Neurobiology of Psychosis. Clinical and Psychosocial Implications

This is a Section of *Epidemiologia e Psichiatria Sociale*, that regularly appears 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 short articles is to provide a better understanding of the neural basis of psychopathology and clinical features of these disorders in order to raise new perspective in every-day clinical practice.

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Language disturbances in schizophrenia

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Abstract. Language disturbances represent a core feature of schizophrenia, affecting social interactions and quality of life. Here we summarize linguistic and pragmatic deficits and illustrate the role of brain imaging studies in delineating the neural substrates of language deficits in patients with schizophrenia.

KEY WORDS: speech, syntax, semantics, pragmatics, prosody, psychosis, brain imaging.

Language represents the most evolved expression of human intelligence. It consists of a "*generative system of sound-meaning connections*" (Bhati, 2005), which allows individuals to communicate ideas and thoughts and, as such, it can be considered the basis of human social behaviour. Linguists use to distinguish between hierarchical but interrelated levels, such as the phonetic (physical sounds composing words), phonological (how sound sequences are recognized as words of specific language), morphological (structure and form of words), syntactic (set of rules, specific for each language, used to combine words in sentences) and semantic (language content/meaning) dimensions. Another aspect is represented by implicit pragmatic knowledge, which refers to a set of para-linguistic factors supporting verbal speech and interfacing communication and context. It includes linguistic and emotional prosody, non-literal expression comprehension, conversational turn respect, correct use of referents in speech, theory of mind (representation of others' mental state), gestures and facial expressions (Aglioti & Fabbro, 2006).

The interest for the neural substrate of language originated from the aphasia studies by Broca (1861) and Wernicke (1874), which suggested left inferior frontal gyrus and left superior/posterior temporal lobe as responsible for speech production and comprehension, respectively. In the last decades, brain imaging techniques have given a strong impulse to the comprehension of the neuro-anatomical basis of language, allowing a general review of the traditional "aphasia" model. This has delineated a more complex, dynamic system involving networks of cortical and sub-cortical brain regions such as

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https://doi.org/10.1017/S1121189X00000270 Published online by Cambridge University Press

prefrontal, frontal, parietal and temporal areas, motor cortex, cerebellum, corpus callosum, and basal ganglia (Bhati, 2005; Stowe *et al*., 2005).

Interestingly, language disturbances represent core features (Covington *et al*., 2005) and diagnostic criteria of schizophrenia as indicated by the DSM-IV (American Psychiatric Association, 1994) and the ICD-10 (World Health Organization, 1993), which cite, respectively, "*disorganised speech*" and "*breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms*". More recently, the link between language and schizophrenia has been strengthened by Crow's theory (Crow, 2008), which has hypothesized that nuclear symptoms of schizophrenia represent a failure in establishing the left hemisphere dominance for language.

Speech deficits in schizophrenia affect both the linguistic (morphosyntactic, semantic) and the communicative (pragmatic) level. At the linguistic level, speech is characterized by word-finding difficulties (Andreasen, 1979), which can lead to stilted speech or neologisms, and also by reduced verbal and speech fluency (Covington *et al*., 2005). In addition, syntactic complexity is impaired in spite of a correct use of syntactic rules (DeLisi, 2001), as also reported by our group (Tavano *et al*., 2008). Conversely, abnormal morphology is quite rare (Covington *et al*., 2005). At the pragmatic level, patients with schizophrenia show difficulties in understanding proverbs, metaphors and idioms as much like sarcasm and irony (Mitchell & Crow, 2005; Tavano *et al*., 2008), having a general predisposition to concretism (Kircher *et al*., 2007). In addition, they use to fill speech with irrelevant pieces of information (Andreasen, 1979), as such as to use ambiguous verbs and referents, with the final effect to confound the hearer. Analysis of speech has in fact shown that subjects suffering from schizophrenia tend to produce incoherent discourse with lack of structure (Elvevag *et al*., 2007; Marini *et al*., 2008). Still, they do not respect turns in conversation and show flattened intonation (Covington *et al*., 2005). Moreover, deficits at the two levels seem to be strictly linked, being the linguistic impairment (microlinguistic dimension) potentially explained by pragmatic and speech planning disturbances (macrolinguistic dimension) (Marini *et al*., 2008). Furthermore, since schizophrenia affects different cognitive domains, linguistic and pragmatic deficits have been linked to a more general impairment in working memory, attention and executive functions, as such as to failure in action/discourse organizing (DeLisi, 2001; Bellani & Brambilla, 2008a; Marini *et al*., 2008).

