

## Auditory Hallucinations and the Brain's Resting-State Networks: Findings and Methodological Observations

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In recent years, there has been increasing interest in the potential for alterations to the brain's resting-state networks (RSNs) to explain various kinds of psychopathology. RSNs provide an intriguing new explanatory framework for hallucinations, which can occur in different modalities and population groups, but which remain poorly understood. This collaboration from the International Consortium on Hallucination Research (ICHR) reports on the evidence linking resting-state alterations to auditory hallucinations (AH) and provides a critical appraisal of the methodological approaches used in this area. In the report, we describe findings from resting connectivity fMRI in AH (in schizophrenia and nonclinical individuals) and compare them with findings from neurophysiological research, structural MRI, and research on visual hallucinations (VH). In AH, various studies show resting connectivity differences in left-hemisphere auditory and language regions, as well as atypical interaction of the default mode network and RSNs linked to cognitive control and salience. As the latter are also evident in studies of VH, this points to a domain-general mechanism for hallucinations alongside modality-specific changes to RSNs in different sensory regions. However, we also observed high methodological heterogeneity in the current literature, affecting the ability to make clear comparisons between studies. To address this, we provide some methodological recommendations and options for future research on the resting state and hallucinations.

**Key words:** psychosis/schizophrenia/fMRI/default mode network/perception

### Introduction

Auditory hallucinations (AH) are vivid perceptions of sound that occur without corresponding external stimuli and have a strong sense of reality. AH feature in 60%–90% of schizophrenia cases, in other psychiatric and neurological conditions, and in a minority of the general population.<sup>1</sup> While many involve voices, nonverbal AH also occur (including environmental sounds, animal noises, and music).

Despite much research on the topic, many questions remain regarding the brain mechanisms of AH.<sup>2</sup> One unanswered question is how they can occur spontaneously from the brain's intrinsic activity. This has been explored by studying the brain in its so-called “resting state,” ie, the spontaneous neural activity and patterns of connectivity between brain regions that are observable when participants are asked to lie still in a scanner and not engage in any particular task.

The International Consortium on Hallucination Research (ICHR) is a global network of researchers, clinicians, and people with lived experience of hallucinations that was created to facilitate multisite collaborations.<sup>3,4</sup> This ICHR report outlines our current knowledge of the

resting state in relation to AH. Although elements of this topic have been reviewed elsewhere,<sup>5,6</sup> this report extends prior work by incorporating evidence from a range of methods and populations, including a specific comparison of auditory and visual hallucinations. This allows us to identify the most important changes to the resting state, establishing what may be specific to AH, what may be specific to a disorder (such as schizophrenia), and what may act as a general marker for unusual perceptions across various populations. A critical review of existing methodologies and potential confounds is also presented.

Here, we first outline the general characteristics of the brain's resting state and introduce some of the most commonly studied resting-state networks (RSNs). In the following sections, we then review functional MRI findings on RSNs relating to schizophrenia and AH and compare them with (1) evidence from other investigative methods (EEG/MEG and structural MRI) and (2) resting-state research on visual hallucinations, both in schizophrenia and in other conditions such as dementia. In the final 2 sections, we evaluate existing methodological approaches, offer a model that summarizes AH findings to date, and discuss the key issues and implications for future research.

### What Is Rest? Intrinsic Activity and Its Networks

Resting-state activity refers to the intrinsic patterns of brain activity that are observable in the absence of an external task.<sup>7</sup> In fMRI, this is typically described in terms of functional connectivity: the correlations between signals in different brain regions.<sup>8</sup> Spatially, the brain's intrinsic activity can be divided into RSNs such as the default mode network (DMN), central executive network (CEN), salience network (SN), and sensorimotor networks.<sup>9,10</sup> Regions involved in these RSNs (table 1) show dense functional connectivity at low frequencies (0.01–0.1 Hz) in the resting state. The DMN is often deactivated during many tasks and may be associated with self-referential or internally directed processing.<sup>9,11</sup> It shows anticorrelated

intrinsic activity to a collection of “task-positive” networks, including the CEN, SN, and sensorimotor networks.<sup>12,13</sup> The CEN has been linked to executive functioning and cognitive control, including working memory and top-down attention.<sup>12</sup> The SN has been associated with monitoring and selecting behaviorally relevant events for further processing.<sup>14,15</sup> Effective goal-directed information processing may require a carefully controlled interaction between the SN and CEN, which may in turn affect processing in sensory and motor networks.<sup>12</sup> Importantly though, intra- and internetwork connectivity is thought to constantly change over time.<sup>16,17</sup> This generates a dynamic spatial structure to intrinsic activity, partly but not fully determined by underlying anatomy.<sup>18,19</sup>

Fluctuations in electrophysiological oscillatory activity also provide a spatiotemporal structure to intrinsic activity: Functional connectivity can be assessed via the synchronization of neural oscillations between different brain regions and frequency bands such as theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (>30 Hz). However, the large majority of resting-state studies on AH have only used fMRI.<sup>6</sup>

### The Resting State and AH: Evidence From fMRI

AH are particularly common in schizophrenia-spectrum disorders (Sz), where they occur alongside other psychotic symptoms (such as delusions), cognitive, and functional changes. Given the primacy of AH in the disorder, RSNs of participants with schizophrenia may provide important clues to those involved in AH.

#### Resting-State Findings in Schizophrenia

**Default Mode Network.** Consistent with a cognitive profile characterized by executive dysfunction, Sz studies often show altered connectivity within the DMN and reduced anticorrelation with areas associated with the CEN, such as dorsolateral prefrontal cortex.<sup>25</sup> Posterior sections of DMN in Sz also show greater connectivity to surrounding sensory areas (such as lateral occipital cortex), which may

**Table 1.** Common Resting-State Networks

Network	Regions	Studies in Healthy Population
Default mode network (DMN)	mPFC, precuneus, PCC, TPJ, MTL	Raichle et al <sup>9</sup> ; Buckner et al <sup>11</sup>
Central executive network (CEN)	dIPFC, supragenual ACC, lateral parietal cortex	Fox et al <sup>20</sup> ; Seeley et al <sup>15</sup>
Salience network (SN)	Right anterior insula, ventral striatum, dorsal ACC	Menon <sup>10</sup> ; Goulden et al <sup>21</sup>
Sensorimotor networks (including language and auditory regions)	HG, left IFG, insula, bilateral STG, inferior temporal cortex, caudate, SMA	Hampson et al <sup>22</sup> ; Beckmann et al <sup>23</sup> ; Lee et al <sup>24</sup>

*Note:* ACC, anterior cingulate cortex; dIPFC, dorsolateral prefrontal cortex; HG, Heschl's gyrus; IFG, inferior frontal gyrus; mPFC, medial prefrontal cortex; MTL, medial temporal lobe; PCC, posterior cingulate cortex; SMA, supplementary motor area; STG, superior temporal gyrus; TPJ, temporoparietal junction.

reflect problems with cognition and unusual experiences in the disorder.<sup>26</sup> When DMN alterations correlate with clinical scores, they often associate with positive symptom ratings<sup>27,28</sup> (for a review, see<sup>29</sup>).

***Salience Network.*** Striatal regions of the SN includes projections of the mesolimbic dopaminergic system (MDS), which are important in assigning novelty and significance to sensorimotor and mental events,<sup>30</sup> while the anterior insula has been implicated in monitoring surprise-based prediction errors during decision-making<sup>31</sup> (see **Box 1**). In terms of RSN dynamics, the SN has been suggested to assign salience by switching attention between the DMN and CEN.<sup>14</sup> Thus, disrupted MDS activity in schizophrenia could result in atypically modulated RSNs. However, evidence of SN dysfunction specific to psychosis has been inconsistent. Two trait studies showed decreases in functional connectivity in Sz during information processing and at rest,<sup>32,33</sup> and another 2 have linked connectivity alterations to general psychotic symptoms.<sup>34,35</sup> Orliac et al<sup>36</sup> showed that reduced connectivity in Sz between SN and DMN was linked to delusion but not hallucination severity. Negative findings of SN dysfunction also exist in Sz,<sup>37</sup> although this may be due to methodological or sampling differences.

