xia, Wang, & He, 2013) implemented in MATLAB. Formal definitions of the metrics used in graph analysis are reported in Table 1.

To find the optimal community structure of the networks, we implemented modularity maximization (Porter, Onnela, & Mucha, 2009) through the application of the widely used and robust Louvain algorithm (Lancichinetti & Fortunato, 2009; Blondel, Guillaume, Lambiotte, & Lefebvre, 2008). An iterative fine-tuning process was used to find participant-specific optimal modular structures (Sun, Danila, Josić, & Bassler, 2009) and to handle the stochastic nature of the Louvain algorithm (Bassett et al., 2011). In the first step, each node was assigned to a distinct module. Then, the optimal community was detected using the Louvain algorithm, and the modularity $Q$ was estimated. This procedure was repeated using the optimal community found in the previous cycle as the starting community affiliation vector, and the process was repeated until $Q$ could not be increased anymore. The agreement matrix was calculated as the matrix whose elements represented the number of times two nodes were assigned to the same module across participants. The group-level modular structure was achieved from the agreement matrix using a community detection algorithm developed for the analysis of complex networks (Lancichinetti & Fortunato, 2012), with the number of repetitions set to 1000.

**Table 1. Formal Definitions of Metrics Used in Graph Analysis**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Formula</th>
<th>Specifications</th>
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</table>
| Modularity ($Q$) | $Q = \sum_{ij}^{N} [A_{ij} - \gamma P_{ij}] \delta(c_i, c_j)$ | $A_{ij}$: observed number of connections between nodes $i$ and $j$  
$P_{ij}$: predicted number of connections between nodes $i$ and $j$  
$N$: number of nodes in the whole network  
$c_i$: module in which the node $i$ is included  
$\delta(c_i, c_j)$: Kronecker delta function is equal to 1 if $c_i = c_j$, 0 otherwise  
$\gamma$: resolution parameter |
| Predicted number of connections ($P_{ij}$) | $P_{ij} = \frac{b_{ji}}{2m}$ | $b_{ji}$: the degree of the node $i$  
$m$: total number of edges in the network |
| Participation coefficient ($PC_i$) | $PC_i = 1 - \sqrt{\frac{1}{M} \sum_{s} \left( \frac{k_{is}}{k_{is}} \right)^2}$ | $M$: number of modules  
$k_{is}$: number of connections of node $i$ to nodes in module $s$ |
During the detection of optimal communities of nodes in the brain, the structural resolution parameter (γ) plays an important role because it weights the null model in the modularity estimation. In this study, γ was varied in the interval [0.3–5.0] with steps of 0.1 to avoid biasing the subsequent analyses (Betzel et al., 2017). Then, the similarity between the consensus structure and the community structure across participants was calculated using the adjusted Rand coefficient (Traud, Kelsic, Mucha, & Porter, 2011) for each γ. Finally, an automated maximization algorithm was implemented in MATLAB to detect one or more γmax associated with local maxima of the Rand coefficient among the 48 tested gammas. The Newman–Grivan procedure was employed to detect significant modules in the consensus structure (s; Newman & Girvan, 2004), as follows. Null models (10,000) were generated using a random permutation of module assignments while maintaining the original size and number of modules. Within each null model, the modularity contribution Qc of each module was calculated as the summation of the real minus the expected number of connections between node pairs. The expected number of connections between each node pair was weighted with node degree (Betzel et al., 2017; Newman & Girvan, 2004). Only modules in which the real modularity contribution was greater than 99.9% of the simulated modularity contributions (p < .001) were considered significant.

The percentage of each predefined network (Di Plinio & Ebisch, 2018) covered by each module was estimated to characterize the modules’ functional fingerprints.

**Brain–Behavior Relationship Analysis**

Global statistics of modularity (Q) and global efficiency as well as nodal statistics of participation (Guimerà & Nunes Amaral, 2005) and efficiency (van den Heuvel & Sporns, 2013) were extracted and analyzed concerning the prospective and retrospective components of the SoA.

