STUDY ON NEUROPSYCHOLOGY OF FIRST EPISODE SCHIZOPHRENIA: CHARACTERIZATION AND CLINICAL CORRELATES

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CERTIFICATE

This is to certify that the dissertation entitled a **"STUDY ON NEUROPSYCHOLOGY OF FIRST EPISODE SCHIZOPHRENIA: CHARACTERIZATION AND CLINICAL CORRELATES."** is a bonafide record of work done by **Dr.V.VIMAL DOSHI** in the Department of Psychiatry, Government Rajaji Hospital, Madurai Medical College, Madurai, in partial fulfilment of the requirement for the award of MD degree Branch XVIII (Psychiatry) under the direct guidance of me.

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DECLARATION

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This is submitted to the Tamil Nadu, Dr. M.G.R. Medical University Chennai, in partial fulfilment of the regulations for the award of MD degree Branch XVIII (Psychiatry).

Place : Madurai

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ABBREVIATIONS

1	DSM	-	Diagnostic And Statistical Manual IV Edition. (TR2000)
2	MINI PLUS	-	Structured Clinical Interview for DSM-IV TR
3	PANSS	-	Positive and Negative Syndrome Assessment Scale
4	SFI	-	Social Functioning Index
5	DSST	-	Digit Symbol Substitution Test
6	DVT	-	Digit vigilance Test
7	FT	-	Finger Tapping
8	Dig-Seq	-	Digit Sequencing Test
9	DOT	-	Dot Test
10	FAB	-	Frontal Assessment Battery
11	COWAT	-	Controlled Oral Word Association Test
12	CAT	-	Category Test (Fluency)
13	CT 1&2	-	Color Trails 1 & 2
14	AVL_1 1 &2	-	Rey's Auditory Verbal Learning Test
15	RCF 1, 2, 3	-	Rey's Complex Figure Test
16	RAV	-	Raven's Progressive Matrices
17	WCST	-	Wisconsin Card Sorting Test
18	CPT	-	Continuous Performance Test
19	SPAN	-	Span of Attention
20	PET	-	Positron Emission Tomography

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INTRODUCTION

Cognitive abnormalities were noted by early investigators of schizophrenia. In the original clinical descriptions of schizophrenia made by Kraepelin, he commented *"Mental efficiency is always diminished to a considerable degree. The patients are distracted, inattentive . . . , they `cannot keep the thought in mind.' "*

"My whole mental power has disappeared; I have sunk intellectually below the level of a beast"(a patient with schizophrenia, quoted by Kraepelin, 1919, p. 25).

Study of cognitive deficits evolved from the traditional 'lesion'-based approach in neuropsychology, which is, inferring regional brain dysfunction based on poor performance on putatively localising neuropsychological tests. On the basis of such an approach, various authors have concluded that schizophrenia is characterized by cognitive test profiles indicative of dysfunction of the frontal lobe, temporal lobe, left or right hemisphere, basal ganglia, etc. (Blanchard & Neale, 1994). This lack of consensus may reflect the heterogeneity of schizophrenia, and may also be a result of the relatively poor localizing ability of many standard neuropsychological instruments. In general, the strongest camps to emerge have been those that claim a disproportionate impairment of memory functioning (McKenna, 1991; Saykin *et al*, 1994) and those arguing for a relatively selective executive dysfunction (Weinberger *et al*, 1986). Others have reported more

widespread neuropsychological dysfunction (Buchsbaum, 1990). An extreme case is put by Meehl who stated:

"I conjecture that whatever is wrong with the schizotaxic CNS is ubiquitous, a functional aberration present throughout, operating everywhere from the sacral cord to the frontal lobes" (Meehl, 1990, p. 14).

Many current workers would agree with Shallice *et al* (1991) who proposed that from a neuropsychological perspective, an attempt to understand the nature of the information-processing impairment of **schizophrenia** should precede an attempt to localise it.

Heinrichs & Zakzanis (1998) carried out a large-scale comprehensive quantitative meta-analysis of cognitive impairment in schizophrenia**,** which involved comparisons of patients with schizophrenia *v.* controls. The greatest impairment is observed in global verbal memory functioning. Palmer *et al* (1997) recently posed *"Is it possible to be schizophrenic yet neuropsychologically normal?"* They gave a comprehensive neuropsychological battery to 171 out-patients with schizophrenia and compared them with 63 healthy controls. Only 27% of the patients with schizophrenia were classified as neuropsychologically 'normal'. It is interesting that Goldberg *et al* (1993), who reported symptomatic improvement with clozapine treatment, with no associated improvement in neuropsychological functioning, concluded:

"This suggests that certain cognitive deficits are relatively independent of psychotic symptoms in schizophrenia, and are probably central and enduring features of the disorder. Cognitive disability appeared to have been rate-limiting in the sample's rehabilitation" (p. 43). Concepts have, therefore, moved from a position where cognitive impairment was not considered to be particularly important in schizophrenia, to the current view, that it may be a central and rate-limiting feature in terms of rehabilitation. Cognitive deficits can manifest as an inability accurately to recognise social cues or to retrieve appropriate responses. Consequently, patients have difficulty acquiring social and interpersonal skills. It is understandable that, during periods of increased arousal such as psychosocial crisis or relapse, this capacity becomes limited and cognitive functions can worsen.

Are cognitive deficits a trait or a state marker? If they are a trait marker one would expect that they remain stable in spite of treatment. Various studies have shown that cognitive dysfunction does remain stable from the acute phase to follow-up after clinical stabilisation, suggesting that these deficits are indeed trait markers. This trait deficiency may exist in addition to state-related cognitive impairments (Saykin *et al*, 1994).

The exact timing of onset of cognitive impairment during the early phase of schizophrenic illness and its progress and course after the first episode are unclear. Furthermore, the clinical significance of cognitive impairment in first-episode psychosis is not well understood, and there is evidence to suggest that it pre-dates

the onset of illness (O'Carroll, 2000). Numerous studies (e.g. Bilder *et al*, 1996; Heinrichs & Zakzanis, 1998) have reported deficits in attention, memory and executive functioning that are now thought to be strongly related to clinical outcome, perhaps more than positive and negative symptoms (Hoff & Kremen, 2003).Some studies suggest that the cognitive impairment in first-episode psychosis differs from that in chronic schizophrenia only in terms of degree of severity (Saykin *et al,* 1994). In the West London study, Joyce *et al*(2002) identified a profile of executive impairment in first-episode psychosis that they suggested differs from previous findings in chronic schizophrenia. A lack of clear understanding of neural and neuropsychological substrates makes it difficult to know whether the cognitive problems that occur are isolated deficits or whether they reflect a more global impairment (Bilder *et al,* 2000).

Drug-free patients with schizophrenia demonstrate significant cognitive impairment. (e.g. Blanchard & Neale, 1994; McCreadie *et al*, 1997; Saykin *et al*, 1994). Although drugs may make a contribution, they do not account for the cognitive impairment that is observed in schizophrenia. Negative features and neuropsychological impairments can cause the greatest problems in terms of rehabilitation and are generally considered to be minimally responsive to conventional neuroleptics. The recent development of novel antipsychotics raised the hope that these may help alleviate both negative symptoms and neuropsychological deficits. However, Hawkins *et al* (1999) state:

"Despite some reports of positive findings, the grounds for thinking that the novel antipsychotics will exert direct and significant effects on neurocognition nevertheless remain inferential, and infirmly so" (p. 6).

The importance of research in this area is of many fold, such that it provides us clues into the biological underpinnings and nature of the possible pathophysiological mechanisms that results in cognitive impairment and secondly from a clinicians view the relevance of cognitive deficits in the course and outcome of the disease is crucial, from another practical point of view any significant cognitive deficit is likely to affect the individual in daily activities with poor coping skills, particularly in terms of setting appropriate goals, goal directed behaviours, self regulation and decision making ultimately ending up with socio occupational difficulties and increasing the burden of the disease.

With this background my study aims to assess neurocognitive functions of I episode Schizophrenia patients and to compare them with normal healthy control population, and to note the relationship between the test performance and various socio demographic and clinical variables.

REVIEW OF LITERATURE

Cognitive functioning in schizophrenia has been recognized since Kraepelin first described dementia praecox in the fifth edition of his Textbook of Psychiatry (Kraepelin, 1896). For years, schizophrenia was recognized as a cognitive disorder, also marked by multiple additional symptoms. In fact, the first research on cognition in schizophrenia and related conditions was published in the 19th and the early years of the last century.

Over the middle of the 20th century, influenced by the advent of medications that effectively treat most of the symptoms of schizophrenia other than deficits in formal cognitive functions, the focus of attention on schizophrenia shifted away from cognition and toward positive symptoms of the illness. At the very end of 20th century, however, there was a resurgence of interest in cognition in schizophrenia. This interest was partially spurred by the realization that functional deficits in schizophrenia are responsible for a large amount of the disability and indirect costs of the illness, and the recognition that cognitive deficits are largely responsible for these functional deficits. Another impetus toward the increased interest in cognition in schizophrenia was the realization that some of the newer medications used to treat schizophrenia had beneficial effects on cognition as well. Finally, the level of sophistication in the diagnosis and sub typing of schizophrenia increased as well, leading to greater replicability of findings and faster progress in understanding some of the subtleties of cognitive impairments.

There is a remarkable agreement on the point that neurocognitive deficits are part and parcel of schizophrenia. In other words, they generally do not derive from the symptoms of the disorder, nor are they a result of medication nor are they induced by institutionalization. On the contrary, many of the neurocognitve deficits seem to reflect predisposition to the illness as opposed to the presence of illness. Hence, the neurocognitive deficits of schizophrenia can be considered central to the disorder. Some neurocognitive deficits are present in children who are at 'high risk' for schizophrenia, with risk for illness usually defined as having a schizophrenic parent (Nuechterlein, 1983; Cornblatt and Erlenmeyer Kimling, 1985; Rutschmann et al., 1986; Cornblatt et al., 1989; Asarnow et al., 1977). These studies indicate that neurocognitive deficits are apparent long before the onset of overt, psychotic symptoms. Further support for the centrality of the deficits is that they endure after a psychotic episode when symptoms have subsided and patients are in remission (Asarnow and MacCrimmon, 1978; Miller et al., 1979; Nuechterlein et al., 1992). Neurocognitive deficits are also found in first degree relatives of patients, who do not have a schizophrenic disorder (Grove et al., 1991; Steinhauer et al., 1991; Mirsky et al., 1992; Green et al., 1997; Keefe et al., 1997). Moreover, these deficits can be observed in non-psychotic individuals who are considered to be in the schizophrenia spectrum because they have clinical symptoms of schizotypal personality disorder or high scores on tests of psychosis proneness (Braff, 1981; Asarnow et al., 1983; Balogh and Merritt, 1985; Lenzenweger et al., 1991).