***Central Executive Network.*** As noted above, anticorrelation between the DMN and task-oriented RSNs such as the CEN is often reduced in Sz.<sup>29</sup> Consistent with executive dysfunction in Sz, resting-state connectivity increases and decreases have been reported in this network<sup>37,38</sup> alongside atypical correlations with frontotemporal regions.<sup>37</sup>

#### *Resting-State Findings Specific to AH*

Given DMN, SN, and CEN alterations in Sz, AH studies have focused on these RSNs, as well as on sensory networks involving auditory and language regions. Studies have either focused solely on participants with AH,<sup>59</sup> compared those with and without AH,<sup>60</sup> or reported correlations with hallucination severity.<sup>61</sup> Few non-Sz resting-state studies of AH exist, although 2 have included people in the general community who regularly experience AH (“nonclinical voice hearers”).<sup>62,63</sup>

***Default Mode Network.*** Various articles have posited a specific link between DMN function and AH. For instance, Northoff and Qin<sup>5</sup> proposed that resting interactions between auditory cortex and parts of the DMN may produce a state of confusion regarding external stimulation and resting-state activity. Support was provided by Jardri et al,<sup>64</sup> who compared hallucinations and “real rest” periods in 20 adolescents with psychosis (participants had either AH, VH, or both). Hallucinations were associated with spontaneous engagement of sensory cortex, specific to modality, alongside disengagement and

### **Box 1: Predictive Coding, Auditory Hallucinations, and Rest**

A further challenge is how to integrate evidence of resting-state alterations with computational models of auditory hallucinations (AH). In parallel to the rising interest in resting-state networks, some researchers have advocated predicting processing approaches to understanding perception.<sup>38</sup> Predictive coding (PC) and Bayesian models of the brain posit that perception and inference are part of a unitary process.<sup>39,40</sup> Under PC, brain systems have a hierarchical organization of message passing that reduces coding of predictable information by minimizing prediction errors (PEs) in internal predictive models about the external environment. Each level of the hierarchy is comprised of functional units signaling feedback predictions and feedforward PEs, the latter being essential teaching signals that prompt updating of internal predictive models. Intuitively, PC suggests that the brain is not merely a passive feature detector, but an active creator of internal, predictive models of the environment, which determine both perception and inference about external stimuli. It follows that abnormalities in encoding of such internal predictive signals could result in abnormal percepts such as hallucinations.<sup>41</sup>

This framework accommodates models of dysfunctional corollary discharge in psychosis (which can be regarded as a special case of predictive coding), as well as findings of deficient mismatch negativity (MMN) in psychosis, as MMN has been considered a type of sensory PE signal.<sup>42</sup> Ample evidence supports deficits in both corollary discharge mechanisms and MMN in schizophrenia<sup>43</sup> with some evidence supporting their relationship to AH.<sup>44</sup> Computational-model-based analyses of EEG and fMRI data have also suggested specific deficits in sensory PE signals in schizophrenia during auditory processing<sup>45</sup> and in hallucinating patients with schizophrenia during speech discrimination,<sup>46</sup> respectively. Deficient PEs have also been linked to increased activity in voice-selective regions of the auditory cortex,<sup>47</sup> a neural phenotype previously linked to AH.<sup>46,48,49</sup>

According to PC and associative learning models more generally, PEs prompt learning by inducing changes in synaptic plasticity that remodel connection strengths encoding predictions.<sup>50</sup> Some fMRI studies have provided evidence for connectivity changes as a function of associative learning in healthy individuals<sup>51–53</sup> and for a relationship between learning and intrinsic connectivity.<sup>54</sup> PC models of psychosis may therefore share a common ground with dysconnectivity views of schizophrenia, which posit that failures in synaptic plasticity (eg, NMDA-dependent plasticity and its modulation by neurotransmitters like

dopamine and acetylcholine) are at the core of the disorder.<sup>55</sup> Key questions to explore are how voice-selective changes to PE in auditory cortex relate to local functional connectivity within surrounding temporal cortex (which could be assessed using methods such as Regional Homogeneity) and long-range functional connectivity with default mode network, salience network (SN), and central executive network. It has also been suggested that the anterior insula, within the SN, is important for integrating interoceptive PEs that give rise to a sense of agency or presence<sup>56</sup>; if this were to be disrupted, it could be involved in the alterations of agency that are common in AH. Recent advances in task-based and resting-state fMRI analysis, including dynamic causal modeling,<sup>57</sup> are a promising avenue to investigate the relationships between abnormal connectivity, predictive learning mechanisms, and unusual experiences such as AH.

weaker integrity of the DMN (as measured by its consistency over time during scanning), suggesting that unstable DMN states may be an important precursor to AH states. Further support came from Alonso-Solis et al,<sup>26</sup> who observed atypical connectivity-specific AH between hubs of the DMN and SN.

Other studies show inconsistent DMN alterations in AH. In a Sz + AH sample, Wolf et al<sup>61</sup> observed no difference in DMN function or correlation with symptoms: Connectivity alterations were observed in precuneus and posterior cingulate but these were specific to an executive control network and a left frontoparietal network, respectively (see below). In contrast, van Lutterveld et al<sup>63</sup> observed increased connectivity in posterior regions of the DMN in a sample of nonclinical AH participants, which may indicate differing routes to AH-proneness in clinical and nonclinical populations.

**Central Executive Network and Salience Network.** While showing no differences in DMN function, Wolf et al<sup>61</sup> observed reduced connectivity in the posterior CEN (precuneus) and increased connectivity in anterior CEN (right middle and superior frontal gyri), with increased middle frontal gyrus connectivity correlating with AH severity. Correlations with AH were also observed within a left-lateralized frontoparietal network that the authors related to speech processing and monitoring: More severe AH associated with decreased anterior cingulate cortex (ACC) connectivity and increased left superior temporal gyrus (STG) connectivity. Correlations between hallucination severity and altered resting connectivity have also been reported for the ACC,<sup>65,66</sup> medial prefrontal cortex (mPFC),<sup>59</sup> and anterior insula.<sup>58</sup>

**Sensorimotor Networks.** Most RSN research on AH has focused on connectivity in auditory and language regions.

Oertel-Knochel et al<sup>67</sup> examined resting connectivity between seeds identified with an auditory language task, observing largely reduced connectivity between left auditory cortex and limbic regions in Sz + AH. Similar results were reported by Shinn et al<sup>65</sup> who observed widespread reductions in connectivity for left primary auditory cortex (PAC), and by Gavrilescu et al,<sup>68</sup> who observed reduced interhemispheric PAC connectivity. However, recent work by Chyzhyk et al<sup>60</sup> identified right rather than left PAC as a key discriminator of AH status in Sz patients, highlighting some inconsistency in current findings.

Based on the role of Broca's and Wernicke's areas in speech processing, other studies have focused on connectivity between left inferior frontal gyrus (IFG) and the posterior STG, respectively. Hoffman et al<sup>69</sup> observed elevated connectivity within a corticostriatal loop including STG (bilaterally), left IFG, and the putamen, in a pattern specific to Sz + AH. In contrast, Sommer et al<sup>70</sup> found reduced connectivity between left IFG and left STG in AH participants, although only in comparison with healthy controls (ie, no clinical group without AH was included). In nonclinical AH, the left STG shows elevated connectivity with right STG and right IFG<sup>62</sup> and acts as stronger connectivity "hub" at rest.<sup>63</sup> Language lateralization may differ between clinical and nonclinical voice hearers,<sup>71</sup> suggesting that extrapolating across these groups may be problematic, but taken together, these results indicate that atypical resting connectivity between left STG and other areas is common in AH.

Altogether, these studies point to a complex interaction between sensory, default mode, executive, and salience networks in AH. Inconsistent findings link overall DMN activity to AH, but there is evidence of DMN instability over time correlating with hallucination occurrence.<sup>64</sup> Associations are also evident between AH and connectivity within SN and CEN, suggesting that problems with salience processing and cognitive control could contribute to a less stable balance between RSNs involved in external, sensory-guided attention.<sup>5</sup> In addition, studies point to altered resting connectivity in left temporal regions implicated in auditory and language processing, although these findings require replication as some results (such as PAC connectivity) appear contradictory. In this context, drawing on evidence from other research methods, modalities, and conditions involving hallucination could help to parse out specific and general RSN properties important to AH.

## Evidence From Neurophysiology and Structural Connectivity

### *From the Resting State to AH in EEG/MEG*

Compared with stimulus-driven research, few EEG/MEG studies have examined the resting state in relation to either AH specifically or positive symptoms more broadly. At rest, Lee et al<sup>72</sup> reported greater amplitude of beta oscillations in those with Sz + AH compared with

Sz, with group differences localizing to left frontoparietal regions implicated in speech and language processing (left medial frontal gyrus and inferior parietal lobule). Andreou et al<sup>73</sup> observed generally increased resting-state gamma oscillations within a left frontotemporoparietal network in Sz participants but surprisingly reduced gamma for those with higher positive symptoms (ie, those with greater levels of hallucinations and delusions had more normalized resting gamma). The actual occurrence of AH has been associated with increased gamma-theta coupling in frontotemporal areas,<sup>74</sup> decreased beta power in left temporal cortex,<sup>75</sup> and increased alpha connectivity between left and right auditory cortices.<sup>76</sup> Analysis of rapid connectivity patterns known as “microstates” has also linked AH occurrence to shortened frontoparietal network patterns linked to error monitoring.<sup>77</sup> Taken together, these findings support the primary role of left-lateralized frontotemporal cortex during AH but highlight how resting markers are likely to encompass a wider network of frontoparietal regions.

#### *Comparisons With Structural Connectivity*

Because of the auditory-verbal nature of many AH, much research on structural connectivity has focused on integrity of the arcuate fasciculus (AF), the main white matter tract linking inferior frontal and superior temporal cortex. Consistent with RSN evidence of STG alterations, AF has generally reduced white matter integrity in Sz + AH compared with controls.<sup>78</sup> There is also some evidence that this is specific to Sz + AH compared with Sz,<sup>79</sup> especially for verbal AH (AVH<sup>80</sup>), while milder alterations to AF are evident in nonclinical voice hearers.<sup>81</sup> However, as in the RSN literature, some studies have reported contrasting results, including elevated connectivity in people with Sz + AH<sup>82</sup> or positive correlations between integrity and AH severity.<sup>83</sup>

A second tract linking STG to frontal and occipital regions (supporting a ventral rather than dorsal language pathway) is the inferior occipital-frontal fasciculus (IOFF). Two studies have reported reduced structural integrity of the left frontotemporal segment of the IOFF being specifically related to AVH.<sup>79,84</sup> Consistent evidence linking AH and structural connectivity elsewhere is so far lacking. Two studies<sup>79,85</sup> have reported reduced structural integrity of the corpus callosum in Sz + AH compared with Sz and healthy controls—consistent with evidence of altered interhemispheric resting connectivity in AH<sup>68</sup>—but an earlier study reported stronger connectivity in an Sz + AH group.<sup>86</sup> There is also some evidence that integrity of the cingulum (thought to be important in DMN connectivity, eg,<sup>87</sup>) may be reduced in Sz + AH, although this has also been observed in Sz-only samples without any correlation to AH.<sup>88</sup> No studies have specifically sought to examine structural connectivity in AH for the main RSNs discussed above. Thus, though there

is emerging evidence of white matter differences beyond the AF, more evidence is needed on AH-specific white matter changes and how they may relate to resting-state pathology.