A two-step robust weighted regression was applied to analyze the participation coefficients excluding poor fitting and overfitting. In the first step, the model was fitted using all the module’s nodes as levels of a random grouping variable, and the prospective component was used as a continuous predictor. In the second step, the analyses were repeated after removing nodes violating model assumptions, that is, with inhomogeneous residuals within the corresponding random grouping as indicated by Anderson–Darling normality tests. Regressions were performed separately for each module to detect module-specific associations between participation measures and the SoA. Results were corrected for multiple comparisons after model diagnostics and outlier removal. Best linear unbiased predictors were extracted to estimate the effect at the nodal level and highlight nodes with the highest contributions, whereas significant effects were detected (Liu, Rong, & Liu, 2008). Individual conditional expectation (ICE) plots were generated to visualize significant effects at both the nodal and modular levels (Goldstein, Kapelner, Bleich, & Pitkin, 2015). The impact of significant results was tested also considering different graph density thresholds (10%, 15%, 20%, 25%, and 30%) through the cost integration approach (Hilger et al., 2017; Ginestet, Nichols, Bullmore, & Simmons, 2011), conforming to current neuroscientific standards (Nichols et al., 2017; van den Heuvel et al., 2017). A Bayesian bootstrap procedure was employed to estimate the reliability of the beta coefficients from the regression analyses (Rubin, 1981). Starting from the hypothesis that the individual intrinsic brain signatures may be associated with the implicit SoA depending on the structural resolution of the modular architecture, and in line with recent multiresolution approaches (Chen et al., 2018; Jeub, Sporns, & Fortunato, 2018), the modularity Q was analyzed using all the γ values in the interval [0.3–5.0]. Three different analyses were implemented to test these associations. First, a simple linear model was fitted for each value of γ using the modularity Q as the dependent variable and the prospective component as a continuous predictor. Second, the link between modularity and the SoA was tested in a multivariate model including all the structural resolutions in a single analysis, with levels of γ being used as repeated measures. Third, a penalized regression (elastic net; Zou & Hastie, 2005) was adopted to account for the many potentially correlated variables, that is, modularity values at different levels of γ. The optimal regularization coefficient of shrinkage (λ) for the penalized regression was chosen as the λ minimizing the mean squared error in 100 Monte Carlo cycles of two-folded cross-validations (Hastie, Tibshirani, & Friedman, 2009). Because the LASSO-penalty in the regression constraints irrelevant variables (irrelevant γ) to be zero, the stability of feature selection was estimated by calculating the frequency of nonzero coefficients in 500 bootstrap cycles (threshold: p < .05). It can be argued that functional connectivity may depend on the level of musical expertise, the fitness of the individuals, handedness, or sex (van der Westhuizen, Moore, Solms, & van Honk, 2017; Kühnis, Elmer, & Jäncke, 2014; Herting & Nagel, 2013). To this aim, the analyses described above were also performed adding years of sports training and music expertise as covariates. In addition, the interaction of the measures of agency and participant’s sex and handedness was considered, and we repeated all the analyses using weighted graphs (Sporns & Betzel, 2016) to explore the stability of the results in relation to the methodology used.

**RESULTS**

**Behavioral Results: Confirming a Significant Prospective SoA in Healthy Participants**

The average perceptual shifts are reported in Table 2 and illustrated in Figure 2A. As expected, we found a strong prospective component, whereas the retrospective component was nearly zero. This effect was confirmed by the
results of the mixed-effects model. Significant effects were found for the factor Tone probability, $p = .02, F(1, 160) = 5.7$, and for the interaction between Tone probability and Trial type, $p = .01, F(1, 160) = 6.1$. The factor Trial type by itself was not significant, $p = .38, F(1, 160) = 0.8$. The statistics observed for the intercept, $p = .06, F(1, 160) = 3.4$, showed that the average perceptual shift ($\Delta$) in the experimental conditions was different from the baseline perceptual shift ($\Delta_{B}$), although only a trend was observed. The prospective component was confirmed by contrasting perceptual shifts between the “action-only” trials of the two probability conditions ($p < .001$, Tukey’s honestly significant difference test).

The results of the bootstrap procedure to estimate the effect sizes are shown in Figure 2B and indicated a medium-to-large effect size regarding the prospective component ($g = 0.39$, bootstrapped 95% CI $[0.19, 0.61]$). Effect sizes related to the retrospective component were rather irrelevant ($g = 0.10$, 95% CI $[−0.04, 0.23]$). Finally, the difference from the baseline was medium to large ($g = 0.38$, 95% CI $[0.08, 0.67]$).

