

## Review Article

# Unawareness in schizophrenia: Neuropsychological and neuroanatomical findings

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### Abstract

The lack of insight in schizophrenia has so far been interpreted as a primary symptom of the illness, namely a defensive mechanism rather than a neurologically-based condition. However, recent findings have emphasized its relationship with damage to specific brain areas as well as the domain specificity in which it may occur. This supports a neuropsychological interpretation of the lack of insight in schizophrenia. The present article reviews the foregoing data, and takes into account the most relevant anatomo-clinical results. There is evidence that the lack of insight in schizophrenia may occur as a neurological disease per se following brain damage that seems related to frontal lobe areas. Additionally, it could either be related to all aspects of the disease or be domain-specific, occurring for one kind of symptom but not for others. These data indicate several analogies with the phenomenon called anosognosia for a neurological deficit.

### Key words

anosognosia, lack of awareness, lack of insight, schizophrenia, tardive dyskinesia, unawareness.

## INTRODUCTION

In Liber V, Epistula IX,<sup>1</sup> Seneca described a lady denying her blindness. This is possibly the first report of unawareness of a neurological deficit. However, the term ‘anosognosia’ was introduced 2000 years later by Babinski<sup>2</sup> to indicate diminished awareness or denial of the existence of deficits due to neurological disease (see Prigatano and Schacter<sup>3</sup> for an extensive review). At that time, the disease was interpreted as a symptom of a body schema disorder build-up by individual somato-sensory experiences.<sup>4</sup> During the 1930s, various authors pictured anosognosia in terms of a generalized defensive mechanism or psychological denial that protected patients from the disease.<sup>5</sup> This approach claimed that premorbid features of personality were the primary cause of illness onset, although certain data then contradicted this perspective. First, anosognosia is more frequent after right-brain damage and during the acute and postacute phases of the ill-

ness; a general defensive mechanism view would predict that anosognosia for both right and left disturbances should increase with time (a goal-directed mechanism would take time to consolidate). Second, anosognosia can be highly selective, occurring as a domain-specific phenomenon: the patient is aware of certain symptoms or functional deficits, but not others. In addition, a patient can be anosognosic in personal reports (i.e. when asked why they are in hospital and what their deficit is), but not in a self-evaluation task (i.e. when they are questioned on their ability to execute a task involving impaired function) and vice versa. These latter data contradict a motivational account of the disease (see Bisiach and Geminiani<sup>1</sup> and Berti *et al.*<sup>6</sup> for an extensive discussion on this topic).

The ‘lack of insight’ into one’s own illness in people with schizophrenia has been a well-known phenomenon ever since Bleuler coined the diagnostic term. The term states a broad construct encompassing unawareness of the disorder, the effects of treatment, social consequences, the occurrence of psychiatric symptoms and difficulty in labelling them. In the past 2 years, the lack of insight has been considered an unconscious or conscious refusal rather than an inability. Nevertheless, numerous authors have recently claimed that anosognosia, the diminished awareness or denial of the existence of deficits due to neurological disease, might have

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similarities with the concept of lack of insight: persistence despite all contrary evidence, confabulations to explain away symptoms, frontal lobe impairments and domain specificity. Accordingly, these authors used the term 'unawareness' (or 'anosognosia') rather than the psychoanalytic 'lack of insight' in order to highlight this neuropsychological point of view (see References 7–11 for a discussion). These findings have been somewhat contradictory, and it has not yet been clearly proven that impaired frontal lobe functioning is a causal explanation for poor insight (while the deficit in cases of anosognosia is certainly related to brain damage). However, the accumulated evidence for a prominent role of the frontal lobe is intriguing, and merits more careful review. The authors will focus on this literature, attempting to discuss its relevance for the understanding of the term 'unawareness'. References from the literature were obtained by both manual and electronic search methods (Medline database combining keywords: anosognosia, unawareness, schizophrenia, lack of awareness, lack of insight and tardive dyskinesia) up to the end of 2005. A historical introduction to the subject is followed by a brief description of the anatomoclinical features of schizophrenia, and then an analysis of those studies dealing with the relationship between unawareness and schizophrenia.

## **ANATOMO-CLINICAL PICTURE OF SCHIZOPHRENIA**

Schizophrenia is a spectrum disease covering several conditions of different etiology. At present, several theoretical interpretations converge to systemic models including neurotransmission, genetic changes and neurodevelopmental malformation of brain structures. The anatomy of schizophrenia is a long-debated issue. The data are sometimes conflicting and yet there is no clear evidence about the specific role of the different brain structures in schizophrenia onset. The literature reports that several brain regions might be involved: ventricles, frontal and temporal lobe subregions, medial temporal and inferior parietal regions, and subcortical structures (see References 12–14 for reviews). From a clinical point of view, schizophrenia is characterized by profound disruption in emotion and cognition, affecting the most fundamental human attributes: language, thought, perception, emotion, and sense of self.

