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EEG ALPHA COHERENCE AND PSYCHOPATHOLOGICAL DIMENSIONS OF SCHIZOPHRENIA

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ABSTRACT

The aim of this study was to evaluate the correlation between psychopathological dimensions in recent-onset neuroleptic-naive schizophrenic patients and EEG alpha coherence in the resting state. 37 neuroleptic-naive, recent-onset schizophrenic patients were assessed on the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms, and psychopathological dimension scores on reality distortion, psychomotor poverty and disorganization were calculated. EEG alpha coherence was computed across 14 intra-hemispheric and 8 inter-hemispheric electrode pairs in the resting eyes closed and eyes open conditions. The relationship between the psychopathological dimension scores and coherence values was assessed using Pearson's product moment correlation with Bonferroni correction for levels of significance. Significant associations between higher psychomotor poverty scores and lower inter-hemispheric coherence values were found across the central and parietal regions in the eyes closed condition and across central regions in the eyes open condition. Reality distortion and disorganization dimensions were not significantly correlated with intra- or inter-hemispheric coherences in both eyes closed and eyes open conditions. However there was a trend for an inverse correlation between disorganization dimension and intra-hemispheric coherence across left frontal, left temporo-parietal and right parieto-occipital regions in the eyes open condition. These findings suggest a possible differential pattern in the extent of brain involvement across the three psychopathological dimensions of schizophrenia in neuroleptic-naive patients with recent-onset illness.

Key words: schizophrenia, dimensions, drug-naive, EEG, alpha coherence, disconnection

Schizophrenia as we understand today is essentially a heterogeneous entity. The heterogeneity is not only in its clinical presentation but probably in the underlying aetiopathophysiological mechanisms as well. Despite a century of research in this area, the evidence supporting distinct pathophysiological mechanisms associated with the traditional categories of schizophrenia is slender. Dimensional approaches which have come up in recent years as an alternative to categorical classification imply that the pathological mechanism responsible for the illness involves several distinguishable processes that vary in relative severity between cases. Each of these underlying processes produces a set of symptoms, the severity of which may depend on the extent of severity of the underlying mechanism, and which vary together over time within a given patient (Liddle, 1999).

Most studies that have examined the dimensional aspects of schizophrenic psychopathology have used the Scale for the Assessment of Negative Symptoms (SANS)

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(Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984) for rating symptomatology. These studies have shown that the symptoms of schizophrenia can be grouped into three orthogonal syndromes, viz., reality distortion, psychomotor poverty and disorganization (Andreasen et al., 1995; Andreasen and Olson, 1982; Andreasen and Grove, 1986; Liddle, 1987a; Arndt et al., 1991; Peralta et al., 1992). Studies that used instruments other than SANS and SAPS have suggested the existence of other domains (Kay and Sevy, 1990; Van der Does et al., 1993). However, the three-dimensional hypothesis still remains the most robustly replicated of all the competing models of schizophrenic psychopathology (Amador & Gorman, 1998) and the same has been validated in patients with illness of recent-onset in developing countries (Kulhara et al. 1986; Gureje et al., 1995).

The underlying neurobiological correlates of these syndromes have been studied using various investigative techniques. Most of such studies till date have attempted to anatomically "localize" abnormalities in schizophrenia. Since schizophrenia is coming to be recognized as a "disconnection syndrome" it may be assumed that abnormalities of functional connectivity could be a key neurobiological feature of this condition. This "disconnection" is essentially a disorder of functional connectivity, which may or may not have macroscopic anatomical correlates (Friston, 1999). There is a growing consensus that schizophrenia is a disorder of functional brain systems involving a failure of integration between brain regions rather than simply isolated localizable deficits (Gruzelier, 1999). Therefore in the present study, we have analyzed the cortical coupling mechanisms in neuroleptic-naïve schizophrenic patients with recent-onset illness by studying the EEG coherence across intra and inter-hemispheric scalp locations.

EEG coherence analysis is a noninvasive technique for studying cortico-cortical associations (Thatcher et al., 1986). Coherence is a measure of the correlation between two EEG signals. The coherence values are computed in the various frequency bands of the EEG. Coherence of EEG signals recorded from electrodes placed over different brain regions is assumed to index anatomic or functional coupling between the brain regions under the electrodes (Shaw et al., 1978). It provides "a frequency-specific, phase-independent, linear index of the degree of coupling of two periodic phenomena" (Scammon et al., 1981). EEG coherence has been found to be a more sensitive tool for studying EEG changes in psychiatric patients than amplitude or power analysis (Tauscher et al., 1998).