Course of Cognitive Deficits:

In a birth cohort study in which 4746 people born in Great Britain during one week of 1946 were followed up to 16 years of age, Jones et al. (1994) have shown that those participants that went on to develop schizophrenia displayed low premorbid levels of educational achievement, retardation in the attainment of neuromotor developmental milestones and premorbid speech abnormalities.Goldstein and Shemansky, 1995 make a strong case that there are groups or clusters of patients with schizophrenia who display rather severe and diffuse cognitive impairments in adulthood which, at least in some patients, may have existed before the emergence of diagnostic symptoms. On the basis of a cluster analysis, Goldstein and Shemansky (1995) identified a group of severely cognitively impaired patients with schizophrenia whose cognitive performance was indistinguishable from the performance of dementia patients.

Other studies clearly suggest that there is also a subgroup of patients with schizophrenia who do not experience intellectual decline or severe cognitive impairment before or after the onset of illness (Schwartz, 1967, Dudek, 1969, Goldstein and Shemansky, 1995).

Based on these findings, it is possible (an attempt was made) to divide the sample of patients with schizophrenia into two groups as follows:

1. To define a group of patients that undergo intellectual deterioration from premorbid levels as defined by a drop of at least 10 points from the premorbid IQ estimate.

2. Identify a group of patients that do not undergo intellectual deterioration from premorbid levels as defined by a drop of <10 points, no change or a slight increase from premorbid IQ estimate. The non-declining group was subdivided further based on previous findings and clinical observation as follows:
    a. Specify a group of premorbidly compromised patients defined as exhibiting premorbid IQs below 90 and no decline in current IQ from the premorbid level.
    b. Describe a cognitively preserved group defined as exhibiting premorbid IQs above 90 and no decline in current IQ from the premorbid level.

The cognitive domains affected in the premorbidly compromised group include memory, visuospatial perception, attention, executive function / working memory, language and psychomotor speed. These findings implicate temporal and parietal cortical dysfunction in the premorbidly compromised group in a stronger way than do the neurocognitive profiles of the other groups. It is also important to note that the premorbidly compromised group is strikingly similar to patients displaying so-called 'deficit' syndromes in neurocognitive measures (Buchanan et al., 1994, 1997). Finally, with respect to the premorbidly compromised group, the pattern of neuropsychological deficits described above would suggest that parieto-

occipital, temporal and frontal functions are compromised, implicating a pan-cortical impairment.

In the Intellectually deteriorated patient group the finding of intellectual decline is consistent with the longitudinal findings of Lubin et al. (1962) and Schwartzman and Douglas (1962), Dalby and Williams, 1986; Goldberg et al., 1993b, 1995; Gold et al., 1994; Frith, 1996; Kremen et al., 1996. This decline in intellect was accompanied by a distinct neurocognitive profile. Specifically, impairment was evident in the cognitive domains of memory, working memory, attention, psychomotor speed and occulomotor scanning. Unlike the premorbidly compromised group, visuospatial perception and lexical access were unaffected. It was recognized that the intellectual decline is not necessarily monolithic in the sense that all areas (or WAIS-R subtests) are not affected equally. Rather, the decline of intellectual abilities appears to reflect impairment in those abilities specifically associated with working memory or those subtests that load highly on the so-called freedom from distractibility factor, such as the DSST. This profile of cognitive impairment implicates fronto-temporal dysfunction as observed in the work of Rappaport and Webb (1950), Lubin et al. (1962), Schwartzmann and Douglas (1962) and Nelson et al. (1990). The intellectually deteriorated groups of schizophrenic patients displayed significant differences from normal on tests of declarative memory such as the immediate and delayed portions of the WMS-R and for all measures in the CVLT (Goldberg et al., 1993b; Paulsen et al., 1995).

Significant differences on measures of attention in schizophrenic patients relative to normal controls on various versions of the CPT (Mirsky et al., 1992; Servan-Schreiber et al., 1996) have been reported. Patients also displayed significant differences from normal controls on the mean percentage of perseverative errors exhibited on the WCST, a measure of executive / fontal lobe function. On a test of psychomotor speed and scanning ability, forms A and B of the Trail Making Test, the intellectually deteriorated schizophrenic patients displayed significant differences from normal controls and intellectually preserved schizophrenic patients.

An unexpectedly large portion (25% of the total sample) of the intellectually intact patients displayed only mild impairment on the cognitive domains of executive function / working memory and attention / vigilance. Cognitively preserved patients displayed no deficits in the cognitive domains of episodic memory or psychomotor speed. In contrast to the premorbidly compromised group, the cognitively preserved group did not display deficits in the fundamental cognitive domains of language and visuospatial perception.

Thus, one course suggests that the disease process manifests itself as cognitive impairment that may be relatively profound and widespread at an early stage of development and is present subsequent to the onset of psychotic symptoms. These premorbidly compromised patients may have experienced early developmental stressors and / or a genetic predisposition leading to the observed cognitive deficits. A second course suggest that the cognitive deficits may become

manifest concurrently with the onset of psychotic symptoms, resulting in a more circumscribed pattern of deficits that encompasses the cognitive domains of executive function, attention and long-term memory. The third course suggests that while cognitive impairment may be concurrent with symptom onset, the debilitating cognitive deficits associated with the disease process may be relatively subtle, being restricted to the domains of executive function / working memory and attention. Deficits of executive function / working memory and attention constitute a necessary and perhaps sufficient type of cognitive impairment in schizophrenia. With the exception of the DSST of the WAIS-R, the number of categories attained on the WCST and correct responding on the CPT were the only cognitive measures that provided significant differences between the cognitively preserved group of patients and the normal control group. As such, these deficits can be considered to be 'core' cognitive deficits in schizophrenia.

Working Memory:

There is solid neuropsychological and imaging evidence that temporo frontal function is disordered in schizophrenia, suggesting that core deficits may be localized in that region. One candidate core function is working memory, a capacity-limited system that enables the holding of information while the individual works on a problem. One of the key characteristics of a working memory task may be the assessment of performance on a primary task such as problem solving, while simultaneously performing a secondary task such as recalling words or digits (Daneman and Carpenter, 1980). The cognitive process of

maintaining the information form the primary task ‘in mind’ while conducting the secondary task is the core of working memory functioning. If the secondary task disrupts the primary one, this is attributable to the limitations of the working memory system.

In its basic form, this model includes a “central executive” (or supervisory attentional system), which allocates between sensory representations depending on the informational analysis required for the specific task, and two “slave” systems, a phonological loop and a visuospatial scratch pad, which retain specialized information over brief periods of time. In this model, executive functions are located in the prefrontal cortex and storage is more posterior, in the motor and sensory systems. Because of the central role of working memory, malfunction of this system can be logically perceived to cause impaired goal-oriented behavior, disorganized cognitive organization, failure of self-monitoring, and other phenotypic manifestations of schizophrenia. There is abundant evidence that schizophrenia patients perform poorly on tests of working memory, and several studies showed correlations between working memory deficits and other neurocognitive abnormalities, including processing speed and executive function. The non-pyschotic relatives of patients with schizophrenia as well as individuals with schizotypal personality also appear to demonstrate working memory deficits, although normally in a milder form.

Correlations of Working Memory with other Cognitive Functions:

The relationship between the phonological loop and WCST performance was assessed by Gold et al., (1997) using the letter-number span test. Although letter-number test performance in schizophrenic patients was associated with several other domains of cognitive functioning including full-scale IQ, trailmaking, memory, attention and verbal fluency, the correlation with WCST categories was particularly high ($r = 0.74$, $P < 0.01$), and was significantly higher than in normal controls. Thus, verbal working memory appears to be a significant component of WCST performance, and may account for a major component of the cognitive impairment that accounts for WCST performance in patients with schizophrenia.

The performance of the schizophrenic patients on tests of visuospatial working memory and executive functions (as measured by a 'Tower of London' test) was even worse that that of patients with frontal lobe lesions, and far worse than that of patients with focal temporal lobe lesions. It is noteworthy that the strategies of schizophrenic patients in performing the spatial working memory test were severely impaired, suggesting that executive functions may in some cases underline the poor working memory performance of patients with schizophrenia.

Schizophrenic patients performed less well than controls on working memory tests as well as on tests of long-term verbal memory. Between-group differences on all three tests of strategic long-term memory (free recall, memory for temporal order and self-ordered pointing) could be accounted for by working memory capacity. Verbal working memory, as measured by the letter-number

span, has been found to be related to general memory functions (Gold et al., 1997), yet visuospatial working memory is not related to delayed recall of verbal material (Keefe et al., 1995). Sullivan et al. (1997) demonstrated that when scores were controlled for age and IQ estimated from the NART, the working memory deficits of schizophrenic patients were far more severe than their deficits in longer term memory functions. This finding was remarkably consistent across verbal and visual stimuli, as well as for working memory for the temporal order of the stimuli. In summary, the relationship between working memory and longer term memory functions is complex and may depend upon the modality of the stimuli and the strategies employed by subjects to encode and retrieve stored information.

The relative impact of distractibility and processing capacity on verbal working memory was assessed by Goldberg et al. (1998) by administering serial span tasks of either three or six digits to schizophrenic patients and healthy controls. Verbal working memory span deficits are more likely to be attributable to processing capacity limitations than attentional deficiencies. The patient performances were affected by the interference task to a greater degree than those of the controls, suggesting that schizophrenic patients may rely more heavily than normal controls on covert articulatory rehearsal strategies. Schizophrenic patients do not perform poorly on verbal working memory tests due to a lack of verbal rehearsal; rather, the fundamental deficit may lie in processing capacity limitations or possible the inability to generate alternative processing strategies.