### Graph Analyses: The Modular Brain Structure

Three resolution parameters, corresponding to $\gamma_1 = 0.6$, $\gamma_2 = 1.2$, and $\gamma_3 = 1.9$, were found to maximize the adjusted Rand coefficients (Figure 3A). We report results related to the modular structure associated with $\gamma_3$ because significant relationships with the SoA were found within this modular configuration. Group-averaged matrices of functional connectivity are reported in Figure 3B and show the nine significant modules found with $\gamma_3$ ($M1 – M9, p < .001$ using the Newman–Girvan procedure).

Anatomical fingerprints of the nine modules with respect to predefined brain functional networks (Di Plinio & Ebisch, 2018) are depicted in Figure 3C. The consensus community detection (with $\gamma_3$) detected five modules encompassing associative cortices in the frontal, parietal, and temporal lobes ($M1$–$M4, M7$). Among these modules, $M1$ was mainly related to default mode and language systems; $M2$ incorporated frontal, insular, and cingulate regions often ascribed to salience and control networks; $M3$ encompassed high-order executive and attentional regions; $M4$ included regions associated with motor attention and social interactions; and $M7$ included regions associated with late stages of visual processing. Furthermore, two sensory modules were detected, namely, $M5$ and $M6$, that were related to sensorimotor/auditory and visual networks.

### Table 2. Perceptual Shifts

<table>
<thead>
<tr>
<th>Group</th>
<th>Condition</th>
<th>Trial Type</th>
<th>$\Delta \pm SE$ (msec)</th>
<th>$\Delta - \Delta_B \pm SE$ (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average perceptual</td>
<td>Baseline</td>
<td>Action only</td>
<td>$-50 \pm 10$</td>
<td>-</td>
</tr>
<tr>
<td>shifts $\pm SE$</td>
<td>50%</td>
<td>Action only</td>
<td>$-45 \pm 8$</td>
<td>$4 \pm 5$</td>
</tr>
<tr>
<td></td>
<td>50%</td>
<td>Action and tone</td>
<td>$-42 \pm 9$</td>
<td>$7 \pm 5$</td>
</tr>
<tr>
<td></td>
<td>75%</td>
<td>Action only</td>
<td>$-33 \pm 9$</td>
<td>$16 \pm 6$</td>
</tr>
<tr>
<td></td>
<td>75%</td>
<td>Action and tone</td>
<td>$-39 \pm 8$</td>
<td>$11 \pm 5$</td>
</tr>
</tbody>
</table>

Average perceptual shifts in the three groups are shown both before ($\Delta$) and after ($\Delta - \Delta_B$) the subtraction of the baseline.

![Figure 2. Behavioral results. (A) Average values and standard errors of perceptual shifts relative to the baseline condition ($\Delta - \Delta_B$), which represent measures of intentional binding. As expected, participants showed a significant effect relative to the prospective component. (B) Bootstrapped effect sizes (Hedges’ $g$) for the prospective component, retrospective component, and intercept. Null distributions were created by scrambling data between experimental conditions in 10,000 bootstrap cycles. Whereas a medium-to-large effect was observed for the prospective component (top) and the intentional binding (bottom), the retrospective component showed a close-to-zero effect size (center). These results replicate findings from Di Plinio et al. (2019).](http://direct.mit.edu/jocn/article-pdf/32/9/1764/1862181/jocn_a_01590.pdf)
Figure 3. Consensus modularity. (A) Local maxima of the Rand coefficient were detected for three gamma values: $\gamma_1 = 0.6$, $\gamma_2 = 1.2$, and $\gamma_3 = 1.9$. (B) Group-averaged functional connectivity matrix ($\gamma_3 = 2.1$). Each significant module ($p < .001$, comparison with 10,000 null models following the Newman–Girvan procedure) is enclosed in a square, distinguishing within-modules (inside the squares) and between-modules (outside the squares) connections. (C) Functional fingerprints of the nine modules identified with $\gamma_3 = 1.9$ as compared with predefined brain networks (Di Plinio & Ebisch, 2018). The width of each circle represents the amount of overlap between each network and each module, calculated as the normalized percentage of each network covered by each module. (D) Modular structural topographies with $\gamma_3 = 1.9$. A full list of regions included in each module is available upon request to the corresponding author. DMN = default mode network; lDMN = lateral DMN; Limb = limbic network; Lan = language network; FPN = frontoparietal network; dDAN/pDAN = distal/proximal dorsal attention network; TPJN = temporoparietal junction network; CON = cingulo-opercular network; SM1/2 = sensorimotor networks; Aud = auditory network; Vis1-3 = visual networks; SUB = subcortical nodes; CER = cerebellar nodes.
relationships between the two measures were found for γ. In particular, the strongest association was found for γ = 1.8, t(57) = 2.5, p = .01, β = 4.3e−4.