#### **Comparisons With VH**

##### *Comparing the Resting State in Auditory and Visual Hallucinations in Schizophrenia*

VH are roughly half as common as AH in schizophrenia<sup>89,90</sup> and are more prominent in neurological conditions with known etiology (such as Lewy Body Dementia [LBD] and Charles Bonnet syndrome<sup>91</sup>) leading to them being less studied in Sz. Indeed, common instruments for assessing hallucinations in Sz either neglect the distinction between AH and VH<sup>92</sup> or primarily focus on AH.<sup>93</sup> Importantly, the majority of Sz who experience VH also experience AH, but not necessarily simultaneously, allowing for comparison between the 2 experiences.

Four studies have specifically compared Sz participants with AH and AH + VH. Because of its proposed role in salience, Rolland et al<sup>94</sup> focused on connectivity of the nucleus accumbens (NAc), finding greater connectivity between NAc and bilateral insula, putamen, parahippocampal gyri, and ventral tegmental area for participants with AH + VH (compared with just AH). Meanwhile, because of its involvement in both VH<sup>95</sup> and AH,<sup>48</sup> Amad et al<sup>96</sup> analyzed hippocampal connectivity in both groups, observing hyperconnectivity to mPFC and caudate in participants with AH + VH specifically. Those with AH + VH also had higher white matter connectivity between the hippocampus and visual cortex and greater hippocampal hypertrophy.

In contrast, Ford et al<sup>97</sup> observed no differences in hippocampal connectivity between AH and AH + VH participants but reported hyperconnectivity between visual cortex and amygdala specific to those with AH + VH. In the same participants, Hare et al<sup>98</sup> identified decreased amplitude of low frequency fluctuations (ALFF) in AH compared with AH + VH, in retrosplenial/inferior precuneus (BA29), left hippocampus, bilateral insula, thalamus, medial cingulate, and the medial temporal lobe. Overall, these findings show much overlap in AH and VH circuitry but also that multisensory elements involve further alterations in connectivity to limbic and striatal cortex.

##### *Comparisons With VH in Other Disorders*

Aberrant perceptual phenomena also occur in a range of other neuropsychiatric disorders but often manifest in the visual rather than auditory domain. They are particularly common in Parkinson's disease (PD) and LBD.<sup>99</sup> Popular models implicate widespread impairments in attention and perception in the manifestation of hallucinations,<sup>100</sup> which are supported by evidence from resting-state studies that

show impaired connectivity within the DMN<sup>101,102</sup> and between attentional networks in the brain.<sup>103</sup> In addition, task-based fMRI has shown that visual misperceptions in PD are associated with increased DMN connectivity to ventral occipitotemporal regions that process object-related visual information.<sup>104</sup> Interestingly, the latter results have strong convergence with the finding that the visual cortices show increased resting connectivity with the amygdala in Sz with AH + VH,<sup>97</sup> suggesting similar yet divergent mechanisms underlying the manifestation of aberrant visual perception in different disorders.

Other neuropsychiatric disorders with VH demonstrate impairments in non-DMN networks. For instance, in post-traumatic stress disorder (PTSD), hallucinations and illusions (ie, misperceptions of actual stimuli) are relatively stereotyped and are closely related to the context in which the original stress occurred (eg, a war veteran with PTSD might hallucinate an enemy combatant or misperceive a telescope as a sniper rifle). Importantly, the primary pathological impairment in PTSD is related to impaired amygdala function<sup>105</sup> and overactivity of regions within the ventral attention network (VAN),<sup>106,107</sup> an RSN that overlaps anatomically and functionally with the SN but also typically includes regions of temporoparietal cortex.<sup>13</sup> Due to this

overactivity, it is assumed that any stimulus that closely matches the object related to the original stressor recruits attentional systems, leading to a rapid (and incorrect) increase in top-down influence over the ventral visual cortex, essentially “priming” the brain to incorrectly interpret the incoming stimulus. Although both LBD and PTSD are phenomenologically distinct from schizophrenia, the impairments in DMN<sup>29</sup> and VAN<sup>108</sup> suggest potential overlap between the different conditions and provide evidence of how hallucinations in different modalities can arise from the interaction of domain-general RSNs (managing salience and attention) with modality-specific regions.

### Current Methodology in Resting-State Studies

The study of RSNs and AH is an emerging field with a variety of often inconsistent findings. In the following section, we consider a number of potential confounds and recommendations for improving comparability and reliability of results.

#### *Resting-State Design and Potential Confounds*

The designs of resting-state studies on AH to date have been far from uniform (see [table 2](#)), which hampers comparison

**Table 2.** Study Characteristics of Resting-State fMRI Studies Into AH

Study	EO/EC	Scan Length (min)	RS Instructions	Presence of AH Asked?
Alonso-Solis et al <sup>26</sup>	EC	6	Pts instructed to close eyes and remain awake	Not reported
Chyzhyk et al <sup>60</sup>	EO	10	Stay awake, keep eyes open, and think of nothing in particular	Yes for some participants
Clos et al <sup>59</sup>	EC	6	Lie in the scanner as still as possible with their eyes closed yet stay awake	Yes
Diederer et al <sup>62</sup>	EC	6	Pts kept eyes closed but stayed awake	Yes
Gavrilescu et al <sup>68</sup>	EC	5	Relax with eyes closed	Yes
Jardri et al <sup>64</sup>	EC	15	Pts kept still in a state of wakeful rest with eyes closed	Yes
Manoliu et al <sup>58</sup>	EC	10	Eyes closed and not to fall asleep	Pts asked about any “feelings of odd situations” during scan.
Oertel-Knochel et al <sup>67</sup>	EO	6.7	Lie still, do not engage in any speech, think nothing specially and look at white fixation cross	Yes
Rotarska-Jagiela et al <sup>28</sup>	EO	6.7	Lie still with eyes open fixating on a white cross presented in the center of visual field.	Not reported
Shinn et al <sup>65</sup>	EO	10	Stay awake, keep eyes open, and think of nothing in particular	Yes for some participants
Sommer et al <sup>70</sup>	EC	6	Pts instructed to lie in scanner as still as possible with eyes closed yet stay awake	Yes
Sorg et al <sup>112</sup>	EC	10	Keep eyes closed and not to fall asleep.	Pts asked about any “feelings of odd situations” during scan.
Van Lutterveld et al <sup>63</sup>	EC	6	Pts kept eyes closed but stayed awake	Yes
Vercammen et al <sup>66</sup>	EC	7.8	Close eyes and try to “clear your mind” but not fall asleep.	No
Wolf et al <sup>61</sup>	EC	6	Relax without falling asleep, keep eyes closed, not think about anything in particular, and move as little as possible	Yes

*Note:* AH, auditory hallucinations; EC, eyes closed; EO, eyes open; Pts, participants. Hoffman et al<sup>69</sup> extracted intermittent resting data from a symptom capture paradigm involving button pressing, and so is not included here.

of study findings. In table 3, we offer some suggestions to improve uniformity across experiments, some of which are specific to AH research and some that are more general. Most important in AH studies are participant instructions and debriefing: Instructing participants to keep their eyes closed is associated with higher functional connectivity within auditory networks<sup>109</sup> (which may not be desirable) and arguably increases the likelihood of participants falling asleep. We therefore suggest that future studies use an eyes-open design. Beyond this, instructing participants to do anything other than relax can lead to signal changes (eg,<sup>110</sup>) and can create demand characteristics: When participants know in advance that they will be asked about AH, this can induce attention effects which confound hallucination-related brain activity.<sup>111</sup> A thorough debrief about unusual experiences after scanning is preferred to online monitoring.