Significant correlations were demonstrated in schizophrenic patients between working memory as measured by backwards digit span (Brebrion et al. 1998) with digit-symbol substitution test performance. A significant correlation between a visuospatial working memory task (remembering the location of WCST cards in a 6 by 4 matrix) and digit-symbol performance has also been reported (Stratta et al., 1997). These data suggest that processing speed may be an important factor underlying working memory deficits in schizophrenia.

Correlations of Working Memory with Negative, Disorganization and Positive symptoms:

In a study of 18 schizophrenic patients who had been withdrawn from oral antipsychotic medication for at least 10 days, a significant correlation ($r = 0.50$, $df = 16$, $P < 0.05$) was reported between visuospatial working memory performance and negative symptoms as measured by either the Negative Symptoms Assessment or the Schedule for the Assessment of negative Symptoms (Carter et al., 1996).

The working memory deficits of schizophrenia do not appear to be accounted for by patients' reduced motivation. It seems likely that the causal relationship between theses two factors is in the opposite direction. Patients who have working memory deficits may be less likely to be motivated to have goals and pursue them. Those patients with severe working memory deficits are likely to be met with failure if they attempt to pursue employment, social and even recreational avenues that require cognitive skill. These repeated failures are likely to cause discouragement and reduced motivation even in people without mental illness.

A correlation of 0.51 between rating of formal thought disorder and performance on a visuospatial working memory test was reported by Spitzer (1993). Formal thought disorder, as rated by the Thought, Language and Communication Scale (Andresasen, 1982), was significantly correlated ($r = 0.65$, $df = 21$, $P < 0.05$) with visuospatial working memory functions.

A few studies have demonstrated correlations between working memory impairment and positive symptoms, in contrast to the absence of such a relationship between positive symptoms and other cognitive deficits. Further more, specific cognitive tests aimed at measuring the inability of patients with schizophrenia to monitor self-generated mental events suggests that to the extent that working memory is involved in self-monitoring, it is correlated with the presence of Positive psychotic symptoms.

Imaging studies and Working Memory:

An 'N-back' task was used in a positron emission tomography (PET) study of eight schizophrenic patients and eight controls matched for age, sex, and parental education (Carter et al., 1998). Despite similar performance, patients had less activation of the right DLPFC than the controls. When the working memory load increased to a two-back task, patients' performance worsened more than that of the controls. The increase in activation of the right DLPFC and the posterior parietal cortex associated with greater working memory load was significantly less in the patients than in the controls. These data may suggest that patients with

schizophrenia are more likely to have impairment in the neural circuitry that mediates verbal working memory.

Effect of drugs on Working Memory:

Conventional antipsychotics block dopamine receptors in the prefrontal cortex which has been found to impair working memory functions in non-human primates under normal conditions (Sawaguchi and Goldman-Rakic, 1994). Furthermore, dopamine agonism with bromocriptine improves visuospatial working memory in normal subjects (Luciana et al., 1992). Whereas in patients suffering from psychosis, who may have an altered system of dopaminergic transmission (Davis et al., 1991), working memory functions may be relatively unaffected by dopaminergic blockade. Very low doses of dopamine receptor antagonists may be useful in treating working memory impairment in psychotic patients. Higher doses of neuroleptics may be ineffective owing to excessive blockade of dopamine receptors in the prefrontal cortex or impaired striatal function producing response deficits (Arnsten and Goldman-Rakic, 1998). Risperidone may improve all three aspects of working memory functions. Risperidone treatment had a greater beneficial effect than haloperidol treatment on verbal working memory as assessed by a digit-span distraction test (Green et al., 1997). The treatment effect remained significant after the effects of adjunctive benztropine treatment, change in psychotic symptoms and change in negative symptoms were controlled.

Executive Dysfunction:

Lezak (1995) defined Executive functions as those capacities that enable a person to engage successfully in independent, purposive, self-serving behavior. (p.42). Green (1998) offered the following definition: Executive functioning refers to a host of neurocognitive activities that are associated with the prefrontal cortex such as planning, problem solving, shifting cognitive set, and alternating between two or more tasks. A simple definition of executive skills still remains elusive, but in general this construct appears to involve those cognitive processes which permit an adaptive balance of initiation maintenance and shifting if responses to environmental demands permitting goal-directed behavior. Although these processes have been attributed historically to frontal cortical functioning, there has been growing recognition o the importance of cortical-subcortical connections in these functions (Cummings, 1993; Evarts et al., 1984). Some of the most commonly used neuropsychological tests of executive skills include the WCST (for abstraction, maintenance and adaptive shifting of cognitive set), the Category Test (abstraction problem solving and set shifting), the Stroop test (response inhibition or selective attention), Tower of London / Hanoi / Toronto (planning), COWAT (strategic search of the lexicon) and Part B of the Trail Making Test (mental flexibility and working memory).

The WCST (Berg, 1948; Heaton et al., 1993) is perhaps the single most widely used measure of executive functioning within the schizophrenia literature, as well as being widely used within general neuropsychological practice and

research (Bulter et al., 1991).The WCST generally is interpreted in terms of abstraction / problem solving skills and ability to shift strategies efficiently in response to environmental feedback (Lezak, 1995). The tendency for schizophrenia patients to show deficient WCST performance has been known for half a century (Fey, 1951). There have been recent suggestions that these deficits may be related at least partially to working memory deficits in schizophrenia (Goldman-Rakic, 1994; Gold et al., 1997), although some findings to the contrary have also been reported (Stratta et al., 1997a).

Perlstein et al. (1998) recently reviewed the literature on the Stroop task in schizophrenia patients. In general, the studies reported that relative to controls, schizophrenia patients have slower speed and a greater number of errors on the interference task. Schizophrenics also appear to show greater than normal facilitation (increased speed) when naming the ink color from color-congruent words. Perlstein et al. suggested that error rates on single-trial versions of the task may be among the most sensitive to the selective attention deficits of schizophrenia.

Tower tasks frequently are employed to measure the planning ability aspect of executive functioning (Shallice, 1982). Several recent investigations indicated that schizophrenic patients have more difficulty on these tasks (requiring more moves) than do normal comparison subjects (Goldberg et al., 1990; Andreasen et al., 1992; Morris et al., 1995; Pantelis et al., 1997).

Among non-aphasic individuals, performance on the COWAT is thought to reflect subject's abilities to generate and utilize an efficient strategy for searching their lexicon. Thus, the COWAT is thought to exemplify the aspects of 'organized search' included in some authors definition of executive skills (e.g. Welsh et al., 1990). Recent findings reported by Joyce et al. (1996) are consistent with the notion that schizophrenics have relative difficulty with fluency tasks due to inefficient access to their semantic store.

Some authors interpret the Trail Making Test (Reitan and Wolfson, 1993), specifically Part B, as an executive task. This alternation between two sequences is thought to require executive control, specifically flexibility of thinking and greater demand for working memory. Numerous investigators have found that Schizophrenia patients have slower performance on this than do normals (Braff *et al*., 1991; Franke *et al*., 1993a).

Correlations of Executive functions with Negative and Positive symptoms:

The severity of 'positive' symptoms generally appears to have a minimal relationship to the severity of executive deficits in schizophrenia (Franke et al., 1992; Morris et al., 1995; Voruganti et al., 1997). In contrast, 'negative' symptoms may be associated more consistently with poor executive functioning. Alternatively, those patients with poor executive functioning may be more likely to show consistent negative symptoms (Lysaker et al. 1997). Several investigators (e.g. Butler et al., 1992; Capleton, 1996; Berman et al., 1997; Rossi et al., 1997; voruganti et al., 1997), have reported an association between severity of negative

symptoms and executive dysfunction as measured by the WCST, as well as the Trail Making Test and COWAT (Berman et al., 1997). Also, using a computerized version of the Tower of London task, Morris et al. (1995) found that, while the number of moves did not correlated with either positive or negative symptoms, response times tended to be longer in those with more negative symptoms. Some studies show those with paranoid subtype to have relatively better performance on the WCST (Seltzer et al., 1997), and Steindl and Boyle (1995) reported that patients with delusions had better performance on the Category Test than did those without delusions. Buchanan et al. (1994) reported that patients with 'deficit syndrome' had poorer performance on the Stroop interference task and Trail Making Part B, as well as on a visuospatial task, relative to other schizophrenia patients.

Executive functions and Neuro Imaging:

A large number of studies (e.g. Weinberger et al., 1986; Parellada et al., 1994; Steinberg et al., 1996; Volz et al., 1997) reveal a failure of schizophrenia patients to demonstrate normal increases in prefrontal activation while performing the WCST. Similar results have been observed in the anterior cingulate gyrus for the Stroop task (Carter et al., 1997) and in the mesial frontal region for the Tower of London test particularly among those patients with more negative symptoms (Andreasen et al., 1992).

Executive functions and Social Functioning:

Lysaker et al. (1995) found that better WCST performance was related to higher levels of work functioning, and this relationship appeared to be at least partially independent of differences in age, education and overall intelligence. Brekke et al. (1997) found a significant correlation between two executive measures (Stroop and COWAT) and levels of independence in living, but not with ratings of work or social functioning. Green (1996, 1998) noted that WCST performance associated consistently with global measures of community functioning and may be associated with skill acquisition in psychosocial training programs, but does not appear to be associated with social problem solving. In addition, verbal working memory has been related to acquisition of psychosocial skills in rehabilitation programs, and may also be related to social problem solving. It must be noted, however, that Green's reviews also suggested that verbal learning or memory, presumably non-executive skills, consistently were related to all three functional domains.

Executive functions and drugs:

Traditional neuroleptics, such as haloperidol, do not appear to have either an adverse or beneficial impact on most neurocognitive abilities, except for partial normalization of some aspects of attention (reviewed in Spohn and Strauss, 1989; Cassens et al., 1990). Similarly chronic administration of neuroleptics appears to have no clear effect on abstraction or problem solving (Cassens et al., 1990). There may be an adverse or beneficial impact on the more attentional aspects of

executive functioning. Verdoux et al. (1995) found improvements on the Stroop task (but not the WCST) after initiation of neuroleptic treatment. Clozapine appears to have a positive impact on verbal fluency (COWAT) (Hagger et al., 1993; Lee at al., 1994), although any effect on other executive skills is less robust. In one of the few double-blind studies, Green et al. (1997) found improvements in verbal working memory following several weeks of treatment with Risperidone as compared with haloperidol. He has also reported finding similar improvements in spatial working memory, as well as psychomotor speed, in currently unpublished studies (reviewed in Green, 1998).