The same effect was observed using a multivariate model. A higher prospective SoA was associated with a higher modularity Q, F(47) = 3.2, p < .001. The effect was still significant after applying the Huynh–Feldt correction for sphericity (p = .049). This relationship was especially strong for γ in the interval [1.3–2.4]. Figure 6A reports the predicted Q for different values of the prospective component. Although modularity is acknowledged as a measure of the internal cohesion of modules, increasing the structural resolution parameter automatically results in a lower Q. This happens because many connections become cross-modular by using additional smaller modules; that is, more connections are excluded in the estimation of Q. To characterize the relationship between a γ-standardized measure of the modularity and the prospective SoA, we also estimated Qadj, that is, modularity adjusted for the value of γ (Qadj = γQ). The association between Qadj and the SoA was still significant, F(47) = 3.1, p < .001, and remained significant also after Huynh–Feldt correction for sphericity (p = .044).

The cross-validated mean square errors (MSE) regarding the elastic net penalized model are shown in Figure 6B. The λ associated with the minimum MSE produced a structure of beta estimates with 10 nonzero significant values. Remarkably, as shown in Figure 6C, the elastic net regression returned nonzero estimates in correspondence to all the significant γ values from the linear regression models. The highest effect was associated with γ = 1.8 (β = 14.1). Modularity values with γ in the interval [1.7–2.2] were significant after the bootstrap procedure used to control for the stability in feature selection (darker colors in Figure 6C).

To further explore the meaning of the results relative to global modularity, we implemented a post hoc analysis of the association between global modularity and the SoA. For each γ and each module MX, we estimated the modularity Q′ by excluding the module MX. Then, we linearly regressed Q′ against the prospective component to find the effect size β′. The contribution C of the module MX was estimated as C_MX = β − β′, that is, as the difference between the effect size obtained considering the whole brain (β) and the effect size obtained excluding the module (β′). To note, this procedure avoids the introduction of magnitude biases. Finally, values of C_MX were associated with each node in MX and summed across γ values. Thus, higher values of C indicate a higher contribution of nodes in the module MX to the association between agency and modularity. The results of this post hoc analysis are illustrated in Figure 6D and show that nodes in sensorimotor and insular regions were the strongest contributors to the association between global modularity and agency using both binary and weighted graphs. No significant effects were found concerning the retrospective component. Measures of global efficiency were not significantly associated with intentional binding.

The Prospective SoA Is Associated with Whole-brain Modularity

The association between the prospective SoA and multiscale global modularity was investigated in multiple ways. Using linear regression models, significant positive relationships between the two measures were found for γ ranging in the interval [1.3–2.4] (Figure 5A). The t statistics for the effect of the prospective component on modularity Q with increasing γ are reported in Figure 5B.
Figure 4. Associations between agency and nodal/modular participation. (A) ICE plot for Module M4, which illustrates the relationships between the prospective component and network measures of participation. Each slope represents the zero-centered predictions of a node’s participation coefficient (y axis) for a given individual score in the prospective component (x axis). Color intensity indicates the effect strength (beta value, estimated using best linear unbiased predictors [BLUPs]). The average effect at the module level is indicated by a thick black line, t(544) = 3.3, p = .001, β = 3.6e−4. (B) Module M4. The size and color intensity of the nodes are regulated according to the strength of the associations (βs) between the prospective component and participation coefficients. (C) Nodes in M4 in which the effect was statistically stronger than the average slope for the module. For each node, the Montreal Neurological Institute coordinates and the effect sizes are indicated. Diamonds indicate left-handed participants. (D) Estimates and relative standard errors for the bootstrap analysis of interactions between the prospective component of the SoA and participation coefficient (Module M4) are reported for each graph threshold analyzed (*p < .05, **p < .005). Each point represents the beta estimate after a single bootstrap cycle. Box plots are also shown. To note, results were significant using all the threshold ranges considered (from 0.10 to 0.30). (E) Estimates and relative standard errors for the bootstrap analysis of interactions between the prospective component of the SoA and participation coefficient (nodal level) are reported for each graph threshold analyzed. To note, results were significant using all the threshold ranges considered (from 0.10 to 0.30). L = left.
Summarizing, the results from linear, multivariate, and penalized regression models showed a significant positive association between the prospective (but not the retrospective) SoA and the global modular organization of the brain with medium structural resolutions (with $\gamma$ in the interval $[1.4\text{–}2.3]$). Importantly, even if it may be considered a suboptimal model, results from linear regression would allow possible comparisons with studies focalizing...