Studies on EEG coherence in schizophrenia have largely focussed on group differences in coherence estimates between schizophrenic patients and control subjects in resting condition as well as during cognitive activation. The authors found only one previous study that has looked into correlations between symptom dimensions and coherence. In this study by Norman et al. (1997), a negative correlation between fronto-temporal alpha coherence and reality distortion was observed in a sample of 73 chronic schizophrenic patients on neuroleptics, while performing a left hemisphere activation task. No significant correlations were observed in the resting eyes closed or eyes open conditions.

Tauscher et al. (1998) found lower left frontal intra-hemispheric alpha coherence in schizophrenic patients compared to healthy controls in the resting eyes open condition. They also found an inverse correlation between the delta coherence at F7-F3 and the PANSS positive symptom subscore. Negative symptoms were found to be inversely correlated with intra- and inter-hemispheric alpha coherence in the resting eyes open condition in a sample of neuroleptic-free schizophrenic patients by Merrin & Floyd (1992).

There have been several other studies which have looked into group differences in alpha coherence values between schizophrenic patients and controls in resting eyes closed and eyes open conditions or during cognitive activation of right or left hemispheres (Winterer et al., 2001; Wada et

al., 1998a; Wada et al., 1998b; Morrison-Stewart et al., 1996; Nagase et al., 1993; Morrison-Stewart et al., 1991; Merrin et al., 1989; Shaw et al., 1983; Giannitrapani, 1980; Flor-Henry et al., 1979). These studies however have varied in their methodology and patient selection criteria.

In the present study we attempted to correlate the resting eyes closed and eyes open, intra and inter-hemispheric alpha coherence values with scores obtained on the three psychopathological dimensions of schizophrenia, viz., reality distortion, psychomotor poverty and disorganization in a sample of neuroleptic-naïve, recent-onset schizophrenic patients. We hypothesized that the psychomotor poverty dimension would be negatively correlated with inter-hemispheric and intra-hemispheric alpha coherence, whereas the other two dimensions would not be correlated significantly with coherence values.

MATERIAL AND METHOD

The sample for the present study consisted of 37 subjects fulfilling the Diagnostic and Statistical Manual-Fourth Edition (DSM-IV) criteria for schizophrenia or schizophreniform disorder (American Psychiatric Association, 1994). The sample was recruited from among the patients who attended the out-patient department of our hospital between September 1997 to August 1998. The diagnosis was confirmed by two psychiatrists (S.R. & S.K.). The inclusion criteria were: age between 17-45 years; age of onset more than or equal to 17 years; duration from onset of illness less than or equal to 3 years; right handed [as assessed by modified Annett's inventory (1976)] and an MMSE score of ≥ 21. The exclusion criteria were: previous exposure to psychotropic drugs, any general medical disorder or neurological disorder including epilepsy; any other comorbid axis I disorders; history of significant head injury; substance dependence (excluding tobacco); significant suicidal or homicidal risk or other disruptive behavior which warrant immediate interventions; history of ECT within the previous 6 months; history of institutionalization, defined as continuous hospital stay for more than 6 months and prominent catatonic features. Written informed consent was obtained after complete description of the study to the subjects.

Assessment of psychopathology

The symptoms were assessed using the SANS and SAPS. The ratings for all the patients were carried out by one psychiatrist (S.R.). The dimensional scores were calculated based on the method described previously by Liddle (1987 a, b). The score on the reality distortion dimension was the sum of the scores for the items measuring auditory hallucinations commenting on the patient's behavior, persecutory delusions and delusions of reference. The score on the disorganization dimension was the sum of the scores for items measuring inappropriate affect, poverty of content of speech and the global rating for formal thought disorder. The psychomotor poverty dimension was scored using items assessing poverty of speech, decreased spontaneous movement and the average of four items reflecting aspects of blunting of affect (affective non-responsivity, unchanging facial expression, paucity of expressive gestures and lack of vocal inflections). The maximum score on each dimension was 15.

Coherence measures

The subjects were seated in a semi-darkened, sound-attenuated and electrically shielded room that was used only for the purposes of EEG recording. The subjects were given some time to acclimatize with the conditions. The EEG Electro-cap was then fixed and electro-conducting gel was applied for all the electrodes. The test conditions included (a) 3 minutes of resting state with eyes closed and (b) 3 minutes of resting state with eyes opened. In order to make the resting condition as uniform as possible across subjects, they were instructed to focus their gaze on a point, one and a half meters in front at eye level in the eyes open condition and direct their eyeballs in the direction of this same point in the eyes closed condition. This would keep eye movement artifacts to a minimum as well as provide some amount of

uniformity to the 'cognitive state' of the patients at the time of EEG recording.