The symptomatology can be subdivided into positive symptoms (traits or behaviors that are 'added' to the personality) and negative symptoms (capabilities or aspects of personality that are 'lost'). Positive symptoms include hallucinations, delusions, disorganized speech and behavior; negative symptoms, in contrast,

consist of the inability to experience pleasure, lack of emotion, loss of motivation and deficits of attention and thought.

Several papers showed that at least 50% of patients with schizophrenia are unaware of their disease (see References 7–15 for instances). This can significantly affect treatment compliance. The neuropsychological data come from studies focused on tardive dyskinesia, positive and negative symptoms. Other components of the complex symptomatology characterizing schizophrenia, for example amnesia, perceptual deficits and incoherent language, do not appear in the literature. The authors' review will, therefore, be focused on these studies.

## **POSITIVE AND NEGATIVE SYMPTOMS**

### **Neuropsychological studies**

A number of authors have shown that unawareness is not related to general cognitive<sup>16,17</sup> or frontal lobe<sup>18–21</sup> impairments. Cuesta and colleagues, for instance,<sup>19</sup> administered to 35 schizophrenics the Wisconsin Card Sorting Test (WCST), a classic measure of abstract conceptual skills and cognitive flexibility which is very sensitive to the acute effects of frontal lobe injury. No correlation was found between poor performance on WCST and unawareness. These results lead to consider unawareness still a primary symptom of schizophrenia or a consequence of clinical/individual variables.<sup>16,19</sup> However, several other papers suggested that unawareness might be linked to a poor performance in tests assessing the frontal lobe functions. For instance, Young and colleagues<sup>22</sup> conducted three separate studies testing 108 patients with chronic schizophrenia diagnosed via the revised 3<sup>rd</sup> edition of the Diagnostic and Statistical Manual (DSM-III-R) criteria. Subjects were administered the standard WCST, measuring the level of awareness with two instruments of demonstrated validity and reliability: the Scale for the Assessment of Unawareness of Mental Disorder (SUMD) and the basic activities of daily living (ADL). The authors showed a clear and consistent association between poor WCST performance and unawareness. In another study, it was proved that such a kind of correlation can be highly specific.<sup>23</sup> In detail, the authors recruited 21 subjects with a diagnosis of schizophrenia based on the Structured Clinical Interview (SCID) for the 4<sup>th</sup> edition of the DSM (DSM-IV). Unawareness was evaluated with the SUMD. The subjects also underwent an extensive neuropsychological examination and it was found that SUMD correlated significantly only with WCST but not with the other neuropsychological test. The relationship between tests assessing frontal lobe func-

tions and unawareness has been confirmed also in several other papers.<sup>24–32</sup>

These results about the associations between unawareness and frontal functions tests are somewhat conflicting. However, the authors must emphasize that many of the above-mentioned studies cannot be easily compared because of several methodological differences such as a-priori hypotheses, sample recruitment, chronicity, unawareness measures and symptomatology. Additionally, unawareness was measured as a unitary variable without considering possible dissociations within the symptomatology (e.g. positive vs negative symptoms or subcomponents of executive functions). Indeed, they often limited the analysis to WCST, which is a non-specific insight measure. As pointed out by Donohoe *et al.*,<sup>33</sup> it is essential to prone patients to cognitive tests which can subdivide executive functions into their different components: inhibition, planning, working memory, regulation of emotion, motivation and so on.

Accordingly, other authors explored whether the association between unawareness and frontal lobe functions could be a domain-specific phenomenon, measuring it separately for positive and negative symptoms. Mohamed and colleagues<sup>34</sup> tested 25 patients with schizophrenia according to DSM-III-R diagnostic criteria. They assessed unawareness of the illness with the SUMD adding four additional subscales based on the breakdown of items from the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS). The scores were unawareness of negative symptoms (UNS), attribution of negative symptoms (ANS), unawareness of positive symptoms (UPS), and attribution of positive symptoms (APS). Patients also had to perform four tests to evaluate executive functions: Verbal Fluency Test, the Design Fluency Test, the Trail-Making Test and a modified version of the WCST. The authors proved that only unawareness for negative symptoms was significantly correlated to a deficit of the executive functions. This link has been described in other papers.<sup>15,35–38</sup> On this basis, Mohamed and colleagues proposed that negative symptoms could be a consequence of damage to the executive functions while the positive symptoms follow damage to other cognitive functions, a general cognitive deterioration or an attempt to protect one's own psychological well-being. However, some of these authors and others described a link between positive symptoms and unawareness.<sup>35,37,39,40</sup> Both Amador *et al.*<sup>7</sup> and Kemp and Lambert<sup>37</sup> noted that increased psychosis and grandiosity (both positive symptoms) were associated with increased misattribution of psychiatric symptoms. This might be a specific aspect of insight that may have

a different etiology than unawareness. As has been demonstrated, schizophrenia patients may have selective unawareness of some attributes of their illness, but not of others.<sup>7,10,33,41</sup>