Figure 5. Associations between agency and global modularity: linear regression. (A) Scatter plots representing values of the prospective component (x axis) against global modularity (y axis) for each value of $\gamma$ tested. Significant ($p < .05$) interactions in binary graphs are indicated with green background colors. Significant ($p < .05$) interactions in weighted graphs are indicated with bold purple axes. Diamonds indicate left-handed participants. (B) The $t$ statistic for the association between global modularity ($Q$) and the prospective component is represented for each $\gamma$ and is shown for binary (top, green color) and weighted (bottom, purple color) graphs. Darker green and purple colors indicate significant associations ($p < .05$).
Covariates included in the analyses, such as sex, handedness, musical expertise indexed by the years involved in musical training, and sportive skills indexed by years of sports training, were not significant and did not interact with the effects of the predictive component.

Results Using Weighted Graphs

The results reported in the previous paragraphs were confirmed using weighted graphs. The modular structure identified with weighted graphs was largely similar to the modular
structure obtained through binary graphs, including a default mode module analogous to M1, a salience/control module analogous to M2, a motor attention module analogous to M4 (including SMG, superior parietal cortex, PMC, and dorsal precuneus), a sensorimotor module analogous to M5, a visual module analogous to M6, a limbic module analogous to M8, and a cerebellar module analogous to M9. The network participation of the motor attention module, corresponding to M4, was positively associated with the prospective component of the SoA, $t(544) = 3.9, p < .001, \beta = 3.1e-4, 95\% CI \{1.5e-5, 4.6e-4\}$, adjusted $R^2 = .88$, thus confirming the results from binary graphs. One difference between weighted and binary graphs was related to the contribution of nodes to the effect: In weighted graphs, the strongest effect was associated with nodes in the dorsal precuneus.

The association between the prospective SoA and multiscale global modularity was also confirmed with weighted graphs. Using linear regression models, significant effects were found for $\gamma$ ranging in the interval $[1.4-2.2]$. The strongest association was found for $\gamma = 1.9$, $t(37) = 2.3$, $p = .026, \beta = 4.3e-4$. The same effect was observed by using a multivariate model, $F(47) = 3.0, p < .001$ (Figure 6E). The effect was still significant after applying the Huynh–Feldt correction for sphericity ($p = .049$) and penalized regression, which returned nonzero estimates in correspondence of five of the seven significant $\gamma$ values from the linear regression models (Figure 6F). Modularity values associated with most $\gamma_i$ in the intervals $[1.5-1.6]$ and $[1.9-2.1]$ were significant after the bootstrap procedure (Figure 6G). The highest effect was associated with $\gamma = 1.9$ ($\beta = 11.6$). As in the case of binary graphs, the strongest contributors to this association were found in the sensorimotor and insular nodes (Figure 6H).

These results demonstrate an association between the SoA and both local and global properties of the resting brain independently of the method used to study the brain connectome (binary graphs, weighted graphs).

**DISCUSSION**

We showed that signatures of intrinsic brain activity are associated with the individual SoA in healthy adults. We focused on intentional binding as a measure of predictive and retrospective components of an implicit SoA (Haggard, 2017; Voss et al., 2010) and on graph-theoretical metrics to describe the intrinsic organization of functional brain networks based on a multiscale, cross-resolution approach (Rubinov & Sporns, 2010; Bullmore & Sporns, 2009). To the best of our knowledge, this is the first study that traces the experimental measure of the SoA to individual differences in the intrinsic functional brain architecture at both local and global scales.

