

Is the Sense of Agency in Schizophrenia Influenced by Resting-State Variation in Self-Referential Regions of the Brain?

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Schizophrenia is a disturbance of the *self*, of which the attribution of agency is a major component. In this article, we review current theories of the Sense of Agency, their relevance to schizophrenia, and propose a novel framework for future research. We explore some of the models of agency, in which both bottom-up and top-down processes are implicated in the genesis of agency. We further this line of inquiry by suggesting that ongoing neurological activity (the brain's resting state) in self-referential regions of the brain can provide a deeper level of influence beyond what the current models capture. Based on neuroimaging studies, we suggest that aberrant activity in regions such as the default mode network of individuals with schizophrenia can lead to a misattribution of internally/externally generated stimuli. This can result in symptoms such as thought insertion and delusions of control. Consequently, neuroimaging can contribute to a more comprehensive conceptualization and measurement of agency and potential treatment implications.

Key words: self/agency/schizophrenia/resting-state activity/default mode network/source monitoring hypothesis

Introduction

How do individuals perceive responsibility for their own actions? That is, on what grounds do agents attribute actions to themselves and believe to be responsible for them? Until fairly recently, the sense of agency (hereafter Sense of Agency [SoA]) has been a rather neglected topic by philosophers.¹⁻⁷ Agency was believed to be a straightforward matter of conscious intentions causing

actions. The self appeared to be the agent, as being capable of inducing physical events as causal consequences of certain of their conscious mental states. This assertion has been contested by the recent development of psychological and neuroscientific methods that have made the phenomenology of agency empirically accessible.^{2,3,8-10} It appears that the genesis of agency and the relation to the self is much less straightforward than it has been previously assumed by philosophers. Rather than agency being based solely on mental causation, SoA appears to be based on the interplay of both unconscious and conscious processes. A phenomenological notion of experiences of agency may thereby play an important role in the integration of conscious and unconscious processes which has raised the interest of philosophers. Gallagher² described agency as the experience that “I am the one who is causing or generating an action.” This implies that agency is a subjective phenomenon; open to the idiosyncrasies of human experience. “If we lacked altogether even a minimal sense of agency for automatically triggered actions,” says Pacherie,¹¹ “our agentive selves would be but fragmented islands on a sea of automaticity”. This vivid quote captures the impressions of those who exhibit a disrupted sense of agency; that is, those suffering from schizophrenia. One can imagine how it must feel to be lost on this sea of automaticity, where agency, and indeed the self, becomes a scattered archipelago. In this article, we refer to the *self* as the subjective experience that oneself is the agent of perception, action, cognition, and emotion; *sense of agency* is understood as the subjective feeling of control or responsibility over one's actions and the subsequent consequences.

In what follows, we suggest that aberrant resting-state activity in the self-referential regions of the brain of individuals with schizophrenia plays an influential role in their attribution of agency. We propose to extend the current models of agency to include the influence of ongoing resting-state activity in the attribution of agency.

The Sense of Agency and Schizophrenia: Phenomenology and Neurobiology

Schizophrenia is fundamentally a disorder of the self.¹²⁻¹⁶ Particular aspects of the self, namely the SoA, appears to be disrupted in individuals with schizophrenia (hereafter referred to as patients).¹⁷ One of the core features of a disrupted SoA is the misidentification of the source of internally generated stimuli, ie, the *agent*.¹⁸⁻²¹ This is the underlying principle of the source monitoring theory.¹⁹ This theory proposes that patients misattribute the source that generated a stimulus,^{18,22-25} which can result in symptoms like thought insertion.¹² From a phenomenological perspective, patients describe thought insertion as “ideas being forced into my head by someone else”. This follows the context of a misattribution of agency, because the source of the “ideas” is misattributed (exogeneous rather than endogenous).

From a neurobiological perspective, the default mode network (DMN) is important to the attribution of agency. The DMN describes a neural network that shows particularly high metabolic and neural activity in the resting state,²⁶⁻³⁰ where resting-state brain activity is defined as the period in which the brain is not engaging with any external stimuli (eg, specific cognitive tasks²⁶). Many of the symptoms of schizophrenia have been attributed to the failure of functional integration or aberrant connectivity in the DMN.³¹ The DMN primarily consists of cortical midline structures, including areas of the prefrontal, cingulate and temporal cortexes (figure 1).^{27,32} Conversely, the set of regions collectively known as the central executive network (CEN), shows the opposite

activity. The CEN includes lateral prefrontal and parietal cortical regions that are implicated mainly in attention and goal-oriented executive functions.³³⁻³⁶ Interestingly, patients demonstrate aberrant spatio-temporal patterns in the ongoing resting state in these regions which can impact the SoA at a neural level.^{26,37}

What Does Neuroscience Have to Say About the SoA?