Learning and Memory:

There is consistent evidence of prominent encoding and retrieval difficulties on the CVLT. The study by Paulsen et al. (1995) revealed marked retrieval deficits, severely impaired total recall and mildly impaired recognition discriminability. The discriminant analysis classified 50% of the sample into a subcortical profile memory impairment group characterized by prominent retrieval difficulties, suggesting frontostriatal dysfunction (Kramer et al., 1988, 1989; Massman et al., 1990; Buytenhuijs et al., 1994).

Executive and Working Memory impairments appear related to poor self generated organizational strategies, which can contribute to free recall deficits in Schizophrenia. Iddon et al. (1998) reached similar conclusions in their study of strategic memory processes during visuospatial sequence generation and verbal list learning tasks. The tasks were administered before, during and after training

sessions that instructed patients in organizational strategies. Control subjects performed similarly on both tasks and benefited from training. Patients did not benefit from training and were impaired on both tasks, with more severe impairments on the verbal task. Patients also made a large number of perseverative errors, suggesting difficulties in central monitoring of their own action and mental activity (Frith and Done, 1989).

Volumetric studies with MRI have described global parenchymal volume reduction and increased cerebrospinal fluid (CSF), as well as more specific frontal and temporal lobe reduction in schizophrenia (Turetsky et al., 1995). Furthermore, Gur et al. (1998) reported correlations between volume change and neuropsychological performance, specific for frontal and temporal lobe volumes in relation to memory. Smaller hippocampal volumes in first-episode and chronic patients (Velakoulis et al., 1999) and associations between volumetric reduction, particularly in the amygdale-hippocampal region, and familial risk for disease onset (Lawrie et al., 1999) have been reported. Mozley et al. (1996) divided a sample of 42 patients with schizophrenia into poor recall and preserved recall groups based on their WMS performance. Patients with more marked impairment demonstrated an increase in left-lateralized superior temporal, mid-temporal and inferior temporal metabolism, and also showed greater laterality for the inferior frontal region. This supports the notion that part of the neurobiology of schizophrenia involves not only hemispheric dysfunction but also pathological 'overactivation' (Gur, 1978). Andreasen and colleagues have used functional

imaging of memory challenge tasks to evaluate disruption in the cortical-cerebellar-thalamic circuitry (Andreasen et al., 1996, 1997; Wiser et al., 1998; Crespo-Facorro et al., 1999). This series of studies has suggested that the neurocognitive profile in schizophrenia is characterized by relative decreases in cerebral blood flow (CBF) within regions of this circuit during word recall tasks. In their study Fletcher and colleagues found that in a healthy control sample, prefrontal activation increased as the memory task became more difficult, whereas the patient group demonstrated initial increases that began to drop off with increasing task demands. Furthermore, patients failed to activate superior temporal and inferior parietal regions. Functional studies using PET have also been used to demonstrate disruption in frontal-temporal connections during a task requiring retrieval of semantic information (Jennings et al., 1998).

Information Processing and attention:

Information processing deficits are a prominent feature of schizophrenia (McGhie and Chapman, 1961; Steronko and Woods, 1978; Green, 1996; Braff, 1999). Deficits in information processing are found in acute and remitted patients with schizophrenia and their relatives, suggesting that information processing may be a phenotypic marker linked to specific information processing dysfunction (i.e. not the whole syndrome) of schizophrenia (Freedman et al., 1997). Because information processing deficits appear to be at least partial predictors of both functional and symptomatic outcome, it appears that these deficits are important and even crucial features in understanding schizophrenia.

The ‘pathway’ by which information processing abnormalities might be associated with the psychotic and deficit symptoms of schizophrenic patient has, at times, been described in terms of an inhibitory failure or an impairment in stimulus gating or filtering (McGhie and Chapman, 1961; Frith, 1979, 1993; Braff and Geyer, 1990; Bulter and Braff, 1991; Braff, 1999). Thus, if a schizophrenic patient is unable to inhibit the normally preconscious alternative meaning of words, they might be inundated with sensory stimuli with resulting thought disorder manifested by abnormal speech patterns (Frith, 1979).

Consistent associations between information processing deficits and the so-called ‘deficit’ symptoms of schizophrenia are noted in studies from Green and Walker, 1984, 1986; Nuechterlein et al., 1986; Braff, 1989; Weiner et al., 1990; Katsanis and Iacono, 1991; Igata et al., 1994; Sweeney et al., 1994; Javitt et al., 1995; Buchanan et al., 1997; Cadenhead et al., 1997; Freedman et al., 1998.

The neural substrates of at least some information processing deficits in patients with schizophrenia have been identified via neuroimaging studies that reveal a significant association between thought disorder and hallucinations and reduced total thalamic volume (Portas et al., 1998). These data also add support to the idea that the thalamus plays a central role in normal sensory gating (Jones, 1985, 1997) and the integration of cortical processing and behavior (Sherman and Koch, 1986; Crosson and Hughes, 1987; Livingstone and Hubel, 1987; Alexander et al., 1990; Swerdlow et al., 1992; Van Essen et al., 1992; Cadehead et al., 1998)

and that these functions may be impaired specifically due to thalamic abnormalities in schizophrenia.

Remitted schizophrenic patients have been shown to have information processing deficits when assessed using VBM (Miler et al., 1979; Saccuzzo and Braff, 1986), CPT (Nuechterlein et al., 1986) and other measures including visual-evoked potential and P300 event-related potential (ERP) paradigms (Rao et al., 1995; Matsuoka et al., 1996).The findings of information processing deficits in clinically unaffected relatives of schizophrenic patients (Cadenhead et al., in press; Cornblatt and Erlenmeyer-Kimling, 1985; Waldo et al., 1991; Green et al., 1997; Young et al., 1998) suggests that these measures are trait related and ultimately can provide intermediate phenotypes for genetic linkage analyses (Freedman et al., 1997), increasing the probability of finding candidate genes for specific deficits (e.g. prepulse inhibition or P50 gating) that are phenotypic markers found to be defective in schizophrenia.

Green (1996) identified secondary verbal memory and vigilance as strong predictors of functional outcome (community outcome, social problem solving and social skill acquisition) in at least two separate studies. Card Sorting was found to be associated with community functioning but not social skill acquisition. Brekke et al. (1997) have reported associations between better community outcome (independent living), as assessed by the Role Functioning Scale (Goodman et al., 1993), and better visuomotor (digit-symbol) and verbal processing (verbal fluency and Stroop), while better social skill acquisition (work functioning), assessed by

the Strauss and Carpenter Outcome Scale (Strauss and Carpenter, 1974), was associated with better complex visuospatial processing (block design). Cadenhead et al. (1997), Penn et al., (1996) the consistent findings of a connection between high responsivity and better social functioning suggest that increased attentional allocation to the environment may lead to an ability to respond accurately to social cues (Brekke et al., 1997). Wykes (1994) reports that patients with schizophrenia who have information processing deficits, as assessed by a reaction time test, do less well in the community (as assessed by social behavior and the ability to live in a more independent setting) at 3 year follow-up, while those without reaction time deficits showed differential improvement in community functioning. Lysaker and Bell (1995) report that the degree of cognitive impairment, not positive or negative symptoms, was associated with improvement in insight during a vocational rehabilitation program. In addition reports, Lysaker et al. (1995a, b) found that poor cognitive performance was associated with less symptomatic improvement and persistence of social skills deficits at follow-up.

Cognitive Functioning, Social adjustment and Community functioning:

Impairments in social functioning are among the hallmark characteristics of schizophrenia (DSM-IV), and these impairments, although present in other clinical disorders (e.g., bipolar disorder), are most pronounced in persons with schizophrenia(Liddle, 1987; Bellack, 1990a; Glynhn et al., 1992; Brekke et al., 1994). Deficits in social functioning are present throughout the course of the disorder. For instance, they are frequently present in patients having a first episode,

may persist despite antipsychotic treatment, and tend to remain stable in severity or even worsen in subsequent phases of the illness (Strauss and Caroenter, 1974, 1977; Tsuang, 1986; Rajkumar and Thara, 1989; Jonsson and Nyman, 1991; Perlick et al., 1992; Harrison et al., 1996). Deficits in social functioning are also present before the onset of psychosis and are evident in individuals with a biological parent who has schizophrenia, suggesting that these deficits are premorbid features of—and may be a vulnerability factor for—schizophrenia. In addition to being implicated in the development of schizophrenia, impairments of social functioning contribute to the rate of relapse (Langfeldt, 1937; Zigler and Glick, 1986; Stephens et al., 1966, 1997; MacEwan and Athawe, 1997). Therefore, it appears that impairments in social functioning represent a core behavioral feature of schizophrenia. These findings not only underscore the importance of social dysfunction in the course of schizophrenia but also suggest that any interventions, psychosocial or pharmacological, that can affect social functioning may have crucial implications for long-term outcome. The role of cognitive impairment as a predictor of social functioning and outcome in schizophrenia has been well established. Cognitive impairment is associated with social perception, social skill, social functioning, the course of illness and response to psychosocial treatment. However, cognitive functioning is also correlated with the severity of negative symptoms, which is associated independently with social skill and social functioning. Cognitive functioning limits (or precludes) the ability to benefit from psychosocial rehabilitation has important implications for the development,

evaluation and modification of interventions designed to improve social functioning in schizophrenia.