At the regional (nodal) and network (modular) levels, participation coefficients were studied as measures of cross-network integration. Our results revealed an association between the prospective SoA and participation coefficients in a frontoparietal module, labeled M4, which consists of frontoparietal regions related to motor attention such as the IPL, PMC, and dorsal precuneus. Associations were confirmed using both binary and weighted graphs. These same regions have been associated with the sense of control over the environment to predispose the body to motor learning (Wolpert et al., 2011) and to generate internal predictions, which are then compared with perceived sensory stimuli (Haggard, 2017; Desmurget & Sirigu, 2009; Gallese, 2000). For example, IPL is a multimodal integration region (Caspers et al., 2011) involved in the translation of motor intentions into meaningful actions (Ra e et al., 2014; Farrer et al., 2003) and in distinguishing the self from other agents to generate a prospective SoA (Ticini, Dolk, Waszak, & Schütz-Bosbach, 2018; Chambon et al., 2015). Furthermore, PMC is involved in monitoring conscious movements (Desmurget et al., 2009) and in higher-order cognitive processes like overt task control (Chambon et al., 2013), whereas the dorsal precuneus has been associated with the perceived experience of agency (Cavanna & Trimble, 2006). Accordingly, certain sensorimotor disorders, such as the alien hand syndrome (Hassan & Josephs, 2016; Assal, Schwartz, & Vuilleumier, 2007) and impaired movement initiation (Desmurget et al., 2009), have been associated with aberrant functioning of the IPL, and others, such as anosognosia for hemiplegia (Vocat, Staub, Stroppini, & Vuilleumier, 2010), have been associated with impaired functioning of the PMC. These impairments often compromise the online adjustment of motor actions in voluntary actions versus externally driven movements (Fried, Haggard, He, & Schurger, 2017).

Taken together, these task-related studies have highlighted the role of regions involved in motor attention and motor learning, such as SMG, PMC, and dorsal precuneus, in sensorimotor processes that support the experience of control over actions and their intended consequences. In this context, our results on the local and modular scales make two major contributions. First, behavioral measures of an implicit, prospective SoA are related to the cross-module integration of a frontoparietal subsystem (Module M4) encompassing regions related to motor control and SoA. Second, within this subsystem, the most prominent contribution of internetwork connections to the prospective SoA comes from the left PMC, SMG, superior parietal cortex, and postcentral gyrus (using binary graphs) or from the bilateral dorsal precuneus (using weighted graphs). Our findings show that the prospective SoA may be rooted in the intrinsic functional connectivity patterns of the same regions that are modulated during motor control. In addition, they suggest that altered internetwork brain connections may shift the individual predisposition to contingent effects conveyed by the contextual sensory feedback, which consequently leads to diversified behavioral responses within the population. To note, the participation coefficients, but not nodal efficiency, were significantly associated with intentional binding. This suggests that the SoA is entailed in the modular structure of the brain because participation...
coefficients are module topography-dependent whereas nodal efficiency is module topography-independent. Conceivably, stronger internetwork connections mediated by this frontoparietal subsystem may be necessary for integrating action consequences with ongoing motor behavior to efficiently acquire a feeling of control over actions and their consequences.

Another intriguing finding in our study concerns the relationship between the prospective SoA and global modularity, but not global efficiency. Post hoc analyses further showed that nodes in the primary sensorimotor and middle-insular cortices were the primary source of this association. Global modularity parameters obtained during a task-free state may be interpreted as describing intrinsic organizational principles that quantify how efficiently a brain is represented by subnetworks or modules (Gallen & D’Esposito, 2019). Previous studies have reported various associations between whole-brain parameters and behavior, such as between modular organization and intelligence (Hilger et al., 2017), between intermodular connections and awareness (Godwin et al., 2015), and between global efficiency and short-term memory skills (Gupta et al., 2018). Expanding on these studies, our findings suggest that brain–behavior associations may exist at multiple hierarchical levels of brain architecture, especially regarding module topography-dependent measures.

It should be noted here that modularity measures may suffer from structural constraints (Betzel et al., 2017). This is a direct consequence of how the modularity itself is estimated: The observed intramodular connections are compared with the expected intramodular connections, which are estimated using null models (Bassett et al., 2011; Newman & Girvan, 2004). The constraint in this procedure arises because the weight of the null model is usually assumed to be unitary (γ = 1), essentially constraining the structural resolution of the network (i.e., the size of the modules). In this study, we overcame this limitation by exploring multiple resolution parameters. The results showed that increased values of modularity within medium–high structural resolutions were associated with increased prospective SoA. This interaction was significant with all the regression models that we tested, using both classic and γ-adjusted modularity and both binary and weighted graphs. These findings indicate that whole-brain features like modularity may explain high-order mechanisms like contextual predictions elicited by SoA when the brain subsystems (modules) fall between a medium size and a small size. Thus, specific resolutions of the modular structure may support specific cognitive functions.

