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Electrophysiological examination of Formal Thought Disorder in schizophrenia

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ABSTRACT

Quantitave EEG profile was recorded for 60 age and sex matched drug free/naive schizophrenia patients, divided into two groups based on the presence and absence of Formal Thought Disorder (FTD) and a group of 30 matched healthy participants. Coherence and power spectrum analysis revealed that as compared to normal controls, schizophrenia patients with FTD had decreased regional power and intra hemispheric coherence; those without FTD had increased regional power and increased intra hemispheric coherence. Inter hemispheric coherence was greater in schizophrenia patients with FTD and lesser in those without FTD, as compared to healthy participants. The data were interpreted in terms of neural dis-connection which in FTD can be attributed to the existence of both a deficit and excess of neural connections, which compensate each other.

1. Introduction

Language is fundamentally a generative system of sound-meaning connections emerging from coordinated and temporally integrated sensory, cognitive, and motor functions of the brain. Individuals with schizophrenia show abnormalities in all these domains of brain function, including symptoms specific to perceiving, comprehending, learning, and expressing language. *Formal Thought Disorder* or disorganized speech stands out to be one of the most elusive symptoms of schizophrenia. From the earliest descriptions of schizophrenia, disordered association (thought disorder) has been recognized as a major feature of the illness. It has also been proposed that many, if not all, other features of schizophrenia may be derived from a *cognitive impairment primarily affecting association mechanisms*. Bleuler (1911, 1950) first identified a disturbance in associations as one of the so-called four *fundamental symptoms* of schizophrenia, which along with autism, ambivalence, and affect, are often referred to as the "four A's" of schizophrenia. According to Bleuler (1911, 1950), formal thought disturbance reflects a breakdown in the associative threads that serve to interweave words, thoughts, and ideas into coherent discourse. A more recent formulation of psychological disintegration is the idea that some experiential symptoms of schizophrenia can be explained by a failure to integrate the intention to act with the perceptual registration of the consequences of such action. At a neurobiological level, this integrative abnormality might correspond to a failure to integrate signals from the intentional (prefrontal) regions and the perceptual (temporal) cortices. Recent physiological and anatomic studies have stressed increasingly the importance of resonant, reciprocal interaction between multiple cortical areas during information processing task rangings from visual perception to language production. Synchronization of EEG activity at high oscillatory frequencies (20–100 Hz) has been proposed to reflect the degree of functional connectivity between cortical areas. Several lines of research, including post-mortem and brain imaging studies, suggest that schizophrenia is characterized by abnormalities in concerted action between spatially distributed networks (Hubl et al., 2004) and reduced cerebral functional connectivity in schizophrenia patients (Bleich Cohen et al., 2009, 2012; Li et al., 2010). Schizophrenia has therefore been described as a "dysconnectivity disorder" (Peled, 1997). However, these findings have been inconsistent. Early studies reported a variety of findings – most typically increased coherence – in contrast to more recent reports that show decreased coherence during different tasks in schizophrenics, in relation to health individuals (Peled, 2004; Winterer et al., 2001; Strelets et al., 2003; Slewa-Younan et al., 2004). Functional imaging studies of thought disorder have correlated the trait for this symptom with resting activity in the inferior frontal cingulated and temporal cortex (Liddle et al., 1992) while articulation of thought disordered speech "online" has been associated with relatively reduced activity in inferior frontal, cingulated and superior temporal cortex, but increased activity in the fusiform region (Mc Guire et al., 1997). But, none of these studies have been consistently replicated. Since 1970s investigators have consistently shown that schizophrenic patients display

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augmented low frequency power and diminished alpha band power (Iacono, 1985; Sponheim et al., 1994). Liemburg et al. (2012) investigated resting state network connectivity of the auditory, language and attention networks and observed decreased connectivity in patients, as compared to controls, between auditory and language networks. Conversely, increased connectivity was present in patients, as compared to controls between attention and language networks; but there was no relationship with severity of symptoms. Schizophrenia is a disorder with diverse symptoms affecting almost all aspects of mental functioning, for example perception, concept formation, language, volition, motor activity, social interaction, and emotion. There is evidence that such deficits are global as well as specific, marked by distinct patterns of association and dissociation of performance across different cognitive tasks. The dominant etiopathological models of schizophrenia in recent times consider that a mixture of genetic, epigenetic and environmental factors induce early anatomical brain lesions in circuits critical for cognition and emotion. These brain insults might affect the normal positioning of neurons and the establishment of connectivity as well as the synaptic pruning through childhood and adolescence, configuring the onset of the clinical syndrome years later (Selemon and Goldman-Rakic, 1999). Alterations in cortical circuit development may result in decreased synaptic connectivity in some regions, but in other brain areas, there may be an excess of neuronal connectivity. Despite Formal Thought Disorder (FTD) being a cardinal symptom of schizophrenia, and in the face of contradictory literature on the connectivity pattern in schizophrenia, research on schizophrenia has rarely focused on trying to relate the issue of functional integration with the symptom of FTD. Hence, the present study purports to explore the relationship between FTD, as one of the core pathologies of schizophrenia, and the status of functional integration in the brain of individuals with schizophrenia with and without FTD. It is believed that resting state functional connectivity may be considered as a reliable tool for identification of dysfunctional networks in the brain associated with psychiatric disorders such as schizophrenia. Analogous to resting state functional activity, the present study has used resting state electrophysiological measurement to assess the substrates of neural connectivity in two subpopulations of schizophrenia. Since the existence of inadequate functional integration in schizophrenia is evident from different studies, we can predict that diminished functional integration will be present in the schizophrenia population, as compared to normal controls. But, the exact nature of this inadequacy has not yet been fully clarified (Breakspear et al., 2003; Foucher et al., 2005) and the significance of EEG power abnormalities in schizophrenia remains unclear. Also, in-spite of the sub-categorization on the basis of presence and absence of FTD, we have actually chosen schizophrenia patients with "positive" symptoms. Hence, we have kept our expectations open regarding the profile of activation – connectivity in the schizophrenia population as contrasted with healthy counterparts and as compared between the two subgroups (Figs. 1–4).