Several empirical models and experimental approaches were developed in order to explore SoA. SoA is often operationally defined as the reported degree of responsibility regarding the result of an action. It is typically quantified by experiments which consist of participants performing an initial action (eg, a button press), followed by an effect/consequence (eg, a tone is produced), and then a perceived responsibility judgement. The effect/consequence is experimentally manipulated, typically by a spatial or temporal distortion (eg, the tone is delayed).³⁹ Generally, experiments show that the closer the spatial/temporal proximity of the initial task to the consequence, the greater the degree of perceived responsibility, ie, the greater the SoA. The Comparator model (CM)^{22,40,41} and the Multifactorial Weighting Model⁴² (MWM) are 2 influential theories of SoA. Essentially, the CM proposes that the SoA is generated by comparing a predicted outcome of intended motor plans to the actual outcome. When the prediction is congruent with the actual outcome, then agency is attributed to the self; if not, then agency is attributed elsewhere (figure 2).^{22,40}

However, the CM has been criticized for being unable to explain how factors that are outside of the physiological system can influence the SoA.^{6,42,43} For example, participants reported greater feelings of agency when primed with self-related pronouns compared with a priming with non-self-related words.⁴⁴ Therefore, cognitive factors can also play a role in the attribution of agency and suggest that physiological information alone is not sufficient to explain the different dimensions of SoA phenomenology.

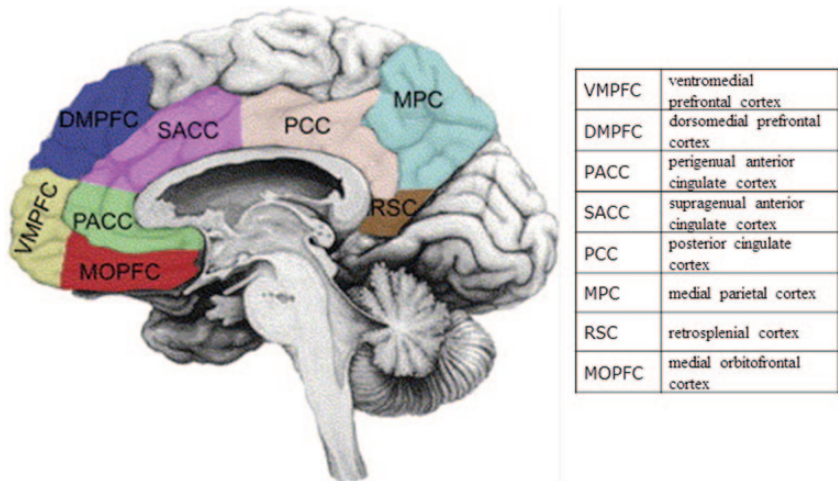


Fig. 1. Midline regions in the cortex (from Northoff⁵¹). The image is a sagittal slice of the brain take in its midline.

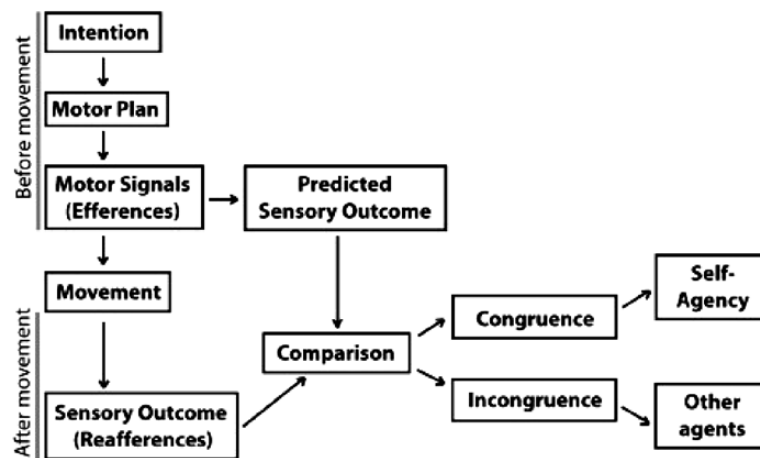


Fig. 2. The comparator model reproduced with permission (from David et al⁸).