Extensive research has documented that patients with schizophrenia demonstrate impairments in their social perception skills, including their ability to perceive accurately the facial expressions of others (Morrison et al., 1988; Gaebel and Wolwer, 1992; Mueser et al., 1997a), to extract relevant social cues (Corrigan et al., 1992), to process contextual factors adequately (Servan-Schreiber et al., 1996) and to identify problems in interpersonal situations (e.g. Donahoe et al., 1990; Bellack et al., 1994). Impairment in cognitive functioning is a core feature of schizophrenia which may limit the ability of patients to identify suitable response options in interpersonal situations (e.g. Bellack et al., 1994). Research provides strong support for the association between cognitive impairment and deficits in both social perception and social skill. The ability to perceive intentions in indirect speech is correlated with IQ in patients with schizophrenia, but not normal controls (Corcoran et al., 1995). Social cue recognition has been found to be correlated with verbal memory and vigilance (Corrigan et al., 1992, 1994a). Deficits in emotion recognition are correlated with generalized perceptual (or neurocogntive) deficits in schizophrenia in numerous studies (e.g. Novic et al., 1984; Feinber et al., 1986; Archer and Hay, 1992; Kerr and Neale, 1993; Mueser et al., 1996; Salem et al., 1996).Penn et al. (1997) suggest that patients with schizophrenia demonstrate a unique impairment in cognitive operations performed on social stimuli (i.e. social cognition), as compared with other stimuli. Social

skills are related to cognitive functioning as established by Mueser et al., 1991, 1995; Brenner et al., 1992; Bellack et al., 1994; Bowen et al., 1994; Corrigan and Toomey, 1995; Lysaker et al., 1995; Penn et al., 1995a; Ikebuchi et al., 1996.The implication of these models is that social functioning is expected to be correlated with cognitive impairment, as supported by extensive research (Spaulding, 1978; Allen, 1990; Breier et al., 1991; Jaeger and Douglas, 1992; Disckerson et al., 1996; Penn et al., 1996; Bartels et al., 1997; Brekke et al., 1997; Spaulding et al., 1997).

Jaeger and Douglas (1992) reported that performance on the Wisconsin Card Sorting Task (WCST) predicted social functioning 18 months later. Cognitive or neurocognitive impairment, measured in various ways, including disorganization on psychiatric rating scales, IQ, performance on the WCST and early information processing measures, is predictive of later vocational outcomes in schizophrenia, including work and work performance (Solinski et al., 1992; Bryson et al., 1998; Nuechterlein et al., 1998; Mueser et al). A simple response processing measure (reaction time) was a robust predictor of poorer functioning in less restrictive environments, lower capacity for independent living and need for higher levels of supervision.

Factor analysis of the SANS suggests that negative symptoms can be divided into three correlated dimensions, including apathy-anhedonia, blunting and alogia-inattention (Sayers et al., 1996). Furthermore, when considered together, only the apathy-anhedonia dimension was related to premorbid functioning, concurrent social functioning and future relapse in a dosage reduction study (Sayers et al.,

1996). Thus, negative symptoms are not a unitary dimension of psychopathology; some dimensions overlap more clearly with cognitive functioning than others, and differential associations may be present between dimensions of negative symptoms and other domain of functioning. Negative symptoms tend to be correlated moderately with the severity of cognitive deficits as for cognitive impairment, negative symptoms are relatively stable over time (McGlashan and Fenton, 1992; Eaton et al., 1995; Husted et al., 1995), are associated with a more severe psychopathology (Robins and Guze, 1970; Keefe et al., 1987; Salokangas et al., 1989; Bailer et al., 1996) and are associated with worse premorbid functioning and a worse outcome (Pogue-Geile, 1989; Mueser et al., 1990a; Gupta et al., 1995; Larsen et al., 1996). The severity of negative symptoms is correlated with both social perception performance (Gaebel and Wolwer, 1992; Schneider et al., 1995; Mueser et al., 1996) and social skill. Negative symptoms are associated with impairment in social functioning (Glynn et al., 1992; Brekke et al., 1994; Palacios-Araus et al., 1995). Liddle (1987) found that negative symptoms were related to poor social relationships and lack of recreational activities, whereas cognitive (disorganization) symptoms were related to poor hygiene and grooming, and impersistence at work.

There is evidence to suggest that social interaction may depend more upon fundamental attentional processes, such as the capacity to orient and reorient to changing stimuli, whereas success in employment and independent living may rely more on the mastery of instrumental tasks requiring neurocognitive skills. The

neurocognitive deficits, but not negative symptoms, are related to the acquisition of social skills in social skills training program. Learning social behavior is more dependent upon intact cognitive processing abilities than the absence of negative symptoms, cognitive impairment would appear to be a determinant of social functioning in patients participating in skills training programs.

Two studies examined the associations between cognitive functioning and social skills following exposure to social skills training (Bowen et al., 1994; Corrigan et al., 1994b), with both studies reporting that vigilance and verbal memory correlated with post-training levels of social skill. These studies are consistent with the hypothesis that cognitive factors are related to social skills acquisition. Mueser et al. (1991) reported that memory (especially verbal memory) predicted both the acquisition of social skills in 30 acute inpatients with schizophrenia or schizoaffective disorder over a 2 week training period and the retention of skills 1 month later. Kern et al. (1992), in a study of social skills training with 17 in-patients with chronic schizophrenia over 8 months, found that vigilance predicted skill acquisition. Auditory attention and verbal memory skills were most predictive of learning new social skills. (Wallace, 1997, Silverstein et al., 1998). Findings indicated that responsiveness to social skills training procedures was predicted by pretreatment verbal memory, verbal fluency and inferential reasoning ability.

The Social and Community functional outcome measures fit into three general categories; (i) success on psychosocial rehabilitation programs; (ii) studies

of laboratory assessment of instrumental skills and social problem-solving ability; and (iii) studies that have considered broader aspects of behavior in community outcome and activities of daily living. Secondary verbal memory was a strong predictor / correlate of all three of the functional outcome domains. Immediate / working verbal memory was associated reliably with skill acquisition. Vigilance was related reliably to both social skill acquisition and social problem solving, and card sorting was related consistently to community outcome. Across all studies published to date, the most consistent predictors and correlates of skill acquisition in rehabilitation programs include secondary verbal memory, immediate / working memory, vigilance and psychomotor speed. This pattern suggests that memory and vigilance are needed for success in skill acquisition programs, and the findings have good face validity. Because rehabilitation programs are similar in format to interactive classes, it makes sense that recall and vigilance would be needed to keep track of the session and to encode new material. Secondary verbal memory and vigilance have both been shown to be highly consistent correlates of laboratory assessments of social problem solving and performance of instrumental skills. The study by Harvey et al. (1998) is notable in that it included three separate groups of elderly patients who differed substantially in their level of adaptive functioning. One group was from a nursing home and had low levels of adaptive functioning. Another group of elderly acute patients had relatively high adaptive functioning, and a group of chronic hospitalized patients was intermediate. The key point is that differences in overall level of adaptive functioning did not affect the patterns of

correlations. For each group, a composite cognitive measure correlated most strongly with adaptive functioning, explaining in the neighborhood of 40-50% of the variance. Negative symptoms correlated slightly less than cognition, and positive symptoms correlated almost not at all.

Penn et al. (1996) reported relationships between affect recognition and adaptive unit behavior, and, not surprisingly, these relationships were stronger than those between basis neurocognition and adaptive unit behavior. Affect perception is the ability to accurately perceive, interpret and process emotional expression in others. The majority have reported that schizophrenia patients are less accurate than normals in their ability to recognize facial and vocal emotion (Turner, 1964; Walker et al., 1984; Feinberg et al., 1986; Borod et al., 1993; Bellack et al., 1996). Perception of affect can be considered a complex social cognitive ability, which relies on the integrity of a select set of more basic neurocognitive processes (Schneider et al., 1995; Bryson et al., 1997; Addington and Addington, 1998). Performance on the measure of early visual processing (The Span of Apprehension) strongly correlated with performance on all affect perception tasks, regardless of the modality of the stimulus presentation. Mueser et al. (1996) found that perception of affect was related to social adjustment on the ward, such as social mixing, personal appearance and hygiene, in a sample of 28 long term schizophrenia in-patients. The most consistent relationships have included the neurocognitive domains of secondary memory, immediate / working memory, vigilance and card sorting as predictors of functional outcome.

Cognitive Functioning and Negative Symptoms:

The 19th century British neurologist Hughlings Jackson was one of the first to use the terms negative and positive symptoms in psychiatry. Crow in the UK, who postulated that there were two syndromes in schizophrenia (1980, 1985), developed this hypothesis more fully. He called these two syndromes type 1 and type 2 schizophrenia. Patients with type 1 had predominantly positive symptoms that were considered to be responsive to neuroleptics, with good premorbid functioning, an acute onset, a better long-term course and outcome, and cognitive deterioration. Type 2 was characterized by mainly negative symptoms that were drug resistant, with poorer premorbid functioning, an insidious onset, a poorer long-term course and outcome, and cognitive deterioration. Crow believed that type 1 reflected reversible hyperdopaminergic activity in a structurally normal brain, and type 2 irreversible neuronal loss in a structurally abnormal brain (1980, 1985). Nancy Andreasen and her colleagues at the University of Iowa were responsible for much of the impetus for empirical work in the area of positive and negative symptoms of schizophrenia (Andreasen, 1982; Andreasen and Olsen, 1982; Andreasen et al., 1986, 1995). Andreasen and Crow reported that those individuals with schizophrenia who had predominantly negative symptoms evidenced more cognitive impairment than those patients with predominantly positive symptoms. Breier and his colleagues (Breier et al., 1990) reported a significant relationship between performance on the Wisconsin Card Sorting Test (WCST) and negative symptoms, as well as a significant association between

verbal fluency and negative symptoms. Liddle (1987a) suggested three factors: the psychomotor poverty syndrome, which is essentially negative symptoms; the disorganization syndrome; and the reality distortion syndrome. Liddle (1987b) reported that the psychomotor poverty syndrome, which best reflected negative symptoms, was associated with impaired abstract thinking and long-term memory. Carpenter and his colleagues (1988) distinguished between two types of negative symptoms, primary and secondary, on the basis of their causative mechanism. Primary negative symptoms are considered to be deficit symptoms. It was proposed that they are a purer form of negative symptoms and are the core enduring feature of the illness. They do require longitudinal observation. Secondary symptoms are considered to be temporary and associated with other factors that are not inherent to schizophrenia, for example depression or side effects from medications. The deficit – non-deficit distinction is stable over time and has long-term predictive validity (Fenton and McGlashan, 1992). There is evidence from several other studies that deficit patients have poorer premorbid adjustment, more neurological signs and more difficulties with eye tracking than non-deficit patients (Buchanan et al., 1990, 1994). Support for the involvement of the frontal and parietal lobes (Tamminga et al., 1992) between negative symptoms and decreased glucose utilization or decreased regional cerebral blood flow (rCBF) in the frontal lobes, and between negative symptoms and decreased rCBF in the inferior parietal cortex. Buchanan et al. hypothesized: “the involvement of the dorsolateral prefrontal circuit in the production of deficit symptoms as it is

composed of the brain regions, e.g. the dorsolateral prefrontal and inferior parietal cortices and the thalamus, implicated in the pathophysiological features of the deficit syndrome". (Buchanan et al., 1994, p. 806).