Recently, Brebion and colleagues<sup>42</sup> examined 40 inpatients meeting DSM-IV criteria for schizophrenia. Positive and negative symptoms were assessed by the Positive and Negative Syndrome Scale for Schizophrenia (PANSS). The authors confirmed the correlation between positive symptoms and unawareness but, in addition, found that unawareness was inversely correlated with unawareness of emotions or social interactions that are considered typical negative symptoms. The authors claimed that positive and negative symptomatology appears to have opposite links to awareness. The variable correlations between different symptom clusters (positive vs negative) may suggest that different elements of awareness may be differentially associated to distinct aspects of schizophrenia.

In summary, neuropsychological findings regarding the association between positive/negative symptoms and executive functions is still a matter of debate. Even when unawareness is analyzed deeply in its subcomponents, the relationships are still unclear. Donohoe *et al.*,<sup>33</sup> for instance, found that unawareness was correlated to working memory deficits but also to general cognitive functions impairments rather than to frontal lobe impairments. These considerations imply that further experiments and theoretical reflections are necessary to shed light on this puzzling topic. Nonetheless, it is fundamental to take into account also the most recent neuroanatomical studies, which have tried to examine directly the association between brain regions and unawareness with structural and functional imaging.

## Neuroanatomical data

The first attempts examined the correlation between awareness and the brain whole volume without taking into account different brain areas. In one of the previously mentioned studies,<sup>38</sup> for example, the authors assessed the relationship between unawareness and the whole brain volumes in a sample of 78 patients with DSM-IV schizophrenia. Unawareness was related to poor WCST performance but not to any global brain measures. The same lack of correlation has been found when considering only the cerebral ventricular enlargement.<sup>43</sup> Nonetheless, other authors looked at the possible association with specific brain regions and subregions. David,<sup>44</sup> for instance, demonstrated that unawareness was specifically associated to dysfunction of prefrontal or parietal lobes. In one of the most 'in-depth' anatomical studies,<sup>45</sup> the relationship between

unawareness and eight different frontal lobe subregions was analyzed in 15 patients with chronic schizophrenia. The authors found that unawareness was associated with a bilateral volume reduction in the middle frontal gyrus, gyrus rectus, and left anterior cingulate gyrus. More interestingly, they tried to correlate specific aspects of unawareness with each anatomic subregion. Overall, unawareness of psychiatric illness was associated with smaller mid-frontal gyrus, right gyrus rectus, and left anterior cingulate gyrus, while the misattribution of specific symptoms was associated with reduced superior frontal gyrus volume. The involvement of these frontal lobe areas in unawareness onset has been confirmed in another study.<sup>36</sup> One problem is that these studies were performed on patients with chronic schizophrenia, thereby making it difficult to identify the effects of illness chronicity and exposure to antipsychotic medications. Shad and colleagues<sup>46</sup> investigated a sample of 35 patients without effects of long-term use of antipsychotic medications and illness chronicity. The authors assessed the unawareness through single questions derived from the items of the Hamilton Depression Rating Scale (HDRS). They analyzed the relationship between dorsolateral prefrontal cortex (DLPFC) volume and unawareness. Unawareness was significantly correlated with a smaller right DLPFC volume as compared to those with preserved insight, independently of global cognitive functioning and illness severity. In a recent paper,<sup>47</sup> the possible dissociation between specific aspects of unawareness and brain subregions<sup>45</sup> was confirmed. The authors demonstrated that the DLPFC was linked to unawareness per se, while Orbito Frontal Cortex (OFC) was linked to symptoms misattribution.

Interestingly, in a different research field, some authors gained important results in order to understand the neuroanatomical basis of unawareness in schizophrenia. Certain data show common cerebral dysfunctions between schizophrenia and dementia with frontal lobes atrophy<sup>48</sup> on the one hand, and common deficits between schizophrenia and dementia in tests for frontal or executive functions on the other.<sup>49</sup> These data reinforce the idea of a close relationship between unawareness in schizophrenia and frontal lobes.