Synofzik's⁴² MWM extended the CM to include higher-order functions as well. They separated SoA into 2 related concepts: Feelings of Agency (FoA) and Judgments of Agency (JoA). FoA involves implicit, lower level sensorimotor process, similar to the components of CM; JoA refers to higher-order factors that can incorporate factors such as contextual cues from the environment, social cues, intentions, and thoughts/beliefs. Following a Bayesian-type statistical system, each of these components is assigned a weight based on the reliability of that information.⁴⁵ Under healthy conditions, the components of FoA provide reliable information, so more weight is ascribed to those components. Whereas, in patients the somatosensory systems becomes disrupted over time due to dysfunctional glutamatergic and dopaminergic systems,^{5,46,47} less weight is assigned to the (increasingly) unreliable components of FoA and more on JoA.^{48,49} Figure 3 provides an illustration of this via a hypothetical weighting system.

Considering an Extended Resting-State-Based Model of SoA

Summing up, the CM^{22,40,41} provided a good starting point to explain the genesis of agency based on physiological/bottom-up processes, and the MWM⁴² extended that to incorporate top-down processes. These models, while supplying a solid foundation to explore agency, may not be complete.

We suggest an extension of these models to include ongoing neurophysiological processes, ie, the brain's intrinsic resting-state activity as a preliminary influence to later processing. In this sense, the brain's resting state can be conceptualized as the background in which all the processes that lead to the generation of the SoA take place. As stated above, the DMN is an important region for the study of the self.⁵⁰ The DMN demonstrates higher activity during self-referential tasks vs non-self-referential tasks.^{27,32,51,52} A meta-analysis found

that externally guided (goal-oriented) decision-making tasks yielded stronger activity changes in lateral frontal and parietal regions of the brain (associated with the CEN), whereas internally guided tasks yielded increased activity in the DMN, including the pregenual anterior cingulate cortex, ventromedial prefrontal cortex, dorsomedial prefrontal cortex, posterior cingulate cortex, and precuneus⁵³ (also see Nakao et al³⁸ and Northoff⁵⁴). Additionally, comparing brain activity while counting heartbeats (endogenous) compared with counting auditory tones (exogenous), Wiebking⁵⁵ found that, in healthy subjects, neural activity in the DMN was negatively correlated with activity in the CEN (ie, as one increases, the other decreases). This supports the idea that when the resting-state activity in the DMN is stronger, the focus is primarily on internal mental contents that are more related to the self (also see Vanhaudenhuyse et al³⁵); and stronger resting-state activity in lateral regions of the CEN leads to increased external mental contents being perceived as originating from the environment (Northoff⁵⁶). Most importantly, this predominance of external mental contents in awareness appears to take place at the expense of the internal mental contents with a reciprocal balance between both: either the load of internal mental contents is high and the ones of external mental contents is low or, conversely, the latter predominate while the former, the internal ones, recede in the background.³⁵ Following the source monitoring hypothesis, disruption of this balance can lead to a blurring between endogenous and exogenous stimuli in schizophrenia.

SoA, Schizophrenia and the Resting State

How is the pattern of resting-state activity in the DMN and CEN relevant to the symptoms of schizophrenia? There is evidence from several different experimental paradigms that ongoing resting-state activity in both the DMN and in the CEN can affect how internal/external