The EEG recording was performed with a 32-channel bio-amplifier system of the Nihon-Kohden type using the EEG-SYS software (NIMH, USA). The amplifiers were calibrated with a 50 μ V sine wave in the 4-8 Hz frequency band, generated by the Nihon-Kohden signal generator. The EEG was recorded from 30 cephalic locations (FP1, FP2, AF3, AF4, F5, F3, F1, Fz, F2, F4, F6, T1, FCz, T2, T3, C5, C3, C1, Cz, C2, C4, C6, T4, T5, P3, Pz, P4, T6, O1, O2) positioned according to the 10/20 International System (Jasper, 1958). A linked-ears reference was employed for the purpose of the study. The use of linked-ears reference does not guarantee high signal-to-noise ratios; however the source of possible error is less compared with that of other reference choices (Rappelsberger and Petsche, 1988). The impedance of all electrodes was kept below 5 kilo ohms. A ground electrode was placed 3 cm anterior to Fz. The signals were digitized at a rate of 256 Hz and converted into ASCII format for further analysis.

Baseline correction of the digital EEG signal was achieved using an autoregressive filter of co-efficient 0.97, and the 50 Hz and other high frequency noises were removed using a bi-directional 150-order Finite Impulse Response (FIR) digital filter with a bandwidth of 0.5-30 Hz (time constant-0.3 seconds). Artifacts due to eye movement, eye blinking, muscle tension or technical errors were excluded by careful visual inspection of the record. For each subject, under each recording condition, the best artifact-free continuous 10-second epoch was selected for further analysis. The EEG signals were then subjected to Fast Fourier Transformation (Cooley and Tukey, 1965), followed by computation of EEG alpha (8.5-12.5 Hz) coherence between the 14 intra-hemispheric (F5-F3, F4-F6, C5-C1, C2-C6, T1-T5, T2-T6, T5-P3, P4-T6, F3-O1, F4-O2, F5-C5, F6-C6, P3-O1, P4-O2) and 8 inter-hemispheric (F5-F6, F3-F4, T1-T2, T5-T6, C1-C2, C5-C6, P3-P4, O1-O2) electrode pair combinations. EEG signal analysis and computation of coherence was carried out using MATLAB (1999).

Statistical analysis

Normal distribution of the coherence values was ascertained by means of the Kolmogrov-Smirnov Goodness of Fit Test. The relationship between coherence values in the eyes closed and eyes open conditions and psychopathological dimension scores was evaluated with the use of Pearson's product moment correlation. Two-tailed tests with $p \leq 0.00119$ were considered significant for the correlation analysis of intra-hemispheric coherences with symptom dimensions after statistical correction. Two-tailed tests with $p \leq 0.00208$ were considered significant for correlation analysis of inter-hemispheric coherences with symptom dimensions. The critical levels of the significance values were arrived at by using the Bonferroni method of statistical correction, considering the fact that multiple comparisons were made. Statistical analyses were carried out using SPSS (1996).

RESULTS

Sample characteristics

The sample for the study consisted of 37 neuroleptic-naïve patients with recent onset of illness. 25 subjects (67.6%) were males and 12 (32.4%) were females. The mean age was 29.19 years (s.d=6.67; range: 18-45). The mean duration of illness was 17.62 months (s.d=12.77; range:1-36) and the mean age of onset of illness was 27.78 years (s.d=6.42; range:17-45). The subjects had a mean of 9.91 years (s.d=2.31; range: 7-15) of education. 30 patients had a diagnosis of schizophrenia whereas 7 were diagnosed to be having schizophreniform disorder.

The mean score on the reality distortion dimension was 8.3784 (s.d=4.9685; range: 0-15).The mean psychomotor poverty dimension score was 5.7365 (s.d.=3.3458; range: 0-13.75).

The mean score on the disorganization dimension was 2.6757 (s.d.=2.2980; range: 0-8).

Correlation between coherence values and psychopathological dimension scores.

Table I shows the correlations between the

alpha coherence at the 14 intra-hemispheric electrode pairs and the psychopathological dimension scores in the eyes closed condition.

TABLE 1
PEARSON'S PRODUCT MOMENT CORRELATION BETWEEN COHERENCE ACROSS INTRA-HEMISPHERIC ELECTRODE PAIRS IN EYES CLOSED CONDITION AND PSYCHO-PATHOLOGICAL DIMENSION SCORES.