In general, longer scan times are preferable (increasing scan time to 13 min greatly improves reliability<sup>114</sup>), and it is important to control for potential effects of head movement, cardiac rate, and respiration.<sup>115–117</sup> Data scrubbing of bad volumes<sup>118</sup> or matching groups for head motion are 2 ways of counteracting potential movement effects. Finally, during data analysis, use of global signal regression to account for nonneuronal artifacts should be avoided, as this can introduce spurious negative correlations.<sup>119</sup>

Resting-State Analysis

There are 2 common approaches to analyzing resting-state fMRI connectivity data: strongly and weakly

Table 3. Recommended Methods for Resting Studies of AH

Basic demographics and pre-interview	Age, gender, sleep patterns, nicotine use, medication, hallucination phenomenology
Participant instructions	Eyes open, relax, keep still. Emphasize not falling asleep
Stimuli	Fixation cross on gray, nonbright background (if eyes open)
Scan length	At least 6 min; over 10 min preferred
Concurrent measures	Head movements, cardiorespiratory signal, sleep monitoring (camera or concurrent EEG)
Debrief	Presence of hallucinations during scanning, emotional state (eg, anxiety), other unusual experiences
Analysis	Seed-based (for hypothesis-testing); common seeds include IFG, STG, TPJ, ACC, hippocampus, insula. ICA-based (preferred); allows analysis of network interactions. Graph-theoretical measures (eg, path-length, betweenness centrality)
Common network frameworks	Triple network (DMN/CEN/SN <sup>10</sup> ) or Yeo et al <sup>113</sup> 7 or 17 network solution

Note: Abbreviations are explained in the first footnote to table 1. AH, auditory hallucinations; CEN, central executive network; DMN, default mode network; ICA, independent component analysis; SN, salience network.

model-driven. In seed-regression analyses, correlations are calculated between an a priori selected region and the rest of the brain. This is a strongly model-driven approach, as the selected seed region represents a spatial hypothesis about the brain state of interest, and is the most common approach used in resting-state AH studies. In contrast, 2 other methods have been used to characterize functional brain dynamics in a multivariate, weakly model-driven approach: independent component analysis (ICA) and graph theory. ICA is a multivariate, data-driven analysis tool of the Blind Source Separation family,<sup>120</sup> which has been shown to be particularly well-suited for analyzing distributed networks of intrinsic brain activity.<sup>121</sup> Unlike seed-based analysis, ICA does not require a priori definition of a seed region or ideal model of activity and provides multiple networks in a single analysis. Moreover, it has been argued that ICA has better test-retest reliability than seed-based methods<sup>122</sup> and may be better at estimating functional statistical maps in the case of unpredictable events such as hallucinations without the need for signaling events’ occurrences online.<sup>64,123</sup> Crucially, when participants hallucinate during a scan, ICA can be used to capture both DMN and hallucinatory fMRI activity: Jardri et al<sup>64</sup> describe a validated procedure for doing so that uses retrospective AH reports from participants. This property of ICA makes possible the exploration of the interplay between DMN and sensory cortices over time during “rest” and “hallucination” periods (defined at the individual IC level), without disrupting intrinsic RSN behavior. Finally, graph theory mathematically describes the architecture of interregional connections (ie, edges) of multiple brain areas (ie, nodes) in relation to efficiency of information processing,<sup>124</sup> which can be used to characterize local or global changes in network architecture. Graph theory can be considered complementary to the other functional connectivity tools, as it is often applied to output of the seed-based or ICA approaches. Its value is in allowing investigators to go beyond simple correlations between regions to examine the relative importance of paths and hubs within a network.

AH and the Resting State: Key Issues and Implications

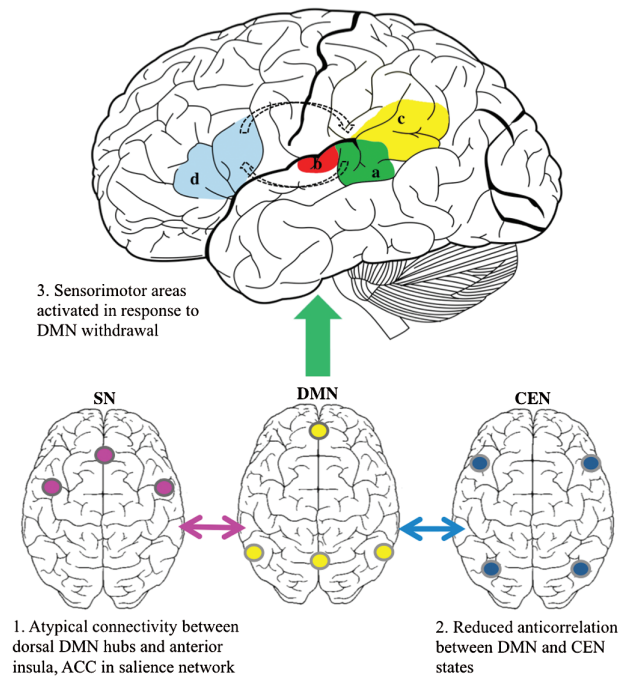
RSNs and AH: A Synthesis of Findings

The investigation of RSNs opens up a range of opportunities for understanding how and why hallucinations occur. The majority of AH research has so far focused on intrinsic connectivity of regions associated with speech, language, and auditory processing, both in fMRI and EEG/MEG: Most consistent are findings of altered connectivity in left posterior temporal regions implicated in speech perception (which are supported by structural evidence), but there are also multiple studies implicating inferior frontal, parietal, limbic, and striatal regions.<sup>6</sup> Such findings broadly support theories that posit disruptions to internal speech and language processes,<sup>125</sup>

although not consistently (cf.<sup>69,70</sup>). This is complemented by a growing body of evidence linking the DMN, CEN, and SN to both AH occurrence and predisposition, lending support to models of hallucinations that go beyond speech processes and emphasize other factors, such as cognitive control and attention.<sup>126</sup> As outlined in prior ICHR collaborations,<sup>127</sup> it is generally accepted that AH are likely to involve multiple cognitive mechanisms in their development, suggesting that a focus on multiple brain networks is required.

Few studies have demonstrated specific trait associations between DMN properties and AH (in comparison with evidence of general links to positive symptoms, eg,<sup>25</sup>). However, the interaction of the DMN with other RSNs<sup>26,58</sup> and dynamic stability of the DMN<sup>64</sup> are both implicated in hallucinatory states and traits. It is possible that atypical interactions of the DMN, SN, and CEN, when *allied* with altered resting connectivity in language and sensory networks, give rise to the collapse of internal states into sensory processing as described by Jardri et al<sup>64</sup> (see figure 1). This also partly supports Northoff and Qin's<sup>5</sup> proposal that AH arise from elevated resting-state activity in auditory areas and irregular modulation by anterior hubs of the DMN: The evidence here does not suggest a direct link between them but implies atypical DMN-SN-CEN interaction *alongside* connectivity alterations to sensory cortices. However, these findings are clearly preliminary and require further testing, especially in the face of inconsistent results and methodological heterogeneity. It will be important to examine how hubs of the domain-general RSNs interact with auditory areas, and the future use of alternative seeds/ROIs or ICA will shed further light on how these other networks contribute to AH.

Comparisons with mechanisms in VH provide an important source of information. Evidence of DMN instability in both AH and VH in psychosis and disruptions to DMN, executive, and salience networks in VH in other disorders imply a similar framework for hallucination susceptibility across different modalities. However, contrasts between AH and AH + VH in schizophrenia also suggest that disruptions to limbic and striatal connectivity may distinguish trait susceptibility for these experiences,<sup>96,97</sup> suggesting that more complex hallucinatory phenomena may require a higher base level of resting connectivity between sensory and limbic regions. Comparison with VH raises the question of whether other RSNs need to be examined in more detail in AH: eg, while a number of AH and Sz studies have focused on the SN, the VAN is relatively unstudied. The SN and VAN overlap in many ways—and the exact relationship between them is still unclear—but definitions of VAN often emphasize right frontoparietal structures (such as IFG and TPJ) rather than just insular and cingulate cortex (eg,<sup>13,128</sup>). Given that functional and structural characteristics of these regions have been related to AH



**Fig. 1.** Initial AH studies focused on resting connectivity in auditory and language regions (upper figure), primarily identifying atypical connectivity of left posterior STG (a), PAC (b), and the TPJ area (c). Findings of atypical resting connectivity between left IFG (d) and STG are inconsistent although both areas are often implicated during AH. More recent findings implicate atypical interaction of the DMN, SN, and CEN in those prone to AH (lower figures). The combination of atypical DMN interaction with SN (1) and CEN (2) and altered resting connectivity in sensory areas could prompt the collapse of internally focused states into activation of auditory cortex (3), which is then reverberated along a frontotemporal loop. The IFG, STG, and surrounding areas are often implicated in symptom-capture studies.<sup>48</sup> Note: ACC, anterior cingulate cortex; AH, auditory hallucination; CEN, central executive network; DMN, default mode network; IFG, inferior frontal gyrus; PAC, primary auditory cortex; SN, salience network; STG, superior temporal gyrus; TPJ, temporoparietal junction.

occurrence and phenomenology,<sup>129,130</sup> the VAN may prove a fruitful avenue for further investigation.

Indeed, the current focus on DMN, CEN, and SN in AH research arguably reflects only one approach to RSNs—the “triple network” model.<sup>10</sup> Other network approaches, such as that used by Yeo et al,<sup>113</sup> use many more functional networks in parallel. Future AH studies may choose to adopt such broader network solutions, especially to allow comparison with research on healthy cognitive function. Understanding of the DMN and other RSNs is also constantly advancing: The early discovery that the DMN is negatively correlated with another set of regions—namely those of the CEN<sup>20</sup>—was called into question by work demonstrating variability in this negative relationship over time.<sup>131</sup> Several subsequent studies have further revealed the complex spatiotemporal patterns of activity that underlie RSNs (eg,<sup>132–134</sup> for a review see<sup>16</sup>), while task studies show that regions

distributed across the whole brain and multiple networks are often involved in “single” processes.<sup>135</sup> In this respect, it is important to recognize that terms such as DMN or CEN are only placeholders for complex and likely cross-network processes, and researchers should be generally wary of treating them as modular, insulated entities.