2. Methods

2.1. Participants

The sample consisted of 60 right handed, male schizophrenia patients, diagnosed as per the ICD 10 criteria and 30 age and sex matched normal controls. Initially a detailed case history was taken from each of the participants through thorough interview. In case of the patient participants, the information was corroborated from the informants, who were usually the primary caregivers.

The diagnosis of schizophrenia was established by psychiatrists in the Out Patient Department of the hospital. Subsequently, the researcher, a trained clinical psychologist, re-confirmed the diagnosis based on the case history and mental status examination. The presence of comorbid psychiatric or significant general medical conditions were also ruled out in the process.

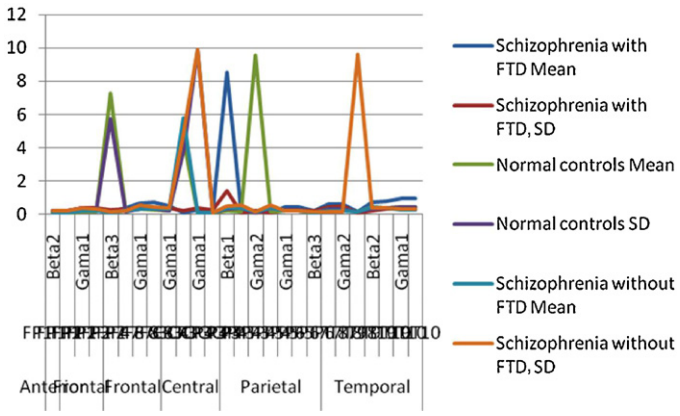

Fig. 1. Graph showing inter hemispheric coherence. FTD represent formal thought disorder; SD represent standard deviation.

The participants of the "*Normal Control*" group were screened out for the presence of any psychopathology by using the General Health Questionnaire (Shamsunder et al., 1986). Only participants with a score of <1 were selected for the study. Presence of past history or family history of psychiatric morbidity was also ruled out from the intensive case history.

Thirty schizophrenia patients were grouped as "*With Formal Thought Disorder*" based on a score of one or more on the Thought, Language and Communication Scale (Andreasen, 1979). Thirty schizophrenia patients were grouped as "*Without Formal Thought Disorder*", based on a score of zero on the Thought, Language and Communication Scale (Andreasen, 1979). The ratings were made after a patient had been evaluated with an ordinary psychiatric interview, lasting for at least 50 min. For an appreciable period of time the patient was permitted to talk spontaneously, without any interruption, in order to observe his speech during this condition. Subsequently, the patient was interrupted at some point in order to see how he responds to this. Most of the ratings are described quantitatively i.e. in terms of how often they occur during an interview, based on the assumption that most interview takes about *fifty minutes*. The scale is scored as *mild* (occasional instances of Thought Language and Communication (TLC) disorder), *moderate* (impaired verbal output which leads to disturbance in communication from time to time), *severe* (significant impairment in communication for substantial part of the interview), and *extreme* (communication is impossible). The evaluation and rating of FTD were done by both the researcher and the supervisor. Those ratings that were taken into consideration were decided upon on the basis of consensus.

As negative symptoms of schizophrenia have been differentially hypothesized to indicate a distinct syndrome, with unique neurophysiological as well as psycho-social correlates (Goldman-Rakic, 1994; Wing and Brown, 1997), presence of negative symptoms was ruled out based on the presence of a negative composite score in the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Kay et al. (1987) had conceived a "*bipolar composite scale*" to express the direction and magnitude of the difference between positive and negative symptoms, by subtracting the negative subscale score from the positive subscale score, which ranges from "−42 to +42". Accordingly, such a score reflects the degree of predominance of one syndrome over the other and its valence is an index of typological characterization. None of the participants had a score of more than three in any of the items of negative subscale.

Handedness was assessed using the Sidedness Bias Schedule (Mandal et al., 1992). The criteria for selection of participants with