Electrode Pairs	Reality Distortion	Psychomotor Poverty	Disorganization
F5F3	.177(.296)	-.223(.184)	-.105(.537)
F4F6	.244(.145)	-.164(.332)	-.306(.066)
C5C1	.148(.382)	-.070(.683)	-.095(.577)
C2C6	.254(.129)	*-.407(.012)*	-.250(1.36)
T1T5	-.062(.715)	.058(.735)	-.2.55(.128)
T2T6	-.087(.609)	-.070(.682)	-.179(.290)
T5P3	-.008(.963)	-.120(.479)	-.208(.217)
P4T6	.181(.285)	-.199(.238)	-.238(.157)
F3O1	.071(.677)	-.160(.343)	.185(.273)
F4O2	.032(.849)	-.72(.671)	-.053(.755)
F5C5	.117(.491)	-.055(.747)	-.83(.626)
F6C6	.247(.140)	*-.370(.024)*	-.206(.221)
P3O1	-.92(.589)	-.076(.656)	-.056(.741)
P4O2	.057(.736)	-.185(.272)	-.180(.287)

No r value with p≤ 0.001. Trends indicated in italics

TABLE 2
PEARSON'S PRODUCT MOMENT CORRELATION BETWEEN COHERENCE ACROSS INTRA-HEMISPHERIC ELECTRODE PAIRS IN EYES OPEN CONDITION AND PSYCHO-PATHOLOGICAL DIMENSION SCORES.

Electrode Pairs	Reality Distortion	Psychomotor Poverty	Disorganization
F5F3	-.139(.412)	.024(.890)	*-.326(.049)*
F4F6	.096(.572)	-.009(.958)	-.156(.357)
C5C1	-.010(.951)	-.027(.874)	.138(.414)
C2C6	-.013(.941)	-.076(.656)	-.095(.578)
T1T5	-.133(.432)	.039(.819)	-.196(.246)
T2T6	-.076(.655)	.121(.474)	-.034(.840)
T5P3	-.082(.629)	-.078(.646)	*-.412(.011)*
P4T6	.129(.446)	-.103(.546)	-.231(.169)
F3O1	.234(.163)	-.173(.307)	.185(.272)
F4O2	.121(.476)	-.109(.519)	-.217(.197)
F5C5	-.138(.416)	.054(.753)	-.056(.744)
F6C6	.077(.652)	-.125(.462)	-.092(.588)
P3O1	.174(.302)	-.300(.071)	-.312(.060)
P4O2	.072(.670)	-.223(.184)	*-.417(.010)*

No r value with p≤ 0.001. Trends indicated in italics

No significant correlations were observed at the p ≤ 0.001 level. However, there was a trend for an inverse correlation between psychomotor poverty scores and alpha coherence across F6-C6 and C2-C6. Table II shows the correlations between the alpha coherence at the 14 intra-hemispheric electrode pairs and psychopathological dimension scores in the eyes open condition.

TABLE 3
PEARSON'S PRODUCT MOMENT CORRELATION BETWEEN COHERENCE ACROSS INTER-HEMISPHERIC ELECTRODE PAIRS IN EYES CLOSED CONDITION AND PSYCHO-PATHOLOGICAL DIMENSION SCORES.

Electrode Pairs	Reality Distortion	Psychomotor Poverty	Disorganization
F5F6	.260(.120)	*-.350(.034)*	-.114(.501)
F3F4	.201(.233)	-.195(.248)	-.247(.140)
T1T2	.167(.322)	-.177(.295)	-.166(.327)
T5T6	.262(.118)	*-.409(.012)*	-.312(.060)
C1C2	.240(.152)	*-.546[3](.000)*	-.199(.238)
C5C6	.165(.329)	-.275(.100)	-.126(.457)
P3P4	.249(.138)	*-.483(.002)*	-.292(.080)
O1O2	.151(.371)	-.176(.296)	.072(.673)

[3] r value with p≤ 0.002. Trends indicated in italics

TABLE 4
PEARSON'S PRODUCT MOMENT CORRELATION BETWEEN COHERENCE ACROSS INTER-HEMISPHERIC ELECTRODE PAIRS IN EYES OPEN CONDITION AND PSYCHO-PATHOLOGICAL DIMENSION SCORES.

Electrode Pairs	Reality Distortion	Psychomotor Poverty	Disorganization
F5F6	-.061(.722)	-.025(.885)	-.177(.294)
F3F4	-.178(.292)	.026(.880)	-.117(.492)
T1T2	-.097(.569)	-.094(.579)	-.051(.767)
T5T6	.195(.248)	-.188(.266)	-.264(.114)
C1C2	.065(.703)	*-.487[3](.002)*	-.130(.444)
C5C6	-.091(.591)	-.004(.981)	.136(.424)
P3P4	-.003(.984)	-.258(.123)	-.025(.885)
O1O2	.243(.148)	*-.405(.013)*	-.137(.420)

[3] r value with p≤ 0.002. Trends indicated in italics

No significant correlations were observed. There was a trend for an inverse correlation between disorganization dimension scores and alpha coherence across F5-F3, T5-P3 and P4-O2. The correlations between the alpha coherences across the 8 inter-hemispheric electrode pairs in the eyes

closed condition are shown in Table III. Significant inverse correlations were observed between psychomotor poverty scores and alpha coherence across C1-C2 and P3-P4. There was a trend for an inverse correlation between psychomotor poverty and alpha coherences across F5-F6 and T5-T6. In the eyes open condition, again, there was significant inverse correlation between psychomotor poverty scores and alpha coherence across C1-C2 and a trend for an inverse correlation across O1-O2 (Table IV).