### *Increasing Study Reliability and Aggregating Data*

In moving forward with resting-state research on AH, improving the comparability and reliability of results is a clear priority. One way of doing this is following a shared “standard” protocol (such as in [table 3](#)); another, more powerful approach is to aggregate data across studies, facilitating the acquisition of a more heterogeneous and representative subject sample.<sup>136</sup> fMRI data are typically pooled using meta-analyses of significant activations (eg,<sup>137</sup>), but such analyses cannot aggregate power across studies as they rarely report effect sizes. A more direct method for aggregating data is by combining (raw) data across centers, also referred to as mega-analysis.<sup>138</sup> Although the instruction and fMRI protocol may differ across studies, this approach allows for the use of the same preprocessing and analysis on all data. Another option consists of multicenter studies in which the scan protocol, participant instructions, scanner, software, hardware, etc. are standardized.<sup>139</sup> Variability between centers can be monitored through the use of acquisition of phantom data and traveling heads, ie, control subjects that are scanned at each site to estimate cross-site variability. Although recent studies indicate that scanner-related variance is low compared with between-subject variability and measurement error,<sup>140,141</sup> it can be modeled by entering study site as a random effects factor capturing variability between study sites.<sup>142</sup> In this vein, the authors of this article are currently planning a mega-analysis of existing resting-state data from research teams within the ICHR: To date, 7 participating centers have agreed to aggregate their data (which includes over 150 participants with AH).

### *Clinical Implications and Directions for Further Research*

As a young field, resting-state research on AH is still at the stage of basic rather than translational science. However, the opportunity to study state and trait markers of AH using resting methods has great clinical potential: In a recent example, Mondino et al<sup>143</sup> demonstrated changes in resting temporoparietal connectivity associated with symptom reduction in patients who had completed 10 weeks of transcranial direct current stimulation for persistent AH. A further way of making resting-state studies more clinically relevant would be to include more detailed examination of hallucinatory phenomenology and contextual factors, both in general and following scanning. While many studies have reported AH symptom correlations, this is usually a total severity score, rather than

specific to different kinds of phenomenological features, and wider environmental and social variables are almost never included. Other key remaining questions, with basic and applied implications, are how resting-state fMRI findings relate to functional connectivity measured with neurophysiological methods (eg,<sup>144</sup>), evidence of changes to anatomical connectivity,<sup>78</sup> and computational models of hallucinations, such as predictive processing approaches (see [Box 1](#)). The use of multimethod studies will go some way to address these issues in future research.

## **Conclusion**

The spatiotemporal dynamics of the brain’s resting state have great potential to offer new insights in the study of hallucinations. Studies of AH highlight altered resting connectivity of speech and language regions, such as the left STG, although there is growing evidence of domain-general resting networks (and thus the brain’s spontaneous activity as a whole) being implicated in Sz + AH and perhaps other kinds of hallucinatory states. Studies of VH suggest that additional networks may be involved, including limbic and striatal regions, although more studies contrasting RSN in VH and AH are needed across different population groups. Alongside this, the study of RSNs is subject to a range of potential confounds and methodological differences, prompting a need to combine efforts and methods across laboratories. A more connected approach will improve comparability and reliability of studies and enhance understanding of how, in the case of AH, a signal may emerge from noise.

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## **References**

1. Johns LC, Kompus K, Connell M, et al. Auditory verbal hallucinations in persons with and without a need for care. *Schizophr Bull.* 2014;40(suppl 4):255–264. doi:10.1093/schbul/sbu005.
2. Allen P, Modinos G, Hubl D, et al. Neuroimaging auditory hallucinations in schizophrenia: from neuroanatomy to neurochemistry and beyond. *Schizophr Bull.* 2012;38:695–703. doi:10.1093/schbul/sbs066.
3. Woodward TS, Jung K, Hwang H, et al. Symptom dimensions of the psychotic symptom rating scales in psychosis: a multisite study. *Schizophr Bull.* 2014;40(suppl 4):S265–S274. doi:10.1093/schbul/sbu014.

4. Thomas N, Rossell SL, Waters F. The changing face of hallucination research: the International Consortium on Hallucination Research (ICHR) 2015 meeting report. *Schizophr Bull.* December 16, 2015. doi:10.1093/schbul/sbv183.
5. Northoff G, Qin P. How can the brain's resting state activity generate hallucinations? A "resting state hypothesis" of auditory verbal hallucinations. *Schizophr Res.* 2011;127:202–214. doi:10.1016/j.schres.2010.11.009.
6. Alderson-Day B, McCarthy-Jones S, Fernyhough C. Hearing voices in the resting brain: a review of intrinsic functional connectivity research on auditory verbal hallucinations. *Neurosci Biobehav Rev.* 2015;55:78–87. doi:10.1016/j.neubiorev.2015.04.016.
7. Northoff G. Immanuel Kant's mind and the brain's resting state. *Trends Cogn Sci.* 2012;16:356–359. doi:10.1016/j.tics.2012.06.001.
8. Fingelkurts AA, Fingelkurts AA, Kahkonen S. Functional connectivity in the brain - is it an elusive concept? *Neurosci Biobehav Rev.* 2005;28:827–836. doi:10.1016/j.neubiorev.2004.10.009.
9. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci U S A.* 2001;98:676–682. doi:10.1073/pnas.98.2.676.
10. Menon V. Large-scale brain networks and psychopathology: a unifying triple network model. *Trends Cogn Sci.* 2011;15:483–506. doi:10.1016/j.tics.2011.08.003.
11. Buckner RL, Andrews-Hanna JR, Schacter DL. The brain's default network: anatomy, function, and relevance to disease. *Ann N Y Acad Sci.* 2008;1124:1–38. doi:10.1196/annals.1440.011.
12. Dosenbach NUF, Fair DA, Miezin FM, et al. Distinct brain networks for adaptive and stable task control in humans. *Proc Natl Acad Sci U S A.* 2007;104:11073–11078. doi:10.1073/pnas.0704320104.
13. Fox MD, Corbetta M, Snyder AZ, Vincent JL, Raichle ME. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proc Natl Acad Sci U S A.* 2006;103:10046–10051. doi:10.1073/pnas.0604187103.
14. Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct.* 2010;214:655–667. doi:10.1007/s00429-010-0262-0.
15. Seeley WW, Menon V, Schatzberg AF, et al. Dissociable intrinsic connectivity networks for salience processing and executive control. *J Neurosci.* 2007;27:2349–2356. doi:10.1523/JNEUROSCI.5587-06.2007.
16. Hutchison RM, Womelsdorf T, Allen EA, et al. Dynamic functional connectivity: promise, issues, and interpretations. *NeuroImage.* 2013;80:360–378. doi:10.1016/j.neuroimage.2013.05.079.
17. Di X, Biswal BB. Dynamic brain functional connectivity modulated by resting-state networks. *Brain Struct Funct.* 2015;220:37–46. doi:10.1007/s00429-013-0634-3.
18. Behrens TE, Sporns O. Human connectomics. *Curr Opin Neurobiol.* 2012;22:144–153. doi:10.1016/j.conb.2011.08.005.
19. Honey CJ, Sporns O, Cammoun L, et al. Predicting human resting-state functional connectivity from structural connectivity. *Proc Natl Acad Sci U S A.* 2009;106:2035–2040. doi:10.1073/pnas.0811168106.
20. Fox MD, Snyder AZ, Vincent JL, Corbetta M, Essen DCV, Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci U S A.* 2005;102:9673–9678. doi:10.1073/pnas.0504136102.
21. Goulden N, Khusnulina A, Davis NJ, et al. The salience network is responsible for switching between the default mode network and the central executive network: replication from DCM. *NeuroImage.* 2014;99:180–190. doi:10.1016/j.neuroimage.2014.05.052.
22. Hampson M, Peterson BS, Skudlarski P, Gatenby JC, Gore JC. Detection of functional connectivity using temporal correlations in MR images. *Hum Brain Mapp.* 2002;15:247–262. doi:10.1002/hbm.10022.
23. Beckmann CF, DeLuca M, Devlin JT, Smith SM. Investigations into resting-state connectivity using independent component analysis. *Philos Trans R Soc Lond B Biol Sci.* 2005;360:1001–1013. doi:10.1098/rstb.2005.1634.
24. Lee MH, Hacker CD, Snyder AZ, et al. Clustering of resting state networks. *PLoS ONE.* 2012;7:e40370. doi:10.1371/journal.pone.0040370.
25. Whitfield-Gabrieli S, Thermenos HW, Milanovic S, et al. Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proc Natl Acad Sci U S A.* 2009;106:1279–1284. doi:10.1073/pnas.0809141106.
26. Alonso-Solis A, Vives-Gilabert Y, Grasa E, et al. Resting-state functional connectivity alterations in the default network of schizophrenia patients with persistent auditory verbal hallucinations. *Schizophr Res.* 2015;161:261–268. doi:10.1016/j.schres.2014.10.047.
27. Garrity AG, Pearlson GD, McKiernan K, Lloyd D, Kiehl KA, Calhoun VD. Aberrant "default mode" functional connectivity in schizophrenia. *Am J Psychiatry.* 2007;164:450–457. doi:10.1176/ajp.2007.164.3.450.
28. Rotarska-Jagiela A, van de Ven V, Oertel-Knochel V, Uhlhaas PJ, Vogeley K, Linden DEJ. Resting-state functional network correlates of psychotic symptoms in schizophrenia. *Schizophr Res.* 2010;117:21–30. doi:10.1016/j.schres.2010.01.001.
29. Whitfield-Gabrieli S, Ford JM. Default mode network activity and connectivity in psychopathology. *Annu Rev Clin Psychol.* 2012;8:49–76. doi:10.1146/annurev-clinpsy-032511-143049.
30. Kapur S, Mizrahi R, Li M. From dopamine to salience to psychosis—linking biology, pharmacology and phenomenology of psychosis. *Schizophr Res.* 2005;79:59–68. doi:10.1016/j.schres.2005.01.003.
31. Rutledge RB, Dean M, Caplin A, Glimcher PW. Testing the reward prediction error hypothesis with an axiomatic model. *J Neurosci.* 2010;30:13525–13536. doi:10.1523/JNEUROSCI.1747-10.2010.
32. Tu P-C, Hsieh J-C, Li C-T, Bai Y-M, Su T-P. Cortico-striatal disconnection within the cingulo-opercular network in schizophrenia revealed by intrinsic functional connectivity analysis: a resting fMRI study. *NeuroImage.* 2012;59:238–247. doi:10.1016/j.neuroimage.2011.07.086.
33. White TP, Joseph V, Francis ST, Liddle PF. Aberrant salience network (bilateral insula and anterior cingulate cortex) connectivity during information processing in schizophrenia. *Schizophr Res.* 2010;123:105–115. doi:10.1016/j.schres.2010.07.020.
34. Palaniyappan L, Simmonite M, White TP, Liddle EB, Liddle PF. Neural primacy of the salience processing system in schizophrenia. *Neuron.* 2013;79:814–828. doi:10.1016/j.neuron.2013.06.027.
35. Wang X, Li F, Zheng H, et al. Breakdown of the striatal-default mode network loop in schizophrenia. *Schizophr Res.* 2015;168:366–372. doi:10.1016/j.schres.2015.07.027.
36. Orliac F, Naveau M, Joliot M, et al. Links among resting-state default-mode network, salience network,