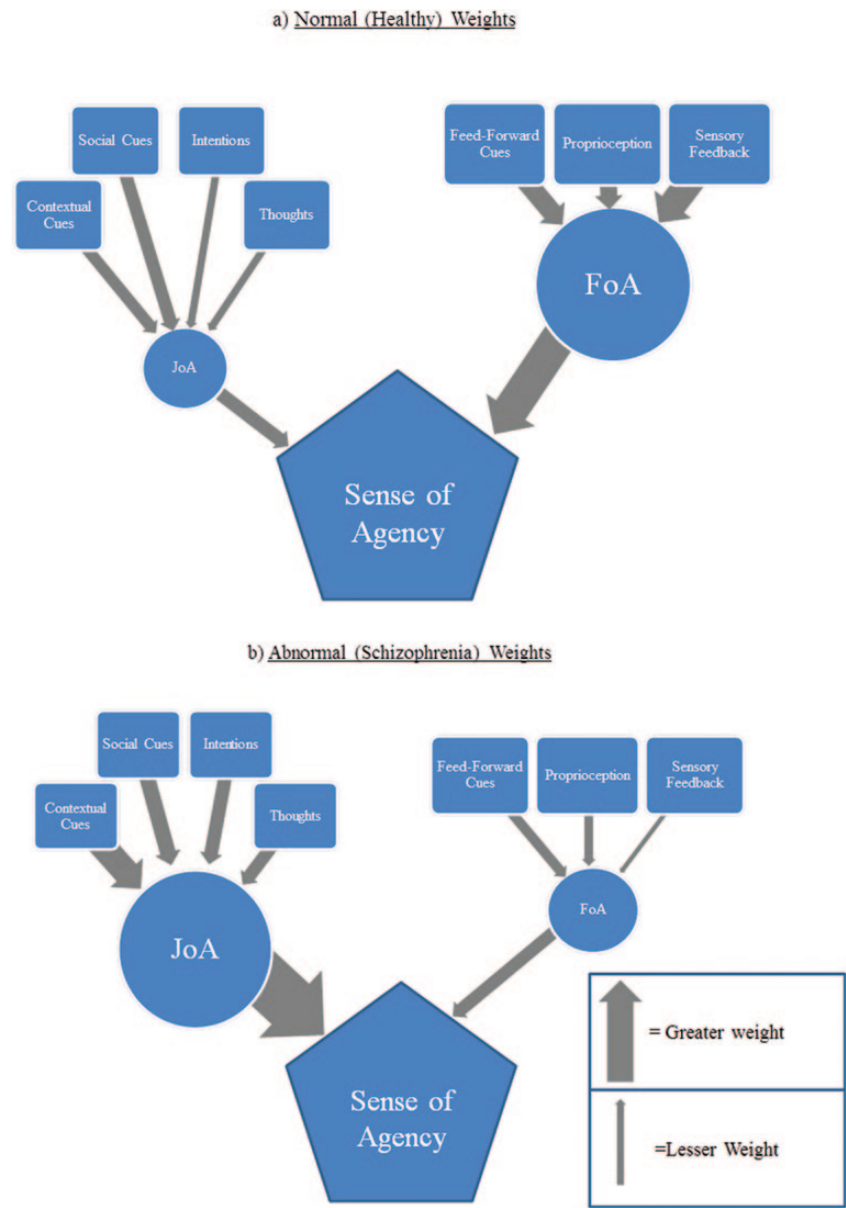


Fig. 3. Multifactorial Weighting Model: Agency is based on the combination of the components of JoA and FoA. Each component is assigned a weight based on its reliability. The girth of the arrow indicates a hypothetical weight assigned to each component. (a) In healthy individuals the components of the reliable FoA are assigned greater weight, whereas in (b) patients rely more on the components of JoA rather than FoA.

stimuli are processed^{31,35,55,57–59} and that DMN activity is related to source attribution.^{54,60,61} Specifically, stronger resting-state activity in the lateral regions of the CEN leads to an increased likelihood that mental contents will be construed as originating from the environment (non-self-related); whereas stronger activity in the DMN yields an increased focus on internal mental contents (self-related).^{61,62} In healthy individuals, when processing internal/external stimuli there appears to be a negative correlation between the activity in the DMN and CEN;^{35,55} ie, when activity in the DMN is stronger and the focus is on internal mental contents,

there is a decrease in activity in the CEN, and vice versa. However, this relationship appears abnormal in patients. For example, when healthy subjects were given psilocybin (a drug that mimics psychosis), the negative correlation of blood-oxygen level-dependent activity between the DMN and the CEN decreased after administering Psilocybin and even became a positive correlation. That is, while participants were experiencing a mild psychosis similar to schizophrenia, a positive correlation of activity was found between the DMN and CEN.⁵⁷ Similarly, individuals at risk for psychosis demonstrated a positive correlation

between the medial prefrontal cortex (associated with the DMN) and the right dorsolateral prefrontal cortex (associated with the CEN).⁶³ The positive relationship between activity in the DMN and the CEN can lead to difficulty separating internally vs externally generated stimuli. Therefore, the relationship between the DMN and the CEN might be linked to the misattribution of agency in patients.

Using the MWM,⁴² we can see how resting-state activity in the DMN and CEN can influence the attribution of agency. As discussed above, due to the degeneration of the sensory system, patients rely less on components of FoA and more on the components of JoA. Then aberrant activity in the DMN and CEN, blurs the judgement of the source of a stimulus (endogenous/exogenous). Figure 4 illustrates this idea.