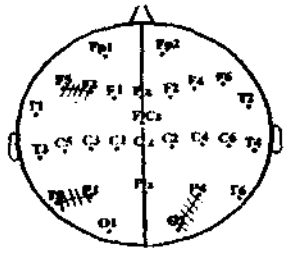

fig-1: **Inverse correlation between disorganization** dimension score and intra-hemispheric alpha coherence values across F5-F3, T5-P3 and P4-O2(trends) in the eyes open condition.

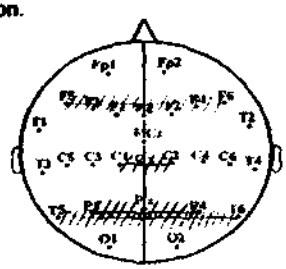

fig-2 :Inverse correlation between psychomotor poverty dimension scores and inter-hemispheric alpha coherence values across C1-C2 and P3-P4 ($p<0.002$) as well as F5-F6 and T5-T6 (trends) in the eyes closed condition.

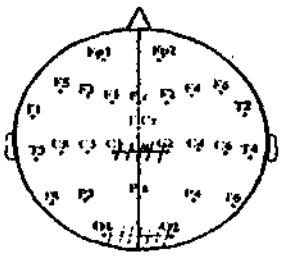

fig-3: Inverse correlation between psychomotor poverty dimension scores and inter-hemispheric alpha coherence values across C1-C2 ($p<0.002$) and across O1-O2 (trend) in the eyes open condition.

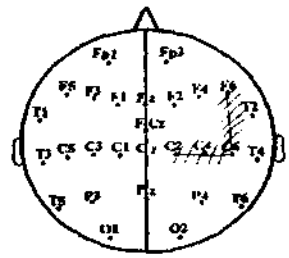

fig-4:**Inverse correlation between psychomotor** poverty dimension scores and intra-hemispheric alpha coherence values across F6-C6 and C2-C6 (trends) in the eyes closed condition.

DISCUSSION

This study evaluated the hypothesis regarding the three psychopathological dimensions of schizophrenia having underlying neural correlates. In particular, the study examined the extent of cortical disconnection associated with the three symptom dimensions using EEG alpha coherence which denotes the extent to which EEG signals in the alpha frequency band across various scalp locations are correlated to each other. Psychopathological dimension scores were correlated with intra- and inter-hemispheric alpha coherences to evaluate the relationship between the three dimensions and extent of dysfunctional connectivity in schizophrenia.

Reality distortion was not significantly correlated to alpha coherence values either intra- or inter-hemispherically in both eyes closed and eyes open conditions indicating that there are no abnormalities of cortico-cortical coupling that could be linked to this dimension. This is in agreement with previous studies that have found either no or minimal abnormalities of brain function associated with positive symptom schizophrenia (Liddle, 1987; Liddle and Morris, 1991; Baxter and Liddle, 1998).

Disorganization dimension was not found to be significantly correlated with alpha coherence values in both eyes closed and eyes open conditions. However, there was a trend for an inverse correlation with intra-hemispheric coherence values in the left frontal (F5-F3), left

temporo-parietal (T5-P3) and right parieto-occipital regions (P4-O2) in the eyes open condition (Figure I). Previous functional imaging studies have revealed a negative correlation of the severity of disorganization dimension with regional cerebral blood flow (rCBF) in ventrolateral prefrontal and parietal association cortices (Liddle et al., 1992; Kaplan et al., 1993). The findings of the present study could be pointing towards abnormalities of cortical coupling in the frontal and parietal regions.

Psychomotor poverty dimension was found to be inversely correlated to inter-hemispheric cortico-cortical coupling across central (C1-C2) and parietal regions (P3-P4) in the eyes closed condition (Figure II) and across central (C1-C2) regions in the eyes open condition (Figure III). There was also a trend for an inverse correlation with alpha coherence values across frontal (F5-F6) and temporal (T5-T6) regions in the eyes closed condition and across occipital (O1-O2) regions in the eyes open condition. A trend for an inverse correlation was noticed between psychomotor poverty and intra-hemispheric alpha coherence values in the right fronto-central (F6-C6) and central areas (C2-C6) in the eyes closed condition (Figure IV). These findings support evidence from previous cerebral perfusion studies in schizophrenia, which suggest a bilateral cortical hypofunction associated with deficit symptoms (Sabri et al., 1997; Tamminga et al., 1992; Wolkin et al., 1992; Cleghorn et al., 1989).