Deficit patients performed significantly less well on two of the four frontal measures (Stroop and Trail making test but not WCST or verbal fluency). Deficit patients performed less well on one of the three visuospatial measures of parietal functioning. Deficit patients did have lower WAIS-R general ability scores.

Recently Buchanan and his colleagues (Buchanan et al., 1997) reported that deficit symptom patients performed less well on the Continuous Performance Test (CPT) and Span of Apprehension task (SPAN) than non-deficit patients and normal controls. Longitudinal studies (Addington et al., 1991) indicate that Negative symptoms were related to poor performance on verbal reasoning and verbal fluency at both assessment periods. Significant associations of poor cognitive functioning and positive symptoms that were observed in the acute phase were no longer significant during the period of remission after a significant improvement in positive symptoms had occurred. Brekke et al. (1995) assessed 40 out-patients using the BPRS as a measure of negative symptoms. At the initial assessment, negative symptoms were associated with poor performance on the Stroop. At the 6 month follow-up assessment, negative symptoms correlated again with Stroop but also with digit-symbol, a measure of visuomotor processing. These results support the persistence of the connection between negative symptoms and poor cognitive functioning. (Addington et al., 1997).Two of the primary measures

of visual attention that have been considered to be vulnerability indicators are the CPT (Nuechterlein, 1991; Cornblatt and Kelip, 1994;) and the forced-choice SPAN (Asarnow et al., 1991). Consistent results have been found more with the CPT than with the SPAN (Harvey et al., 1985). Furthermore, it has been suggested that deficits on the CPT and SPAN may be negative symptom-linked vulnerability indicators. Deficits on the CPT and the SPAN have been reported to be associated with negative but not positive symptoms (Nuechterlein et al., 1986; Asarnow et al., 1991; Strauss et al., 1993). In both multi-episode and first-episode samples, deficits on the CPT and SPAN have been found to remain stable over time despite an improvement in symptoms (Asarnow and MacCrimmon, 1982; Nuechterlein et al., 1986, 1992; Cornblatt et al., 1989b; Winters et al., 1991).

These results supported the conclusion that the deficit in attention was not simply linked to negative symptoms that were present concurrently, which would be expected if attention deficits were secondary to clinical symptomatology (Nuechterlein et al., 1986).One possible explanation suggested by Harvey is that cognitive impairment is an autonomous feature of the symptomatology of schizophrenia but it does overlap with negative symptoms (Harvey et al., 1996). These authors published a 1 year follow-up with 174 elderly chronic patients (average age of 75 years) (Harvey et al., 1996). In this study, negative symptoms and cognitive functioning were stable over time. Cognitive impairment was more stable than negative symptoms. There was a consistent finding, however, of a concurrent correlation between the composite measure of cognitive functioning

and negative symptoms. These authors conclude that cognitive functioning and negative symptoms are actually discernible but related constructs.

In summary, there are replicated results of associations between negative symptoms and information processing tasks such as backward masking, the CPT and the SPAN. Associations of negative symptoms with verbal ability, verbal and visual memory, visuospatial and motor tasks have also been replicated, as has performance on the WCST and other measures of frontal lobe functioning. McGlashan and Fenton (1992) outlined three negative symptom phases that may be separate or that may represent qualitatively different underlying processes at work. The first phase is associated with compromised premorbid functioning and suggests a link between negative symptoms and the vulnerability to schizophrenia. This may be genetic in origin. The second negative symptom process is associated with the acute and / or florid states of schizophrenia. At this time, similarly to positive symptoms, negative symptoms are relatively unstable and may vary with treatments and environmental stress. The third negative symptom process is associated with the longer term more chronic phase of the illness. In this stage, negative symptoms are more prominent, persistent, resistant to intervention and can be functionally disabling.

I Episode and Chronic Schizophrenia:

The possibility that first-episode schizophrenia has a different profile of executive functioning compared with the chronic state has been raised by Joyce *et al*(2002). They found that patients with first-episode psychosis were quicker to initiate responses than were controls, but took the same time to complete each task. In contrast, people with chronic schizophrenia have normal initial thinking times but are slower in thinking about subsequent moves than are controls (Pantelis *et al*, 1999). Joyce *et al* suggest that pre-existing pathophysiological processes in the prefrontal cortex that underlie executive impairment further deteriorate at the onset of psychosis and continue to worsen with time.

Saykin *et al*(1994) identified 37 neuroleptic-naïve patients with first-episode schizophrenia and compared them with 65 previously treated patents and 131 healthy controls. They concluded that verbal memory and learning is selectively compromised relative to other functions and that memory impairment is not secondary to anticholinergic medication. When attention and executive functioning were controlled for, deficits in verbal memory were still present. This finding suggests that deficits in verbal memory are not secondary to lack of attention or deficits in sequential executive functioning. Patients in their first episode also appear to have severe impairments in sequencing, organisational flexibility (Mohamed *et al*, 1999), planning ability and strategy use (Hutton *et al,* 1998). Findings indicating that first-episode patients perform less well on free recall than on verbal memory tests have led to the suggestion that difficulty with free recall is

possibly secondary to impaired executive functioning (Hutton *et al*, 1998). Mohamed *et al*(1999) found that aspects of executive functioning such as sequencing, organisation and flexibility were highly impaired in first-episode psychosis compared with controls. A slightly later study (Bilder *et al*, 2000) reports that executive and motor dysfunctions were relatively less impaired than memory and attention in first-episode patients.

AIMS AND OBJECTIVES

Aim:

To study the neuropsychological performance of I episode Schizophrenic patients and its clinical correlates.

Objectives:

1. To assess the NeuroPsychological performance and social functioning of Patients and controls.
2. To compare NeuroPsychological performance of patients with controls.
3. To identify the relationship between social functioning and NeuroPsychological performance.
4. To identify the relationship between psychopathology and NeuroPsychological performance.

Hypothesis:

1. Patients display poorer performance when compared to controls in Finger tapping test.
2. Patients display poorer performance when compared to controls Digit symbol substitution test.
3. Patients display poorer performance when compared to controls Digit vigilance test.
4. Patients display poorer performance when compared to controls Digit sequencing test.
5. Patients display poorer performance when compared to controls Dot test.

6. Patients display poorer performance when compared to controls Controlled oral word association test.
7. Patients display poorer performance when compared to controls Category test.
8. Patients display poorer performance when compared to controls Frontal Assessment Battery.
9. Patients display poorer performance when compared to controls Rey's Auditory Verbal Learning test.
10. Patients display poorer performance when compared to controls Color trails tests 1 and 2.
11. Patients display poorer performance when compared to controls Rey Ostrerrieth complex figure test.
12. Patients display poorer performance when compared to controls Raven's matrices.
13. Relationship between Neuropsychological performance and Educational status is significant.
14. Relationship between Neuropsychological performance and Illness duration is significant.
15. Relationship between Neuropsychological performance and Social functioning is significant.
16. Relationship between Neuropsychological performance and Negative symptoms is significant.

17. Relationship between Neuropsychological performance and Positive symptoms is significant.
18. Relationship between Neuropsychological performance and General psychopathology is significant.
19. Relationship between Neuropsychological performance and Anergia is significant.
20. Relationship between Neuropsychological performance and Thought disturbance is significant.
21. Relationship between Neuropsychological performance and Activation is significant.
22. Relationship between Neuropsychological performance and Paranoid / Belligerence is significant.
23. Relationship between Neuropsychological performance and Depression is significant.

METHODS

Setting:

The study was conducted in Government Rajaji Hospital, Madurai which is a tertiary level teaching hospital. The project protocol received approval form the ethics committee of the institution.

Study Design:

Crossectional observational case control study.

Period of Study:

6 months – Nov 2006 – April 2007

Subjects:

Cases: Consecutive patients attending out patient section of Psychiatry department fulfilling the selection criterion are included in the study.

Controls: Healthy individuals accompanying patients attending medical outpatient section of Department of Internal Medicine fulfilling the selection criterion.

Selection Criterion:

Subjects of the study are chosen based on the following criterion.

Inclusion Criterion:

1. Subjects between 18-45 years of age
2. Formal Education – 8 years

3. Fulfilling DSM IV diagnosis of schizophrenia, Acute schizophreniform disorder, schizoaffective disorder using structured clinical interview MINI plus.
4. Patients in their I episode of illness.
5. Duration of illness < 2 years
6. Patients and their first degree relatives giving consent.

Exclusion Criterion:

1. History of Psychoactive substance intake – last month
2. Fulfilling DSM IV criterion for sub abuse / dependence – last year
3. History of Psychotropic drug intake– 1 year.
4. History of ECT –last 6 months
5. History of Head injury
6. History of Neurological / General Medical Condition
7. Axis I / Axis II disorders except those mentioned in inclusion criterion.

Tools Employed:

1. MINI PLUS – Structured diagnostic clinical interview for diagnosing schizophrenia, Acute schizophreniform disorder, schizoaffective disorder based on DSM –IV criterion.
2. Socio demographic data: including, Age, Sex, Education, Duration of illness.
3. PANSS: Positive and Negative symptom rating scale to assess the psychopathology with gives scoring of positive symptoms, negative

symptoms, general psychopathology, anergia, thought disturbance, activation, paranoid, depression.