- and symptomatology in schizophrenia. *Schizophr Res.* 2013;148:74–80. doi:10.1016/j.schres.2013.05.007.
37. Woodward ND, Rogers B, Heckers S. Functional resting-state networks are differentially affected in schizophrenia. *Schizophr Res.* 2011;130:86–93. doi:10.1016/j.schres.2011.03.010.
  38. Clark A. Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behav Brain Sci.* 2013;36:181–204. doi:10.1017/S0140525X12000477.
  39. Fletcher PC, Frith C. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. *Nat Rev Neurosci.* 2009;10:48–58. doi:10.1038/nrn2536.
  40. Friston K. The free-energy principle: a unified brain theory? *Nat Rev Neurosci.* 2010;11:127–138. doi:10.1038/nrn2787.
  41. Jardri R, Denève S. Circular inferences in schizophrenia. *Brain.* 2013;136:3227–3242. doi:10.1093/brain/awt257.
  42. Wacongne C, Changeux J-P, Dehaene S. A neuronal model of predictive coding accounting for the mismatch negativity. *J Neurosci.* 2012;32:3665–3678. doi:10.1523/JNEUROSCI.5003-11.2012.
  43. Mathalon DH, Ford JM. Corollary discharge dysfunction in schizophrenia: evidence for an elemental deficit. *Clin EEG Neurosci.* 2008;39:82–86.
  44. Fisher DJ, Labelle A, Knott VJ. Alterations of mismatch negativity (MMN) in schizophrenia patients with auditory hallucinations experiencing acute exacerbation of illness. *Schizophr Res.* 2012;139:237–245. doi:10.1016/j.schres.2012.06.004.
  45. Heinks-Maldonado TH, Mathalon DH, Houde JF, Gray M, Faustman WO, Ford JM. Relationship of imprecise corollary discharge in schizophrenia to auditory hallucinations. *Arch Gen Psychiatry.* 2007;64:286–296. doi:10.1001/archpsyc.64.3.286.
  46. Horga G, Schatz KC, Abi-Dargham A, Peterson BS. Deficits in predictive coding underlie hallucinations in schizophrenia. *J Neurosci.* 2014;34:8072–8082. doi:10.1523/JNEUROSCI.0200-14.2014.
  47. Belin P, Zatorre RJ, Lafaille P, Ahad P, Pike B. Voice-selective areas in human auditory cortex. *Nature.* 2000;403:309–312. doi:10.1038/35002078.
  48. Jardri R, Pouchet A, Pins D, Thomas P. Cortical activations during auditory verbal hallucinations in schizophrenia: a coordinate-based meta-analysis. *Am J Psychiatry.* 2011;168:73–81. doi:10.1176/appi.ajp.2010.09101522.
  49. Horga G, Parellada E, Lomeña F, et al. Differential brain glucose metabolic patterns in antipsychotic-naïve first-episode schizophrenia with and without auditory verbal hallucinations. *J Psychiatry Neurosci.* 2011;36:312–321. doi:10.1503/jpn.100085.
  50. Friston KJ, Stephan KE. Free-energy and the brain. *Synthese.* 2007;159:417–458. doi:10.1007/s11229-007-9237-y.
  51. Ouden HEM den, Daunizeau J, Roiser J, Friston KJ, Stephan KE. Striatal prediction error modulates cortical coupling. *J Neurosci.* 2010;30:3210–3219. doi:10.1523/JNEUROSCI.4458-09.2010.
  52. Horga G, Maia TV, Marsh R, et al. Changes in corticostriatal connectivity during reinforcement learning in humans. *Hum Brain Mapp.* 2015;36:793–803. doi:10.1002/hbm.22665.
  53. Wimmer GE, Daw ND, Shohamy D. Generalization of value in reinforcement learning by humans. *Eur J Neurosci.* 2012;35:1092–1104. doi:10.1111/j.1460-9568.2012.08017.x.
  54. Gerraty RT, Davidow JY, Wimmer GE, Kahn I, Shohamy D. Transfer of learning relates to intrinsic connectivity between hippocampus, ventromedial prefrontal cortex, and large-scale networks. *J Neurosci.* 2014;34:11297–11303. doi:10.1523/JNEUROSCI.0185-14.2014.
  55. Stephan KE, Friston KJ, Frith CD. Dysconnection in schizophrenia: from abnormal synaptic plasticity to failures of self-monitoring. *Schizophr Bull.* 2009;35:509–527. doi:10.1093/schbul/sbn176.
  56. Seth A, Suzuki K, Critchley H. An interoceptive predictive coding model of conscious presence. *Front Psychol.* 2012;2:395. doi:10.3389/fpsyg.2011.00395.
  57. Stephan KE, Penny WD, Moran RJ, den Ouden HEM, Daunizeau J, Friston KJ. Ten simple rules for dynamic causal modeling. *NeuroImage.* 2010;49:3099–3109. doi:10.1016/j.neuroimage.2009.11.015.
  58. Manoliu A, Riedl V, Zherdin A, et al. Aberrant dependence of default mode/central executive network interactions on anterior insular salience network activity in schizophrenia. *Schizophr Bull.* 2014;40:428–437. doi:10.1093/schbul/sbt037.
  59. Clos M, Diederer KJM, Meijering AL, Sommer IE, Eickhoff SB. Aberrant connectivity of areas for decoding degraded speech in patients with auditory verbal hallucinations. *Brain Struct Funct.* 2014;219:581–594. doi:10.1007/s00429-013-0519-5.
  60. Chyzhyk D, Graña M, Öngür D, Shinn AK. Discrimination of schizophrenia auditory hallucinations by machine learning of resting-state functional MRI. *Int J Neural Syst.* 2015;25:1550007. doi:10.1142/S0129065715500070.
  61. Wolf ND, Sambataro F, Vasic N, et al. Dysconnectivity of multiple resting-state networks in patients with schizophrenia who have persistent auditory verbal hallucinations. *J Psychiatry Neurosci.* 2011;36:366–374. doi:10.1503/jpn.110008.
  62. Diederer KJM, Neggers SFW, de Weijer AD, et al. Aberrant resting-state connectivity in non-psychotic individuals with auditory hallucinations. *Psychol Med.* 2013;43:1685–1696. doi:10.1017/S0033291712002541.
  63. van Lutterveld R, Diederer KJM, Otte WM, Sommer IE. Network analysis of auditory hallucinations in nonpsychotic individuals. *Hum Brain Mapp.* 2014;35:1436–1445. doi:10.1002/hbm.22264.
  64. Jardri R, Thomas P, Delmaire C, Delion P, Pins D. The neurodynamic organization of modality-dependent hallucinations. *Cereb Cortex.* 2013;23:1108–1117. doi:10.1093/cercor/bhs082.
  65. Shinn AK, Baker JT, Cohen BM, Öngür D. Functional connectivity of left Heschl's gyrus in vulnerability to auditory hallucinations in schizophrenia. *Schizophr Res.* 2013;143:260–268. doi:10.1016/j.schres.2012.11.037.
  66. Vercammen A, Kneegting H, den Boer JA, Liemburg EJ, Aleman A. Auditory hallucinations in schizophrenia are associated with reduced functional connectivity of the temporo-parietal area. *Biol Psychiatry.* 2010;67:912–918. doi:10.1016/j.biopsych.2009.11.017.
  67. Oertel-Knochel V, Knöchel C, Matura S, et al. Association between symptoms of psychosis and reduced functional connectivity of auditory cortex. *Schizophr Res.* 2014;160:35–42. doi:10.1016/j.schres.2014.10.036.
  68. Gavrilescu M, Rossell S, Stuart GW, et al. Reduced connectivity of the auditory cortex in patients with auditory hallucinations: a resting state functional magnetic resonance imaging study. *Psychol Med.* 2010;40:1149–1158. doi:10.1017/S0033291709991632.
  69. Hoffman RE, Fernandez T, Pittman B, Hampson M. Elevated functional connectivity along a corticostriatal loop and the mechanism of auditory/verbal hallucinations in