A previous study that has examined the association between EEG coherence and symptom dimensions in schizophrenia (Norman et al., 1997) did not find any significant correlations in the resting state in both eyes closed and eyes open conditions. However, it may be pointed out that the subjects included in this study were not drug-naïve. A number of previous studies have not found significant differences in coherence between schizophrenic patients and controls in the resting eyes closed and eyes open conditions (Morrison-Stewart et al., 1996; Morrison-Stewart et al., 1991). These studies, however, have focussed on group differences across schizophrenics and control subjects and did not evaluate correlates of psychopathological dimensions.

There are several methodological advantages, which this study has over previous studies on coherence in schizophrenia. All the subjects were drug-naïve thus ruling out confounding effects of medications, which could limit the inferences that could be derived from previous studies. Including only patients with recent-onset schizophrenic illness ensured homogeneity of the sample. This minimizes the effect of chronicity of illness on EEG coherence. The sample size is sizeable when one considers the fact that all subjects included in the study were neuroleptic-naive schizophrenic patients with recent-onset illness.

The present study has computed EEG alpha coherence in the resting eyes closed and eyes open conditions. Several previous studies have computed alpha coherence while subjects performed various cognitive activation paradigms. However, it must be borne in mind that the choice of a reference condition in behavioral research especially schizophrenia research, is not straightforward (Liddle, 1996).

The findings of the present study point towards the possibility of a differential cortical involvement across the three psychopathological dimensions of schizophrenia. Psychomotor poverty dimension was found to be associated with inter-hemispheric dysfunctional connectivity across central and the parietal regions and possibly in the frontal, temporal and occipital regions as well. There is also a suggestion of aberrant intra-hemispheric connectivity in the right fronto-central and central regions. This study does not provide any definite indicators for aberrant functional connectivity associated with the disorganization and reality distortion dimensions. However there could be a suggestion of aberrant intra-hemispheric connectivity in the left frontal, left temporo-parietal and right parieto-occipital regions associated with the disorganization dimension. Since the reality distortion dimension was not found to be associated with impairment in alpha coherence either intra- or inter-hemispherically, it may be presumed that the neurochemical abnormality that generates the

symptoms subsumed under this dimension does not result in aberrant functional connectivity.

The findings of this study may have implications with regard to response to medications and overall prognosis in patients with schizophrenia. It has already been established that schizophrenic patients having a predominance of deficit symptoms and disorganization symptoms respond unsatisfactorily to typical neuroleptics and in general have a poorer prognosis as compared to those with predominantly psychotic symptoms (Crow, 1980; Harrow et al., 1983). This well-established clinical observation may thus be explained as due to a more widespread impairment of neural circuits in these dimensions when compared to the reality distortion dimension. It is interesting to note that a previous study (Merrin and Floyd, 1992) which demonstrated a negative correlation between negative symptoms and inter-hemispheric alpha coherence reported reversal of these findings following drug treatment.

This study provides further evidence in favor of the 'disconnection hypothesis' of schizophrenia. It also suggests that the extent of disconnection might vary across the three symptom dimensions in a sample of neuroleptic-naïve recent-onset schizophrenic patients, with reality distortion not being associated with disturbances in functional connectivity and psychomotor poverty associated with significant inter-hemispheric dysfunctional connectivity. Disorganization dimension showed a trend for an association with disturbed intra-hemispheric connectivity. More studies utilizing various functional techniques are required to further delineate the neurobiological correlates of symptom dimensions of schizophrenia.

REFERENCES

Amador, X.F. & Gorman, J.M. (1998) Psychopathological domains and insight in schizophrenia. *Psychiatric Clinics of North America* 21, 27-42.

American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders, Edn. IV, Washington DC: *American Psychiatric Association.*

Andreasen, N.C. (1983) The Scale for the Assessment of Negative Symptoms (SANS). Iowa City: The University of Iowa.

Andreasen, N.C. (1984) The Scale for the Assessment of Positive Symptoms (SAPS). Iowa City: The University of Iowa.

Andreasen, N.C., Olsen, S. (1982) Negative vs positive schizophrenia: definition and validation. *Archives of General Psychiatry,* 39, 789-794.

Andreasen, N.C. & Grove, W.M. (1986) Evaluation of positive and negative symptoms in schizophrenia. *Psychiatry and Psychobiology,* 2,108-121.