We suggest that the relationship between the SoA and global modularity might be explained by the reliance of prospective intentional binding effects on multimodal predictive mechanisms constituting a general principle of brain functioning (Clark, 2013; Kording et al., 2007; Wolpert, 1997). In line with this hypothesis, several researchers have proposed a link between predictive coding and the self (Apps & Tsakiris, 2014; Friston, 2012; Kannape & Blanke, 2012). For instance, an essential feature of the self is the ability to generate probabilistic inferences as effenter copies (Friston & Kiebel, 2009; Synofzik, Vogserau, & Newen, 2008; Feinberg, 1978), which are then compared with sensory perceptions (Apps & Tsakiris, 2014; Wolpert et al., 2011). According to internal prediction models, such comparisons are needed to generate prediction errors (Sato & Yasuda, 2005) that favor the adjustment of the motor response (Bédard & Sanes, 2014). The relevance of such considerations is underlined by the crucial importance of the SoA for self-awareness (Haggard, 2017; Ruvolo et al., 2015; Taylor et al., 2014; Gallagher, 2000). Further research is needed to directly explore the interplay between global brain properties and predictive coding.

The relation between the SoA and the integrative functioning of brain networks may also potentially impact clinical contexts. We argue that a suboptimal prospective SoA, commonly observed in neuropathological conditions related to distributed cortical abnormalities such as psychosis (de Bézenac et al., 2018; Moore & Fletcher, 2012; Voss et al., 2010) and in altered awareness (Schooler et al., 2014; Berberian et al., 2012), may arise through two nonexclusive neurophysiological processes. On the one hand, failure of the brain to adopt its structural resolution to the ongoing behavioral context may favor polluted probabilistic estimates of action consequences. On the other hand, inaccurate sensorimotor predictions may result from aberrant intrinsic patterns of nodal functional connectivity in specific brain modules involved in agency tasks. Our report provides a first neurophysiological whole-brain backbone to psychological models of a prediction-based SoA that can be evaluated in clinical samples of psychopathology.

Some limitations of this study need to be mentioned. The study focuses on implicit (prospective and retrospective) measures of the SoA because explicit judgments of agency may be affected by cognitive biases (Synofzik et al., 2008; Wegner, 2002), implicit beliefs (Hoogeveen, Schjoedt, & van Elk, 2018; Desantis, Roussell, & Waszak, 2011), and attentional biases (Wen, Yamashita, & Asama, 2016). Accordingly, we argue that implicit behavioral measurements, rather than self-report measures, could be more suitable to start exploring the link between the SoA and intrinsic features of the brain. Moreover, this study replicates intentional binding effects from previous investigations (Di Plinio et al., 2019; Voss et al., 2010), supporting the robustness of the prospective intentional binding effect that reflects the implicit SoA (Moore & Obhi, 2012; Moore & Haggard, 2008). This cross-study robustness should also dispel potential concerns about the imbalance of the number of trials across conditions. Some general problems related to studies based on individual differences need to be mentioned, such as low experimental control. To limit such potential confounds, control analyses were performed using the years of sports training and music expertise as covariates (Kühnis et al., 2014; Herting & Nagel, 2013), showing that the effects reported in this study were independent of these factors. Finally, the
sample size may be considered small for individual differences analyses. However, the reliability of our results was demonstrated by applying bootstrapping procedures at the nodal, modular, and global levels. Furthermore, results were confirmed across multiple thresholds (retaining from 10% to 30% of the connections) and using both binary and weighted graphs.

In conclusion, we showed that both whole-brain intramodular connections and local intrinsic intermodular connections support the prospective SoA. Comparing predictions and intentions with action feedback is an essential feature of human brain function. This process may be favored by a neural substrate showing, on the one hand, a modular architecture represented by highly interconnected, adaptably rewiring subsystems and, on the other hand, efficient exchange of information mediated by motor-control brain systems. The balance of these two components may predispose to more efficient processing of extrinsic self-information, while aberrant network behavior may be a potential marker of increased psychosis-like traits (Di Plinio, Perrucci, Aleman, & Ebisch, 2020). Future studies may consider combining implicit and explicit measures of personal biases and their relationships with interindividual components may predispose to more efficient processing of extrinsic self-information, while aberrant network behavior may be a potential marker of increased psychosis-like traits (Di Plinio, Perrucci, Aleman, & Ebisch, 2020). Future studies may consider combining implicit and explicit measures of personal biases and their relationships with interindividual differences in brain activity and connectivity.

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