Conclusion

Current theoretical frameworks regarding the attribution of agency implicate both bottom-up and top-down processes in the genesis of SoA. Here we propose that the brain's ongoing resting-state activity may influence these processes at an even more fundamental level. The Comparator Model suggests that the SoA is created by comparing predicted to actual sensory feedback. When predicted and actual sensory inputs match, agency is attributed to the self. When actual input diverges from predicted, agency is attributed externally. In the MWM, agency is closely linked to higher-order cognitive processes rather than merely comparing predicted and actual sensory information. In the case of schizophrenia, both models suggest that the physiological processes that

become disrupted over the course of the disorder, thus distort the attribution of agency. This misattribution of agency can explain a number of the positive symptoms of schizophrenia.

Where though does the increased noisiness in schizophrenia originate? We suggest that the pattern of ongoing resting state in self-referential regions of the brain influences the SoA at the neural level. In healthy individuals, when mental contents are externalized, there is stronger activity in the lateral regions of the CEN,^{61,62} but when mental contents are internalized, there is stronger activity in the DMN.^{35,55} In patients, however, activity in the DMN is decreased during rest- and task-evoked activity, which may explain psychotic symptoms such as thought insertion.^{31,58,64} Therefore, the pattern of that activity could provide an abnormal baseline against which sensory and cognitive activity is set. Since the pattern of neural activity in the DMN and CEN is related to the attribution of agency, and agency is a major component of the self, aberrant activity in these regions can lead to a disordered sense of self.

This could be experimentally validated by examining the pattern of resting-state activity in the DMN/CEN during an internal/external source attribution task. Clinically, assessing and regulating the aberrant pattern in the DMN and CEN could be a treatment target to reduce psychopathological symptoms. Furthermore, if the pattern of the resting state in the DMN and CEN is directly implicated in psychopathological symptoms of the self, then this would support the emerging concept of “spatiotemporal psychopathology”, see Northoff^{65,66} for further details.

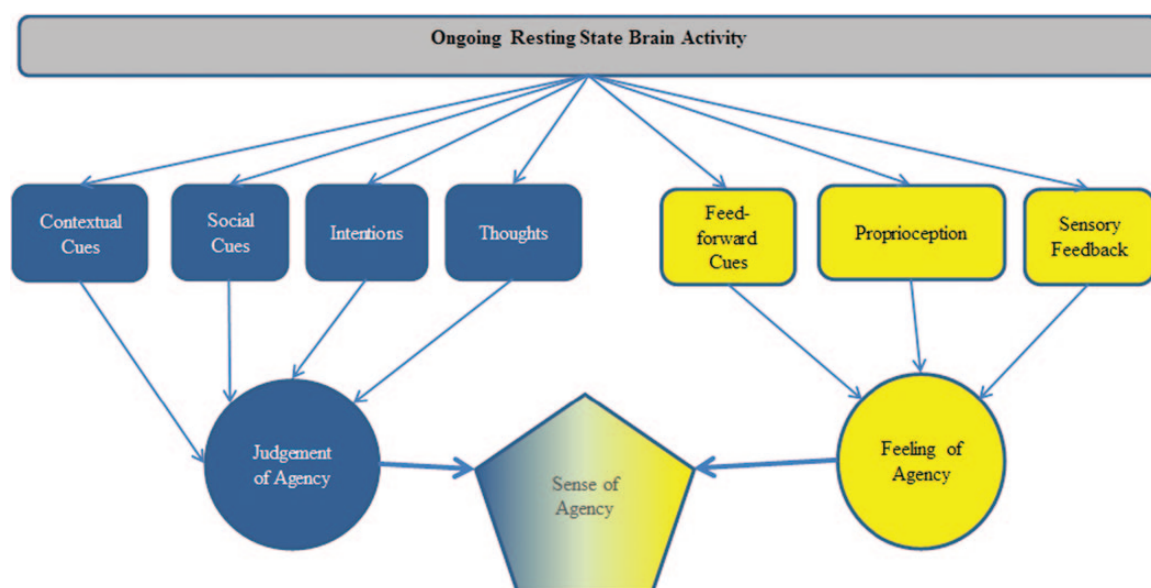


Fig. 4. Ongoing resting state activity provides the background against which the components of the MWM are incorporated into the generation of the SoA.

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