Andreasen, N.C., Arndt, S., Alliger, R., Miller, D. & Flaum, M. (1995) Symptoms of schizophrenia: methods, meanings and mechanisms.*Archives of General Psychiatry* ,52,341-351.

Annett, M. (1976) A coordination of hand preference and skill replicated. *British Journal of Psychology* , 67, 587-592.

Arndt, S., Alliger, R.J. & Andreasen, N.C. (1991) The distinction of positive and negative symptoms: the failure of a two-dimensional model. *British Journal of Psychiatry,* 158, 317-322.

Baxter, R.D. & Liddle, P.F. (1998) Neuropsychological deficits associated with schizophrenic syndromes. *Schizophrenia Research,* 30, 239-250.

Cleghorn, J.M., Nahmias, C., Szechtman, H. & Szechtman, B. (1989) Inferior parietal region implicated in neurocognitive impairment in schizophrenia. *Archives of General*

Psychiatry, 46, 58-59.

Cooley, J. & Tukey, J. (1965) An algorithm for the machine calculation of complex Fourier series. *Mathematics of Computation*, 19, 297-301.

Crow, T.J. (1980) Molecular pathology of schizophrenia: more than one disease process? *British Medical Journal*, 280,1-9.

Flor-Henry, P., Koles, Z.J., Howarth, B.G. & Burton, L. (1979) Neurophysiological studies of schizophrenia, mania and depression. In Hemisphere Asymmetries of Function in Psychopathology, (Eds.) Gruzelier J, Flor-Henry P, pp 189-222, Amsterdam: Elsevier/North Holland Biomedical Press.

Friston, K.J. (1999) Schizophrenia and the disconnection hypothesis. *Acta Psychiatrica Scandinavia, 99 (Suppl.395)*, 68-79.

Giannitrapani, D. (1980) The coherence of the EEG in normal and schizophrenic subjects. *Electroencephalography and Clinical Neurophysiology*, 49, pp 108.

Gureje, O., Aderibigbe, Y.A. & Obikoya, O. (1995) Three syndromes in schizophrenia: validity in young patients with recent onset of illness. *Psychological Medicine*, 25, 715-725.

Harrow, M., Silverstein, M. & Marengo, J. (1983) Disordered thinking: does it identify nuclear schizophrenia? *Archives of General Psychiatry*, 40, 765-771.

Jasper, H. (1958) The ten-twenty system of the International Federation. *Electroencephalography and Clinical Neurophysiology*, 10, 371-375.

Kaplan, R.D., Szechtman, H., Franco, S., Szechtman, B., Nahmias, C., Garnett, E.S., List, S. & Cleghorn, J.M. (1993) Three clinical syndromes of schizophrenia in untreated subjects: relation to brain glucose activity measured by positron emission tomography (PET). *Schizophrenia Research*, 11, 47-54.

Kay, S.R. & Sevy, S. (1990) Pyramidical model of schizophrenia. *Schizophrenia Bulletin*, 16, 537-545.

Kulhara, P., Kota, S.K. & Joseph, S. (1986) Positive and negative subtypes of schizophrenia: a study from India. *Acta Psychiatrica Scandinavia*, 74, 353-359.

Liddle, P.F. (1987a) The symptoms of chronic schizophrenia: a re-examination of the positive-negative dichotomy. *British Journal of Psychiatry*, 151, 145-151.

Liddle, P.F. (1987b) Schizophrenic syndromes, cognitive performance and neurological dysfunction. *Psychological Medicine*, 7, 49-57.

Liddle, P.F. (1996) Functional imaging-schizophrenia. *British Medical Bulletin*, 52 (3), 486-494.

Liddle, P.F. (1999) The multidimensional phenotype of schizophrenia. In Schizophrenia in a Molecular Age (Review of Psychiatry Series Vol.18), (Ed.) Tamminga CA, pp 1-28, Washington DC: American Psychiatric Press.

Liddle, P.F. & Morris, D.L. (1991) Schizophrenic syndromes and frontal lobe performance. *British Journal of Psychiatry*, 158, 340-345.

Liddle, P.F., Friston, K.J., Frith, C.D., Hirsch, S.R, Jones, T. & Frackowiak, R.S.J. (1992) Patterns of cerebral blood flow in schizophrenia. *British Journal of Psychiatry*, 160,179-186.

MATLAB, Version 5.3.1. (1999) USA: Mathwork Inc.

Merrin, E.L. & Floyd, T.C. (1992) Negative

symptoms and EEG alpha activity in schizophrenic patients. *Schizophrenia Research* ,8, 11-20.

Merrin, E.L. & Floyd, T.C. (1996) Negative symptoms and EEG alpha in schizophrenia: a replication. *Schizophrenia Research*, 19, 151-161.