4. Social functioning index: This assesses the social functioning of patients in the domains of personal, work, family and community.
5. A battery of Neuropsychological tests which include:
    a. Finger Tapping
    b. Digit Symbol Substitution Test
    c. Digit Vigilance Test
    d. Digit Sequencing Test
    e. Dot Test
    f. Controlled Oral Word Association Test
    g. Category Fluency
    h. Frontal Assessment Battery
    i. Color Trails Test 1 & 2
    j. Rey's Auditory Verbal Learning Test
    k. Rey's Ostrerrieth Complex Figure Test
    l. Raven's Progressive Matrices

Fifty four consecutive patients fulfilling DSM IV diagnosis of schizophrenia, acute schizophreniform disorder, schizoaffective disorder by using MINIPLUS were screened for selection criterion. 34 patients were included in the study. Details of exclusion: 4 had a history of seizure disorder, 2 had a history of head injury, 8 had history of substance intake in the last month, 5 had history of

medical illness (2-diabetes, 2-renal failure, 1-IHD), 1 fulfilled criterion for schizoid personality disorder.

After getting informed consent from the patients and their first degree relatives, socio demographic data about the patient were collected. patients are then assessed using PANSS and SFI. Then the Neuropsychological tests were carried out. All the tests were administered by a single investigator and approximate duration for a single subject was between 3-3½ hrs which was done in two sessions.

Thirty healthy subjects, accompanying patients to medical outpatient department were included in the study based on the selection criterion. Subjects having family history mental illness / neurological illness were excluded from the study (4 were excluded, - 2 had family history of seizure disorder, 1 family history of mental retardation, 1 had family history of bipolar disorder). All the subjects willingly participated in the study and consent were obtained. Then socio demographic details were collected. Controls were then administered all the same neuro psychological tests. Approximate duration was around 2hrs and it was conducted in a single session.

DATA ANALYSIS AND RESULTS

Analysis of Data:

1. Socio Demographic variable between Patients and controls were analysed using chi-square test.
2. Neuropsychological test scores between Patients and controls were analysed using student t test.
3. Correlational analysis between socio-demographic, psychopathology, social functioning and Neuropsychological test were done using Pearson correlation analysis.

Results:

The present study is a case control study comparing cases defined as subjects diagnosed having schizophrenia, acute schizophreniform disorder, in their I episode of their illness with controls as healthy subjects accompanying patients to medical outpatient department.

Table1. Socio demographic data of Patients

Socio demographic details	Number(n=34)	%
Age greater than 30	17	50
Age Less than 30	17	50
Sex Men	17	50
Women	17	50
Education 8 to 12	20	58.8
Greater than 12	14	41.2

Males and females were equally distributed between 34 cases (17 males & 17 females). Similarly 50 percent of patients were above 30 years and 50 percent of the patients were 30 and below. Mean age of the sample is 29.74 ± 7.44.

B. Illness Details of Patients:

In the **Patients group** 12 had diagnosis of Acute schizophreniform disorder and 22 had diagnosis of schizophrenia. Mean duration of illness was 10.29± 7.33 months. Mean social functioning of the group 51.09 ± 3.12. Psychopathology of the group was assessed using PANSS describing positive, negative, general psychopathology, anergia, thought disturbance, activation, paranoid and depression scores.

Table -2 Illness Details

S.No	Illness Parameters	Mean	S.D
1	Social functioning index	51.09	10.64
2	Duration of illness	10.29	7.33
3	Positive	35.18	3.19
4	Negative	30.68	4.98
5	General psychopathology	74.74	10.26
6	Anergia	17.21	3.37
7	Thought disturbance	18.29	2.74
8	Paranoid	13.56	1.85
9	Depression scores	14.97	2.04

C. Comparison of Socio Demographic Data:

With respect to control population 15(50percent) were male and 15(50 percent) were female. 13 (43.3 percent) persons were above 30 years and 17 (56.67 percent) below 30 years. 19 (63.33 percent) persons had educational levels above 12 years and 11 (36.67 percent) persons were between 8-12 years.

Table 3: Socio Demographic Data of Patients and Controls

Socio demographic details	Patients (N=34)	Controls (N=30)	$\chi 2$
Sex Men Women	17 17	15 15	0.06
Age greater than 30 Age Less than 30	17 17	17 13	0.08
Education 8 to 12 Greater than 12	20 14	11 19	2.31

No significance in Chi square was observed between Patients and controls.

Comparison of Patients and controls socio demographic data with respect to chi-square test shows no significant difference between the two groups. Both groups are comparable in Age, Sex, and Educational Status.

D. Comparison of NeuroPsychological test scores of Patients

and Controls:

12 NeuroPsychological tests were administered to patients and controls yielding 17 different scores. Higher scores in finger tapping, Digit sequencing, Controlled oral word association test, Dot test, Auditory verbal learning, Rey's visual learning and Raven's indicate better performance and low scores indicate poor performance. Tests which assess time namely, Digit symbol substitution, Digit vigilance test and color trails test gives scores in seconds, in which higher the score poorer the performance.

I. Tests for Speed of Processing:

Mean score in finger tapping test is 41.06 ± 4.82 for Patients and 45.43 ± 1.99 for controls. On applying student 't' tests differences in both groups reached statistical significance to the level of 0.01. Tests which measure mental speed are digit symbol substitution and color trails 1. Mean scores of digit symbol substitution 380.88 ±142.19 and 183.4 ±21.52 for Patients and controls respectively. In color trails 1, Mean score of the Patients 109.79 ±29.37 where as for controls 48.17 ±8.64. Applying student 't' test to Patients and controls shows that performance between two groups reached statistical significance (P<0.01).

Table-4-Tests for Speed of Processing

Tests	Patients(N=34)		Controls(N=30)		t value
	Mean	Std.dev	Mean	Std.dev	
Finger tapping	41.06	4.82	45.43	1.99	4.63**
DSST	380.88	142.12	183.4	21.52	7.80**
Color trails1	109.79	27.37	48.17	8.64	12.84**

*p <0.05 ** p <0.01 DSST-Digit symbol substitution test.

II. Tests of Working Memory and Sustained Attention:

Digit sequencing and Dot tests were used for assessing verbal and visual working memory. Digit vigilance test is employed for measuring sustained attention. In digit vigilance test patients took longer time (691 ± 206.68) than controls (390.03 ± 32.06). Errors scores were also greater for Patients (11.91 ± 5.81) than controls (1.07 ± 0.72). Mean length of the digits in Digit Sequencing are for Patients (3.76 ± 0.78) whereas for controls (4.48, 0.36). Dot test reveals that patients perform poorly (2.53 ± 0.61) than controls 3.

Table-5-Working Memory and Sustained Attention

Tests	Patients(N=34)		Controls(N=30)		t value
	Mean	Std.dev	Mean	Std.dev	
DVT	691.00	206.68	390.03	32.06	7.76**
DVT-E	11.91	5.81	1.07	0.74	9.88**
Digit-seq	3.76	0.78	4.48	0.36	5.58**
DOT test	2.53	0.61	3.00	0.00	4.64**

*p<0.05 ** p<0.01

DVT-Digit vigilance test.DIG-SEQ-Digit sequencing.DOT-Dot test.

When means scores between patient and controls were compared, all the tests reach statistical significance to the level of 0.01.

III. Executive Functions and Linguistic fluency:

The tests included under executive functions are Color Trails 2(Mental Flexibility), Raven's progressive matrices (Planning and Abstraction) and Frontal assessment battery(Programming and inhibitory control). Linguistic Fluency is assessed using Controlled Oral Word Association Test and Category Fluency.

Patients on an average generated 8.04 ± 2.62 words in COWAT, 9.79 ± 2.96 words in category tests, whereas the corresponding scores for controls were 12.6 ± 1.65, 16.2 ± 1.10. Regarding color trails 2, patient took longer 223.21 ± 65.43 when compared to controls (107.57± 17.63). In Raven's matrices composite score of the 3 sets for the patients and controls (Mean 23 ±5.19, 27.97 ± 1.92) following table gives the scores of both patients and control.

Table-6 Executive Functions and Linguistic Fluency

S.No	Tests	Patient (N=34)		Control (N=30)		t value
		Mean	S.D	Mean	S.D	
1	COWAT	8.05	2.62	12.6	1.65	10.64**
2	CAT	9.79	2.96	16.2	1.10	11.34**
3	FAB	9.29	2.01	13.5	0.78	11.53**
4	Raven	23	5.19	27.97	1.92	8.10**
5	Color trails 2	223.21	65.43	107.57	17.63	10.49**

*p <0.05 **p <0.01
COWAT- Controlled oral word association test. CAT-Category fluency. FAB-Frontal assessment battery.

All the test scores show statistically significant differences between patient's performance when compared to controls (P<0.01).

IV. Tests for New Learning Ability:

Rey's word list learning and Rey Ostrerrieth complex figure tests were used for assessing verbal and visual memory total number of words recalled in 5 successive trails for patients (39.82 ± 9.4) whereas for controls (63.27± 2.1). In delayed recall the patient on an average recalled 8.56 ± 2.6 words whereas all the controls were able to recall 15 words. Scores of the complex figure tests were also given in the table below:

Table-7 New Learning Ability Verbal and Visual

Tests	Patients(N=34)		Controls(N=30)		t
	Mean	Std.dev	Mean	Std.dev	
AVL1	39.82	9.37	63.27	2.1	14.10**
AVL2	8.59	2.61	15	0	15.26**
RCF1	32.91	2.68	36.9	4.93	4.34**
RCF2	16.59	4.36	29.73	1.52	21.62**
RCF3	13.09	4.17	27.37	1.52	21.62**

*-p <0.05 **- p<0.01

AVL1&2-Rey's auditory verbal learning test immediate and delayed recall.RCF1,2&3-Rey's complex figure test copy, immediate, delay.

On applying t tests all the values were highly significant when compared to controls (P<0.01).

E. Correlation between Socio Demographic Data and Neuro Psychological Test Performance:

Neuropsychological test scores were assessed for any significant correlation between socio demographic details and social functioning index using Pearson correlation analysis.

Table 8- Socio Demographic Data Vs Speed of Processing

Tests	Age	Education	Illnes- dura	SFI
Finger Tapping	-0.17	0.10	-0.26	0.20
DSST	0.09	-0.51**	0.28	-0.48**
Color Trails1	0.10	-0.51**	0.18	-0.42*

*p <0.05 ** p <0.01 DSST-Digit symbol substitution test.