Imaging and post-mortem studies have tried to delineate the neural basis of language disturbances in schizophrenia. Specifically, volume reduction in the left superior temporal gyrus (STG), which is involved in phonological perception, semantic processing and increased syntactic complexity (Bhati, 2005; Demonet *et al*., 2005), is one of the most replicated finding (Shenton *et al*., 2001), being impaired even in the first phases of the illness (Takahashi *et al*., 2009). Also, reduced or reversal asymmetry of planum temporale (PT), corresponding to Wernicke's area, has often been reported (Shapleske *et al*., 1999). In addition, several studies have shown abnormalities of the corpus callosum (Shenton *et al*., 2001; Brambilla *et al*., 2005), which is likely to interface syntax and prosody, as such as to transfer auditory information (Friederici *et al*., 2007). Deficits of cerebellum, a brain region subserving the ordering of syllables into rhythmic sentences, the temporal organization of internal speech and motor articulation of language (Ackermann, 2008; Bhati, 2005), as well as of frontal cortex, containing Broca's area and whose sub-areas are differentially involved in processing syntactic and semantic information (Vigliocco, 2000), have also been reported in schizophrenia (Shenton *et al*., 2001). Furthermore, the basal ganglia, which have also been proposed to play a role in regulating normal language processing (Dominey & Inui, 2009), have consistently been found to be altered (Glenthoj *et al*., 2007).

In Table I language deficits in schizophrenia are tentatively summarized along with the description of the potential neural networks involved, as detected by functional and diffusion imaging studies (Kircher *et al*., 2005; 2007; Leitman *et al*., 2007; Park *et al*., 2008; Andreasen *et al*., 2008).

In conclusion, language abnormalities represent a prominent feature of schizophrenia and may ultimately affect social adaptation (Bellani & Brambilla, 2008b). In this perspective, specific strategies for rehabilitating language deficits should be planned, especially for patients at the early phases of the illness. Finally, although imaging studies have lead to a better comprehension of the neural basis of language impairment in schizophrenia, future studies should identify the role of each network in sustaining particular linguistic disturbance, considering the balance between right and left hemispheres.

https://doi.org/10.1017/S1121189X00000270 Published online by Cambridge University Press

Table I - Linguistic and pragmatic deficits in schizophrenia

Linguistic aspects	Deficits in schizophrenic speech	Potential neural substrates in schizophrenia
Phonetic/Phonological	- linguistic and emotional prosody deficits (see pragmatic aspects)	Primary and secondary auditory pathways
Morphological	- paragrammatic errors (rare) - neologisms	
Syntactic	- reduced syntactic complexity (production) - disruption of receptive syntax (comprehension)	Right posterior temporal cortex; left superior frontal cortex
Semantic (word level)	- verbal and semantic paraphasias (rare) - anomias (rare) - stilted speech - neologisms (they may be due to lexical access impairment, which may explain reduced verbal and speech fluency)	Altered prefrontal modulation of prefrontal-temporal network
Semantic (narrative level; speech coherence)	Impaired discourse coherence given by: - use of ambiguous verbs and referents - speech filled with irrelevant pieces of information (or derailment) - lack of discourse structure	Areas involved in working memory and executive functions, especially regions recruited in planning/ordering
Pragmatic	- impaired proverbs, metaphors, idioms comprehension (predisposition to concretism) - impaired sarcasm and irony comprehension - no respect of turns in conversation - flattened intonation - linguistic prosody deficits (difficulty in differentiate declarative or interrogative sentences by prosodic sentence contour) - emotional/affective prosody deficits (difficulty in distinguish emotions by prosodic sentence contour) - Theory of Mind deficits (difficulty in representation of others' mental state)	Non-literal expression comprehension (concretism): left inferior frontal and right lateral temporal cortex Emotional prosody: primary and secondary auditory pathways; corpus callosum; peri-amygdala areas; enhanced right lateralization (or reduced left lateralization) in parietal and temporal lobe Theory of Mind: left orbitofrontal cortex (OFC); left ventrolateral prefrontal cortex (VLPFC); medial prefrontal cortex

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https://doi.org/10.1017/S1121189X00000270 Published online by Cambridge University Press

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https://doi.org/10.1017/S1121189X00000270 Published online by Cambridge University Press