- patients with schizophrenia. *Biol Psychiatry*. 2011;69:407–414. doi:10.1016/j.biopsych.2010.09.050.
70. Sommer IE, Clos M, Meijering AL, Diederer KJM, Eickhoff SB. Resting state functional connectivity in patients with chronic hallucinations. *PLoS ONE*. 2012;7:e43516. doi:10.1371/journal.pone.0043516.
  71. Diederer KJM, De Weijer AD, Daalman K, et al. Decreased language lateralization is characteristic of psychosis, not auditory hallucinations. *Brain J Neurol*. 2010;133(pt 12):3734–3744. doi:10.1093/brain/awq313.
  72. Lee S-H, Wynn JK, Green MF, et al. Quantitative EEG and low resolution electromagnetic tomography (LORETA) imaging of patients with persistent auditory hallucinations. *Schizophr Res*. 2006;83:111–119. doi:10.1016/j.schres.2005.11.025.
  73. Andreou C, Nolte G, Leicht G, et al. Increased resting-state gamma-band connectivity in first-episode schizophrenia. *Schizophr Bull*. 2015;41:930–939. doi:10.1093/schbul/sbu121.
  74. Koutsoukos E, Angelopoulos E, Maillis A, Papadimitriou GN, Stefanis C. Indication of increased phase coupling between theta and gamma EEG rhythms associated with the experience of auditory verbal hallucinations. *Neurosci Lett*. 2013;534:242–245. doi:10.1016/j.neulet.2012.12.005.
  75. Van Lutterveld R, Hillebrand A, Diederer KJM, et al. Oscillatory cortical network involved in auditory verbal hallucinations in schizophrenia. *PLoS ONE*. 2012;7:e41149. doi:10.1371/journal.pone.0041149.
  76. Sritharan A, Line P, Sergejew A, Silberstein R, Egan G, Copolov D. EEG coherence measures during auditory hallucinations in schizophrenia. *Psychiatry Res*. 2005;136:189–200. doi:10.1016/j.psychres.2005.05.010.
  77. Kindler J, Hubl D, Strik WK, Dierks T, Koenig T. Resting-state EEG in schizophrenia: auditory verbal hallucinations are related to shortening of specific microstates. *Clin Neurophysiol*. 2011;122:1179–1182. doi:10.1016/j.clinph.2010.10.042.
  78. Geoffroy PA, Houenou J, Duhamel A, et al. The arcuate fasciculus in auditory-verbal hallucinations: a meta-analysis of diffusion-tensor-imaging studies. *Schizophr Res*. 2014;159:234–237. doi:10.1016/j.schres.2014.07.014.
  79. Ćurčić-Blake B, Nanetti L, van der Meer L, et al. Not on speaking terms: hallucinations and structural network disconnection in schizophrenia. *Brain Struct Funct*. 2015;220:407–418. doi:10.1007/s00429-013-0663-y.
  80. McCarthy-Jones S, Oestreich LKL, Australian Schizophrenia Research Bank, Whitford TJ. Reduced integrity of the left arcuate fasciculus is specifically associated with auditory verbal hallucinations in schizophrenia. *Schizophr Res*. 2015;162:1–6. doi:10.1016/j.schres.2014.12.041.
  81. De Weijer AD, Neggers SFW, Diederer KMS, et al. Aberrations in the arcuate fasciculus are associated with auditory verbal hallucinations in psychotic and in non-psychotic individuals. *Hum Brain Mapp*. 2013;34:626–634. doi:10.1002/hbm.21463.
  82. Hubl D, Koenig T, Strik W, et al. Pathways that make voices: white matter changes in auditory hallucinations. *Arch Gen Psychiatry*. 2004;61:658–668. doi:10.1001/archpsyc.61.7.658.
  83. Rotarska-Jagiela A, Oertel-Knochel V, DeMartino F, et al. Anatomical brain connectivity and positive symptoms of schizophrenia: a diffusion tensor imaging study. *Psychiatry Res Neuroimaging*. 2009;174:9–16. doi:10.1016/j.psychres.2009.03.002.
  84. Oestreich LKL, McCarthy-Jones S, Australian Schizophrenia Research Bank, Whitford TJ. Decreased integrity of the fronto-temporal fibers of the left inferior occipito-frontal fasciculus associated with auditory verbal hallucinations in schizophrenia. *Brain Imaging Behav*. 2015;1–10. doi:10.1007/s11682-015-9421-5.
  85. Wigand M, Kubicki M, Clemm von Hohenberg C, et al. Auditory verbal hallucinations and the interhemispheric auditory pathway in chronic schizophrenia. *World J Biol Psychiatry*. 2015;16:31–44. doi:10.3109/15622975.2014.948063.
  86. Mulert C, Kirsch V, Whitford TJ, et al. Hearing voices: a role of interhemispheric auditory connectivity? *World J Biol Psychiatry*. 2012;13:153–158. doi:10.3109/15622975.2011.570789.
  87. Teipel SJ, Bokde ALW, Meindl T, et al. White matter microstructure underlying default mode network connectivity in the human brain. *NeuroImage*. 2010;49:2021–2032. doi:10.1016/j.neuroimage.2009.10.067.
  88. Knöchel C, O'Dwyer L, Alves G, et al. Association between white matter fiber integrity and subclinical psychotic symptoms in schizophrenia patients and unaffected relatives. *Schizophr Res*. 2012;140:129–135. doi:10.1016/j.schres.2012.06.001.
  89. Blom JD. Hallucinations and other sensory deceptions in psychiatric disorders. In: Jardri R, Cachia A, Thomas P, Pins D, eds. *The Neuroscience of Hallucinations*. New York, NY: Springer; 2013:43–57. [http://link.springer.com/chapter/10.1007/978-1-4614-4121-2\\_3](http://link.springer.com/chapter/10.1007/978-1-4614-4121-2_3). Accessed January 24, 2016.
  90. Waters F, Collerton D, Ffytche DH, et al. Visual hallucinations in the psychosis spectrum and comparative information from neurodegenerative disorders and eye disease. *Schizophr Bull*. 2014;40(suppl 4):S233–S245. doi:10.1093/schbul/sbu036.
  91. Collerton D, Dudley R, Mosimann UP. Visual hallucinations. In: Blom JD, Sommer IEC, eds. *Hallucinations*. New York, NY: Springer; 2012:75–90. [http://link.springer.com/chapter/10.1007/978-1-4614-0959-5\\_6](http://link.springer.com/chapter/10.1007/978-1-4614-0959-5_6). Accessed January 24, 2016.
  92. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13:261–276.
  93. Andreasen N. *Scale for the Assessment of Positive Symptoms*. Iowa City, IA: University of Iowa; 1984.
  94. Rolland B, Amad A, Poulet E, et al. Resting-state functional connectivity of the nucleus accumbens in auditory and visual hallucinations in schizophrenia. *Schizophr Bull*. 2015;41:291–299. doi:10.1093/schbul/sbu097.
  95. Oertel V, Rotarska-Jagiela A, van de Ven VG, Haenschel C, Maurer K, Linden DEJ. Visual hallucinations in schizophrenia investigated with functional magnetic resonance imaging. *Psychiatry Res*. 2007;156:269–273. doi:10.1016/j.psychres.2007.09.004.
  96. Amad A, Cachia A, Gorwood P, et al. The multimodal connectivity of the hippocampal complex in auditory and visual hallucinations. *Mol Psychiatry*. 2014;19:184–191. doi:10.1038/mp.2012.181.
  97. Ford JM, Palzes VA, Roach BJ, et al. Visual hallucinations are associated with hyperconnectivity between the amygdala and visual cortex in people with a diagnosis of schizophrenia. *Schizophr Bull*. 2015;41:223–232. doi:10.1093/schbul/sbu031.
  98. Hare SM, Pasquerello D, Damaraju E, et al. A multi-site voxelwise analysis of the amplitude of low-frequency fluctuations in schizophrenics: exploring the effects of hallucination type. *Schizophr Bull*. 2015;41:S226–S226.