## TARDIVE DYSKENISIA

Patients with chronic schizophrenia may show involuntary movements of the tongue, lips, face, and trunk independently of neuroleptic treatment.<sup>50</sup> A peculiar feature of tardive dyskinesia is that patients can be completely unaware of their own motor deficit.<sup>51-56</sup> Interestingly, it might be dissociated along the self/other continuum. In other words, the ability to detect

and judge the performance of others might be unimpaired. Smith and colleagues,<sup>56</sup> for example, used the Abnormal Involuntary Movement Scale (AIMS) to evaluate the presence and severity of tardive dyskinesia in 377 patients with schizophrenia.

The authors asked patients to judge both their own behavior and that of others. The number of recognized deficits was significantly greater when they had to judge others' behaviors.

The authors hypothesized that the automonitoring deficits could prevent the awareness of one's own deficit but not that of others.

As for the positive and negative symptoms, some studies focused on the possible relationship between unawareness and frontal lobe functions. Waddington and colleagues<sup>57</sup> examined 47 subjects with a DSM-III diagnosis of schizophrenia. Patients were examined for tardive dyskinesia and neuropsychological test performance. Results showed an association between unawareness of the movements and the poor performance on WCST. The association has been confirmed by other authors.<sup>58,59</sup>

Unawareness for tardive dyskinesia, as well as for positive and negative symptoms, may occur as a domain-specific phenomenon. Arango and colleagues,<sup>51</sup> for instance, were interested in examining whether unawareness of motor dysfunction and lack of insight into mental dysfunction are related. They selected 43 patients in a specialized motor disorder institute and used the SUMD to assess insight of 43 patients with schizophrenia and tardive dyskinesia. Unawareness of tardive dyskinesia was weakly correlated with poor insight. The authors concluded that patients with schizophrenia can be aware of some symptoms but not of others. Dissociations have been found also within tardive dyskinesia. Sandyk and colleagues,<sup>60</sup> found that unawareness of one's own involuntary movement could be dissociated among different muscle groups. In other words, patients could be unaware of their dyskinesia for a specific movement but not for another, akin to what has been reported for patients with anosognosia for hemiplegia who may be aware of the deficit in a specific body part but not in other areas. Lastly, another study<sup>61</sup> reported that patients with schizophrenia may show motor deficits when requested to perform an act, but not during the spontaneous behavior itself.

## CONCLUSIONS

Despite the dramatic disabling nature of schizophrenia, many patients are completely unaware of their own disease. This phenomenon makes rehabilitation more difficult and is a bad prognostic factor for recov-

ery. Conversely, unawareness in schizophrenia may provide us with many important hints for understanding the monitoring process of our own conditions, disclosing implicit mental contents, and shedding light on the neural structures underlying conscious mental processes. For a long time, unawareness in schizophrenia has been described as a symptom without further specifying its own etiological nature. Nevertheless, recent neuropsychological findings seem to suggest an interesting possibility, namely that unawareness in schizophrenia might be very similar to the neurological-based condition known as anosognosia. These data can be summarized into two points:

- (i) unawareness in schizophrenia might occur as a neurological disorder per se due to frontal lobes damage. This conclusion is supported by data showing association between unawareness in schizophrenia and deficits of the executive functions,<sup>15,22–32,34–40,42,57–59</sup> damage to frontal lobe areas<sup>36,44–47</sup> as well as with cognitive and brain impairments in dementia due to frontal lobe lesions,<sup>48,49</sup> and
- (ii) unawareness in schizophrenia might occur *in* the illness as a whole or *within* different domains of it. This is supported by the dissociation between unawareness for negative and positive symptoms<sup>15,34,36,38–42</sup> and by its occurrence only for a specific movement<sup>51,60</sup> or only when questioned.<sup>61</sup>

Yet the analogy between unawareness in schizophrenia and anosognosia is not yet definitive and unquestionable. For instance, some studies found that unawareness was not associated with frontal lobe functions/areas; others showed that it was associated to general cognitive deficits. Here, the authors have tried to stress the importance of deepening the neurological basis of unawareness in schizophrenia as well as its possible manifestation as a domain-specific phenomenon. This should allow clarification of the role of defensive mechanisms or general mental deterioration and a more satisfying anatomo-functional picture of unawareness in schizophrenia. Since unawareness is a poor prognostic factor for functional recovery, the etiology of the insight problem is imperative in order to tailor and manage the treatment accordingly. The authors hope that this review can contribute to stimulate further research and theoretical discussions about the neurocognitive features of awareness in schizophrenia.

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