

NEUROBIOLOGY OF PSYCHOSIS. CLINICAL AND PSYCHOSOCIAL IMPLICATIONS

This is a new Section of *Epidemiologia e Psichiatria Sociale*, called *Neurobiology of Psychosis, Clinical and Psychosocial Implications*, that will regularly appear in each issue of this Journal to describe relevant neuroscience topics. In particular, studies investigating the relationship between neurobiology and psychosocial psychiatry in major psychoses will be debated. The aim of these articles is to provide a better understanding of the neural basis of psychopathology and clinical features of these disorders in order to raise new perspectives in every-day clinical practice.

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Is there a neurobiological basis of insight in schizophrenia?

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Several definitions have been proposed to describe 'insight', which is a construct of different dimensions and is generally considered, although there is not an univocal definition, the awareness of illness. Jaspers (1964) phenomenologically differentiated the sole awareness of illness from insight, which indicated a correct interpretation of the type and severity of one's own symptoms. He wrote: "*The term awareness of illness is applied to the patient's attitude when he expresses a feeling of being ill and changed, but there is no extension of this awareness to all his symptoms nor to the illness as a whole. It does not involve any objectively correct estimate of the severity of the illness nor any objectively correct judgement of its particular type. Only when this is present ... can we speak of insight.*" Differently, Aubrey Lewis (1934) defined insight as "*the correct attitude to morbid change in oneself*" and firstly related insight to schizophrenia, where the lack of insight is common (Sartorius *et al.*, 1972).

David (1990) deconstructed insight dimensions in schizophrenia in three major categories: awareness of illness, recognition that symptoms are abnormal and awareness of the need for treatment. Successively, Amador *et al.* (1993) suggested five different dimensions for insight in schizophrenia: awareness of having a mental illness, awareness of the effects of medication, awareness of the consequences of mental illness, awareness of symptoms of mental disorder and attribution of symptoms to a mental disorder. In schizophrenia lack of insight is relevant to outcome measures, correlating with treatment non-adherence, lower psychosocial functioning, poor prognosis, involuntary hospitalization, higher utilization of emergency services and cognitive impairments (Aleman *et al.*, 2006; Drake *et al.*, 2007; Nosé *et al.*, 2003; Keshavan *et al.*, 2004; Shad *et al.*, 2004).

In this regard, there is a growing interest in understanding the neurobiology of insight. Several neuropsychological studies have supported the hypothesis that cognitive deficits secondary to brain abnormalities may be the basis of poor insight in schizophrenia (Larøi *et al.*, 2000; Young *et al.*, 1993), particularly in prefrontal lobes, which sustain higher cognitive functions, such as self monitoring, inhibition and mental flexibility (Damasio, 1996). Indeed, specific structural changes of prefrontal cortex have been found to be associated to

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poor insight in schizophrenia by magnetic resonance imaging (MRI) studies (Table I). Specifically, in first-episode antipsychotic-naïve patients (Shad *et al.*, 2004; 2006) poor awareness of symptoms inversely associated with right dorsolateral prefrontal cortex (DLPFC) size, whereas misattribution of symptoms positively correlated with right orbitofrontal cortex (OFC) (Shad *et al.*, 2006). In chronic patients, impaired insight into symptoms correlated with smaller volumes of right OFC, bilateral middle frontal gyrus, and left anterior cingulate (Flashman *et al.*, 2001, Sapara *et al.*, 2007), whereas lower level of insight into illness associated with smaller size of left inferior frontal gyrus (Sapara *et al.*, 2007). Moreover,

abnormally smaller total brain size were found in patients with schizophrenia and unawareness of illness (Flashman *et al.*, 2000), although no significant correlations were reported between degree of insight and brain volumes in another MRI study (Rossel *et al.*, 2003). This suggests that prefrontal sub-regions may sustain diverse insight dimensions in schizophrenia, being also different between first-episode and chronic patients. It may also be possible that some findings are spurious due to the small sample size of the studies and the multiple comparisons performed. Furthermore, different prefrontal landmarks and insight measures were used across studies, which may also confound the literature findings.

Table I. – Magnetic resonance imaging studies exploring the structural basis of insight in schizophrenia.

Study	Subjects	Age (years)	Insight Scale	Findings
Flashman <i>et al.</i> , 2001	15 chronic patients	31.9±11	SUMD	Unawareness of illness and symptom misattribution inversely correlated, respectively, with bilateral middle and superior frontal gyrus volumes
Rossel <i>et al.</i> , 2003	78 chronic male patients	33.7±8.50	SAI-E	-Poor WCST performance inversely correlated with insight -No significant correlations between total insight score and total brain matter volumes
	36 healthy controls	33.4±8.93		
Shad <i>et al.</i> , 2004	first-episode patients:		Insight item of HDRS	-Inverse correlation between insight and right DLPFC volumes -Poor insight correlated with WCST perseverative errors
	17 good insight	23.35±7.83		
	18 poor insight	26.13±6.70		
Shad <i>et al.</i> , 2006	14 first-episode patients	26.23±7.50	SUMD	-Awareness of symptoms negatively correlated with right DLPFC volumes -Attribution of symptoms positively associated with right medial OFC volumes
	21 healthy controls	24.29±5.73		
Sapara <i>et al.</i> , 2007	28 chronic patients	39.00±10.51	BIS SAI-E	Lower insight into symptoms and into illness correlated, respectively, with smaller volumes of right OFC and left inferior frontal gyrus (controlled for duration of illness)
	20 healthy controls	35.90±13.68		

SUMD=Scale Unawareness of Mental Disorders; SAI-E=Schedule for the Assessment of Insight; HDRS=Hamilton Depression Rating Scale; BIS=Birchwood Insight Scale; WCST=Wisconsin Card Sorting Test; DLPFC=dorsolateral prefrontal cortex; OFC=orbitofrontal cortex.

In conclusion, although the structural underpinnings have not yet been completely elucidated, specific areas of prefrontal cortex (i.e. DLPFC, OFC, anterior cingulate) may support poor insight in schizophrenia. A better understanding of the neurobiology of insight will help to develop specific cognitive remediation to enhance lack of insight in early phases of the illness, potentially leading to improvement of functional outcome. Interestingly, based on the consistent correlation of poor performance at the *Wisconsin Card Sorting*

Test (WCST) with lack of insight in schizophrenia (Shad *et al.*, 2007), WCST may represent a specific cognitive target to explore amelioration of insight in clinical practice. Therefore, future large longitudinal imaging and neuropsychological studies should further investigate the role of each prefrontal sub-regions in sustaining different insight dimensions in first-episode patients as well as the effects of psycho-social and cognitive rehabilitation in improving insight in schizophrenia.

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