99. Harding AJ, Broe GA, Halliday GM. Visual hallucinations in Lewy body disease relate to Lewy bodies in the temporal lobe. *Brain*. 2002;125:391–403. doi:10.1093/brain/awf033.
100. Muller AJ, Shine JM, Halliday GM, Lewis SJG. Visual hallucinations in Parkinson's disease: theoretical models. *Mov Disord*. 2014;29:1591–1598. doi:10.1002/mds.26004.
101. Yao N, Shek-Kwan Chang R, Cheung C, et al. The default mode network is disrupted in Parkinson's disease with visual hallucinations. *Hum Brain Mapp*. 2014;35:5658–5666. doi:10.1002/hbm.22577.
102. Goetz CG, Vaughan CL, Goldman JG, Stebbins GT. I finally see what you see: Parkinson's disease visual hallucinations captured with functional neuroimaging. *Mov Disord*. 2014;29:115–117. doi:10.1002/mds.25554.
103. Shine JM, Keogh R, O'Callaghan C, Muller AJ, Lewis SJG, Pearson J. Imagine that: elevated sensory strength of mental imagery in individuals with Parkinson's disease and visual hallucinations. *Proc Biol Sci*. 2015;282:20142047. doi:10.1098/rspb.2014.2047.
104. Shine JM, Muller AJ, O'Callaghan C, Hornberger M, Halliday GM, Lewis SJ. Abnormal connectivity between the default mode and the visual system underlies the manifestation of visual hallucinations in Parkinson's disease: a task-based fMRI study. *Npj Park Dis*. 2015;1:15003.
105. El Khoury-Malhame M, Reynaud E, Soriano A, et al. Amygdala activity correlates with attentional bias in PTSD. *Neuropsychologia*. 2011;49:1969–1973. doi:10.1016/j.neuropsychologia.2011.03.025.
106. Daniels JK, McFarlane AC, Bluhm RL, et al. Switching between executive and default mode networks in posttraumatic stress disorder: alterations in functional connectivity. *J Psychiatry Neurosci*. 2010;35:258–266. doi:10.1503/jpn.090175.
107. Fani N, Jovanovic T, Ely TD, et al. Neural correlates of attention bias to threat in post-traumatic stress disorder. *Biol Psychol*. 2012;90:134–142. doi:10.1016/j.biopsycho.2012.03.001.
108. White TP, Gilleen J, Shergill SS. Dysregulated but not decreased salience network activity in schizophrenia. *Front Hum Neurosci*. 2013;7:65. doi:10.3389/fnhum.2013.00065.
109. Patriat R, Molloy EK, Meier TB, et al. The effect of resting condition on resting-state fMRI reliability and consistency: a comparison between resting with eyes open, closed, and fixated. *NeuroImage*. 2013;78:463–473. doi:10.1016/j.neuroimage.2013.04.013.
110. Benjamin C, Lieberman DA, Chang M, et al. The influence of rest period instructions on the default mode network. *Front Hum Neurosci*. 2010;4:218. doi:10.3389/fnhum.2010.00218.
111. Van Lutterveld R, Diederik K, Schutte M, Bakker R, Zandbelt B, Sommer I. Brain correlates of auditory hallucinations: stimulus detection is a potential confounder. *Schizophr Res*. 2013;150:319–320. doi:10.1016/j.schres.2013.07.021.
112. Sorg C, Manoliu A, Neufang S, et al. Increased intrinsic brain activity in the striatum reflects symptom dimensions in schizophrenia. *Schizophr Bull*. 2013;39:387–395. doi:10.1093/schbul/sbr184.
113. Yeo BTT, Krienen FM, Sepulcre J, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J Neurophysiol*. 2011;106:1125–1165. doi:10.1152/jn.00338.2011.
114. Birn RM, Molloy EK, Patriat R, et al. The effect of scan length on the reliability of resting-state fMRI connectivity estimates. *NeuroImage*. 2013;83:550–558. doi:10.1016/j.neuroimage.2013.05.099.
115. Birn RM, Diamond JB, Smith MA, Bandettini PA. Separating respiratory-variation-related fluctuations from neuronal-activity-related fluctuations in fMRI. *NeuroImage*. 2006;31:1536–1548. doi:10.1016/j.neuroimage.2006.02.048.
116. Shmueli K, van Gelderen P, de Zwart JA, et al. Low-frequency fluctuations in the cardiac rate as a source of variance in the resting-state fMRI BOLD signal. *NeuroImage*. 2007;38:306–320. doi:10.1016/j.neuroimage.2007.07.037.
117. Van Dijk KRA, Sabuncu MR, Buckner RL. The influence of head motion on intrinsic functional connectivity MRI. *NeuroImage*. 2012;59:431–438. doi:10.1016/j.neuroimage.2011.07.044.
118. Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*. 2012;59:2142–2154. doi:10.1016/j.neuroimage.2011.10.018.
119. Murphy K, Birn RM, Handwerker DA, Jones TB, Bandettini PA. The impact of global signal regression on resting state correlations: are anti-correlated networks introduced? *NeuroImage*. 2009;44:893–905. doi:10.1016/j.neuroimage.2008.09.036.
120. Hyvärinen A, Oja E. Independent component analysis: algorithms and applications. *Neural Netw*. 2000;13:411–430.
121. Van de Ven VG, Formisano E, Prvulovic D, Roeder CH, Linden DEJ. Functional connectivity as revealed by spatial independent component analysis of fMRI measurements during rest. *Hum Brain Mapp*. 2004;22:165–178. doi:10.1002/hbm.20022.
122. Foucher JR. Perspectives in brain imaging and computer-assisted technologies for the treatment of hallucinations. In: Jardri R, Cachia A, Thomas P, Pins D, eds. *The Neuroscience of Hallucinations*. New York, NY: Springer; 2013:529–547. [http://link.springer.com/chapter/10.1007/978-1-4614-4121-2\\_27](http://link.springer.com/chapter/10.1007/978-1-4614-4121-2_27). Accessed January 24, 2016.
123. Van de Ven VG, Formisano E, Röder CH, et al. The spatiotemporal pattern of auditory cortical responses during verbal hallucinations. *NeuroImage*. 2005;27:644–655. doi:10.1016/j.neuroimage.2005.04.041.
124. Rubinov M, Sporns O. Complex network measures of brain connectivity: uses and interpretations. *NeuroImage*. 2010;52:1059–1069. doi:10.1016/j.neuroimage.2009.10.003.
125. Allen P, Aleman A, McGuire PK. Inner speech models of auditory verbal hallucinations: evidence from behavioural and neuroimaging studies. *Int Rev Psychiatry*. 2007;19:407–415. doi:10.1080/09540260701486498.
126. Waters F, Badcock J, Michie P, Maybery M. Auditory hallucinations in schizophrenia: intrusive thoughts and forgotten memories. *Cognit Neuropsychiatry*. 2006;11:65–83. doi:10.1080/13546800444000191.
127. Waters F, Allen P, Aleman A, et al. Auditory hallucinations in schizophrenia and nonschizophrenia populations: a review and integrated model of cognitive mechanisms. *Schizophr Bull*. 2012;38:683–693. doi:10.1093/schbul/sbs045.
128. Weissman DH, Prado J. Heightened activity in a key region of the ventral attention network is linked to reduced activity in a key region of the dorsal attention network during unexpected shifts of covert visual spatial attention. *NeuroImage*. 2012;61:798–804. doi:10.1016/j.neuroimage.2012.03.032.
129. Sommer IE, Diederik KJM, Blom J-D, et al. Auditory verbal hallucinations predominantly activate the right inferior frontal area. *Brain*. 2008;131:3169–3177. doi:10.1093/brain/awn251.
130. Plaze M, Paillère-Martinot M-L, Penttilä J, et al. “Where do auditory hallucinations come from?”—a brain morphometry

- study of schizophrenia patients with inner or outer space hallucinations. *Schizophr Bull.* 2011;37:212–221. doi:10.1093/schbul/sbp081.
131. Chang C, Glover GH. Time-frequency dynamics of resting-state brain connectivity measured with fMRI. *NeuroImage.* 2010;50:81–98. doi:10.1016/j.neuroimage.2009.12.011.
  132. Schaefer A, Margulies DS, Lohmann G, et al. Dynamic network participation of functional connectivity hubs assessed by resting-state fMRI. *Front Hum Neurosci.* 2014;8:195. doi:10.3389/fnhum.2014.00195.
  133. Smith SM, Miller KL, Moeller S, et al. Temporally-independent functional modes of spontaneous brain activity. *Proc Natl Acad Sci U S A.* 2012;109:3131–3136. doi:10.1073/pnas.1121329109.
  134. Liu X, Duyn JH. Time-varying functional network information extracted from brief instances of spontaneous brain activity. *Proc Natl Acad Sci U S A.* 2013;110:4392–4397. doi:10.1073/pnas.1216856110.
  135. Gonzalez-Castillo J, Hoy CW, Handwerker DA, et al. Tracking ongoing cognition in individuals using brief, whole-brain functional connectivity patterns. *Proc Natl Acad Sci U S A.* 2015;112:8762–8767. doi:10.1073/pnas.1501242112.
  136. Potkin SG, Ford JM. Widespread cortical dysfunction in schizophrenia: the FBIRN imaging consortium. *Schizophr Bull.* 2009;35:15–18. doi:10.1093/schbul/sbn159.
  137. Turkeltaub PE, Eden GF, Jones KM, Zeffiro TA. Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage.* 2002;16:765–780.
  138. Turner JA. The rise of large-scale imaging studies in psychiatry. *GigaScience.* 2014;3:29. doi:10.1186/2047-217X-3-29.
  139. Costafreda SG. Pooling FMRI data: meta-analysis, mega-analysis and multi-center studies. *Front Neuroinformatics.* 2009;3:33. doi:10.3389/neuro.11.033.2009.
  140. Costafreda SG, Brammer MJ, Vêncio RZN, et al. Multisite fMRI reproducibility of a motor task using identical MR systems. *J Magn Reson Imaging.* 2007;26:1122–1126. doi:10.1002/jmri.21118.
  141. Suckling J, Ohlssen D, Andrew C, et al. Components of variance in a multicentre functional MRI study and implications for calculation of statistical power. *Hum Brain Mapp.* 2008;29:1111–1122. doi:10.1002/hbm.20451.
  142. Friedman L, Glover GH, Fbirn Consortium. Reducing inter-scanner variability of activation in a multicenter fMRI study: controlling for signal-to-fluctuation-noise-ratio (SFNR) differences. *NeuroImage.* 2006;33:471–481. doi:10.1016/j.neuroimage.2006.07.012.
  143. Mondino M, Jardri R, Suaud-Chagny M-F, Saoud M, Poulet E, Brunelin J. Effects of fronto-temporal transcranial direct current stimulation on auditory verbal hallucinations and resting-state functional connectivity of the left temporo-parietal junction in patients with schizophrenia. *Schizophr Bull.* 2016;42:318–326. doi:10.1093/schbul/sbv114.
  144. Mantini D, Perrucci MG, Del Gratta C, Romani GL, Corbetta M. Electrophysiological signatures of resting state networks in the human brain. *Proc Natl Acad Sci U S A.* 2007;104:13170–13175. doi:10.1073/pnas.0700668104.