Merrin, E.L., Floyd, T.C. & Fein, G. (1989) EEG coherence in unmedicated schizophrenic patients. *Biological Psychiatry*, 25, 60-66.

Morrison-Stewart, S.L., Williamson, P.C., Corning, W.C., Kutcher, S.P. & Merskey, H. (1991) Coherence on electroencephalography and aberrant functional organization of the brain in schizophrenic patients during activation tasks. *British Journal of Psychiatry*, 159, 636-644.

Morrison-Stewart, S.L., Velikonja, D., Corning, W.C. & Williamson, P. (1996) Aberrant interhemispheric alpha coherence on electroencephalography in schizophrenic patients during activation tasks. *Psychological Medicine*, 26, 605-612.

Nagase, Y., Okubo, Y., Matsuura, M., Kojima, T. & Toru, M. (1993) EEG coherence in unmedicated schizophrenic patients: Topographical study of predominantly never-medicated cases. *Biological Psychiatry*, 32, 1028-1034.

Norman, R.M.G., Malla, A.K., Williamson, P.C., Morrison-Stewart, S.L., Helmes, E. & Cortese, L. (1997) EEG coherence and syndromes in schizophrenia. *British Journal of Psychiatry*, 170, 411-415.

Peralta, V., de Leon, J. & Cuesta, M.J. (1992) Are there more than two syndromes in schizophrenia? A critique of the positive-negative dichotomy. *British Journal of Psychiatry*, 161, 335-343.

Rapplesberger, P. & Petsche, H. (1988) Probability mapping: power and coherence analysis of cognitive processes. *Brain Topography*, 1, 46-53.

Sabri, O., Erkwoh, R., Schreckenberger M, Owega, A., Sass, H. & Buell, U. (1997) Correlation of positive symptoms exclusively to hyperperfusion or hypoperfusion of cerebral cortex in never-treated schizophrenics. *Lancet*, 349, 1735-1739.

Scammon, M.E., Kennard, M.M., Stroebel, C.F. & Glueck, B.C. (1981) A user-interactive graphics-based computer system for analysis of the EEG. *Behavior Research Methods and Instrumentation*, 13, 517-524.

Shaw, J.C., Colter, N. & Resek, G. (1983) EEG coherence, lateral preference and schizophrenia. *Psychological Medicine*, 13, 299-306.

SPSS for Windows, Version 7.5.1 (1996) USA: SPSS Inc.

Tamminga, C.A., Thaker, G.K., Buchanan, R., Kirkpatrick, B., Alphs, L.D., Chase, T.N. & Carpenter, W.T. (1992) Limbic system abnormalities identified in schizophrenia using positron emission tomography with fluorodeoxyglucose and neocortical alterations with deficit syndrome. *Archives of General Psychiatry*, 49, 522-530.

Tauscher, J., Fischer, P., Neumeister, A., Rappelsberger, P. & Kasper, S. (1998) Low frontal electroencephalographic coherence in neuroleptic-free schizophrenic patients. *Biological Psychiatry* ,44, 438-447.

Thatcher, R.W., Krause, P.J. & Hrybyk, M. (1986) Cortico-cortical associations and EEG coherence: a two-compartmental model. *Electroencephalography and Clinical Neurophysiology*, 64, 123-143.

Van der Does, A.W., Dingemans, PMAJ, Linszen, D.H. Dingemans, P.M., Nugter, M.A.

& Scholte, W.F.(1993) A dimensional and categorical approach to the symptomatology of recent-onset schizophrenia. *Journal of Nervous Mental Disorders*, 181, 744-749.

Wada, Y., Nanbu, Y., Jiang, Z.Y., Koshino, Y. & Hashimoto, T. (1998a) Interhemispheric EEG coherence in never-medicated patients with paranoid schizophrenia: analysis at rest and during photic stimulation. *Clinical Electro-encephalography*, 29, 170-176.

Wada, Y., Nanbu, Y., Kikuchi, M., Koshino, Y. & Hashimoto, T. (1998b) Aberrant functional organization in schizophrenia: analysis of EEG coherence during rest and photic stimulation in drug-naive patients. *Neuropsychobiology*, 38, 63-69.

Winterer, G., Egan, M.F., Radler, T., Hyde, T., Coppola, R. & Weinberger, D.R. (2001) An association between reduced interhemispheric EEG coherence in the temporal lobe and genetic risk for schizophrenia. *Schizophrenia Research*, 49, 129-143.

Wolkin, A., Sanfilipo, M., Wolf, A.P., Angrist, B., Brodie, J.D. & Rotrosen, J. (1992) Negative symptoms and hypofrontality in chronic schizophrenia. *Archives of General Psychiatry*, 49, 959-965.

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