From the table it was noted that Education and Social Functioning Index correlated significantly with tests of Mental Speed (DSST and Color Trails1). No significant correlation was observed between age and illness duration.

Table 9-Socio Demographic Data VS Working Memory and Sustained Attention

Tests	Age	Education	Illnes-dura	SFI
DVT	-0.02	0.33	0.17	0.47**
DVT-E	0.16	-0.23	0.24	-0.55**
DIG-SEQ	-0.10	0.49**	-0.33	0.54
DOT	-0.03	0.42*	-0.43*	0.56**

*p<0.05 ** p<0.01

DVT-Digit vigilance test. DIG-SEQ-Digit sequencing. DOT-Dot test.

From the table it was noted that there is significant association between Education and Verbal(Dig-Seq) and Visual Working Memory(DOT Test) whereas illness duration correlated only with Visual Working Memory. Social Functioning Index has significant correlation with both the measures of sustained attention (DVT) and Visual Working Memory.

Table 10-Socio Demographic Data Vs Executive Functions and Linguistic Fluency

Tests	Age	Education	Illnes-dura	SFI
COWAT	0.16	0.53**	-0.25	0.49**
CAT	0.11	0.36*	-0.17	0.46**
FAB	-0.04	0.64**	-0.20	0.37*
CT2	0.01	-0.47**	0.22	-0.44**
RAV	-0.09	0.54**	-0.56**	0.63**

*p <0.05 **p <0.01

COWAT- Controlled oral word association test. CAT-Category fluency. FAB-Frontal assessment battery.

From the table it was noted that Education and Social Functioning Index correlated significantly with Linguistic fluency(COWAT and CAT), Frontal Assessment Battery, Mental Flexibility(Color Trails 2) and Raven's(Abstraction and Planning ability). Illness duration correlated negatively with Raven's (Abstraction and Planning).

Table 11-Socio Demographic Data VS New Learning Ability Verbal and Visual

Tests	Age	Education	Illnes-dura	SFI
AV1	-0.01	0.44**	-0.05	0.26
AV2	0.00	0.45**	-0.01	0.24
RCF1	-0.25	0.42*	-0.34**	0.38*
RCF2	-0.10	0.49**	-0.35*	0.50**
RCF3	-0.12	0.51**	-0.35*	0.58**

*-p <0.05 **- p<0.01

AVL1&2-Rey's auditory verbal learning test immediate and delayed recall.RCF1,2&3-Rey's complex figure test copy, immediate, delay.

Results indicate that Education has significant correlations with both Verbal and Visual New Learning Ability whereas Social Functioning index has significant correlations only with Visual New Learning,

F. Correlations between Psychopathology and Neuropsychological Tests:

Neuropsychological test scores were assessed for any relationship between positive, negative and general psychopathology symptoms using Pearson correlation analysis.

Table 12-Correlation of Symptoms with Speed of Processing

Tests	POSIT	NEGAT	GEN-PSY
Finger Tapping	0.37*	-0.20	0.06
DSST	-0.46**	0.46**	0.12
Color Trails1	-0.53**	0.37*	0.12

*p <0.05 ** p <0.01 DSST-Digit symbol substitution test.

Both Positive and Negative symptoms has significant correlation with tests of Mental Speed (DSST and Color Trails 1).

Table 13-Correlation of Symptoms with Working Memory and Sustained Attention

TESTS	POSIT	NEGAT	GEN-PSY
DVT	-0.54**	0.50**	0.03
DVT-E	-0.49**	0.46**	0.00
DIG-SEQ	0.34	-0.51**	-0.07
DOT	0.39*	-0.39*	-0.10

*p<0.05 ** p<0.01

DVT-Digit vigilance test. DIG-SEQ-Digit sequencing. DOT-Dot test.

Negative symptoms have strong negative correlation with both Verbal and Visual Working Memory and Positive correlation with tests of Sustained Attention. Positive symptoms also have negative correlation with tests of sustained attention.

Table 14-Correlation of Symptoms with Executive Functions and Linguistic Fluency

Tests	POSIT	NEGAT	GEN-PSY
COWAT	0.36*	-0.41*	-0.11
CAT	0.46**	-0.20	0.02
FAB	0.28	-0.41*	-0.13
CT2	-0.57**	0.36*	0.28
RAV	0.14	-0.31	-0.23

*p <0.05 **p <0.01

COWAT- Controlled oral word association test. CAT-Category fluency. FAB-Frontal assessment battery.

From the table it was noted that Positive symptoms correlated significantly Linguistic Fluency (CAT and COWAT) whereas Negative symptoms have significant correlation with Frontal Assessment Battery and Mental Flexibility (Color Trails 2).Also, Positive symptoms have significant negative correlation with Mental Flexibility.

Table 15-Correlation of Symptoms with New Learning Ability Verbal and Visual

Tests	POSIT	NEGAT	GEN-PSY
AV1	0.24	-0.33	-0.16
AV2	0.24	-0.30	-0.13
RCF1	0.26	-0.10	-0.01
RCF2	0.22	-0.08	-0.10
RCF3	0.23	-0.15	-0.12

*-p <0.05 **- p<0.01 AVL1&2-Rey's auditory verbal learning test immediate and delayed recall.RCF1,2&3-Rey's complex figure test copy, immediate, delay.

Results indicate no significant correlation exist between symptoms and new learning ability.

G. Correlations between Symptom Dimensions and Neuropsychological Tests:

Anergia Thought, Activation, Paranoid and Depression scores from PANSS were tested for correlation with neuropsychological test scores.

Table 16-Symptom Dimensions with Speed of Processing

Tests	ANERGIA	THT-DIS	ACTI	PARAN	DEPR
Finger Tapping	-0.15	0.25	0.30	0.16	0.08
DSST	0.51**	-0.19	-0.40*	-0.21	-0.23
Color Trails1	0.42*	-0.25	-0.41*	-0.21	-0.27

*p <0.05 ** p <0.01 DSST-Digit symbol substitution test.

Anergia has significant Positive correlation with Tests of Mental Speed (DSST and Color Trails1) whereas Activation has significant negative correlation with the same scores.

Table 17-Symptom Dimensions with Working Memory and Sustained Attention

Tests	ANERGIA	THT-DIS	ACTI	PARAN	DEPR
DVT	0.50**	-0.16	-0.27	-0.23	-0.27
DVT-E	0.50**	-0.21	-0.15	-0.04	-0.25
DIG-SEQ	-0.53**	0.15	0.38*	0.00	0.35*
DOT	-0.33	0.18	0.21	0.09	0.36*

*p<0.05 ** p<0.01

DVT-Digit vigilance test. DIG-SEQ-Digit sequencing. DOT-Dot test.

Results indicate that Anergia has significant Positive and Negative correlation with Sustained Attention(DVT) and Verbal Working Memory(Digit- sequencing) respectively.

Table 18-Symptom Dimensions with Executive Functions and Linguistic Fluency

Tests	ANERGIA	THT-DIS	ACTI	PARAN	DEPR
COWAT	-0.40*	027	0.21	-0.04	0.11
CAT	-0.25	0.33	0.26	0.11	0.13
FAB	-0.42*	0.28	0.23	0.00	0.09
CT2	0.39*	-0.21	-0.44**	-0.27	-0.28
RAV	-0.11	0.14	0.29	0.04	0.14

*p <0.05 **p <0.01

COWAT- Controlled oral word association test. CAT-Category fluency. FAB-Frontal assessment battery.

Results show that only Activation has significant negative correlation with Mental Flexibility.

Table 19-Symptom Dimensions with New Learning Ability Verbal and Visual

Tests	ANERGIA	THT-DIS	ACTI	PARAN	DEPR
AV1	-0.36*	0.07	0.14	0.08	0.26
AV2	-0.33	0.13	0.11	0.07	0.30
RCF1	-0.01	0.38	0.11	0.06	0.05
RCF2	-0.03	0.19	0.26	-0.03	0.13
RCF3	-0.09	0.21	0.27	-0.05	0.16

*-p <0.05 **- p<0.01

AVL1&2-Rey's auditory verbal learning test immediate and delayed recall.RCF1,2&3-Rey's complex figure test copy, immediate, delay.

Results indicate only one symptom dimension has significant Anergia has significant negative correlation with verbal learning.

DISCUSSION

Cognitive disturbances in Schizophrenia is well established and well characterized. Some researchers believe cognitive deficits to be the core feature underlying the development of Positive, Negative and Disorganization symptoms. Cognitive disturbance provide a bridge between Neuroanatomical substrate (through functional Neuroimaging) and various symptom dimensions leading to the coupling various Neuroanatomical lesions with psychopathology. On the other hand type, degree and nature of the cognitive deficit determines the Social Vocational and Community Functioning of the patients.

Literature establishing the nature and type of cognitive deficits in schizophrenia and chronic non affective psychosis are numerous. But consensus regarding the origin, course and resolution (if any) of cognitive symptoms is yet to emerge. Similarly controversies abound the state or trait nature of cognitive deficits. Characterization and enumeration of Cognitive Deficits in I Episode of Psychosis is still at its infancy. Whether cognitive deficit predates the clinical psychotic breakdown or improves with decrease in symptoms is still not clearly explained. As cognitive deficits are intimately linked to functional recovery, study of cognitive deficits in I episode psychosis is need of the hour.

This study compares the cognitive performance of I episode psychotic patients with Age, Sex, Education matched healthy controls. Cases were chosen based on the Structured Clinical Interview and rigorous and strict application of

Selection Criterion ensured the non interference of confounding factors in the assessment of cognitive function. Control populations with family history of neurologic and psychiatric diseases are also excluded from the study. Symptom rating scale (PANSS) and Social Functioning Index (SFI) are well standardized and validated.

Neuropsychological tests were chosen based on the recommendations of National Institute of Mental Health workshop on ***M***easurement ***A***nd Treatment ***R***esearch ***T***o ***I***mprove ***C***ognition ***I***n ***S***chizophrenia (MATRICS) program (In which a panel of experts agreed upon the 6 Cognitive Domains which significantly distinguish and are most sensitive to cognitive dysfunction in Schizophrenia). The domains were Speed of Processing, Vigilance, Working Memory, Executive Functions, New Learning Ability Verbal and New Learning Ability Visual. 13 Neuropsychological tests(yielding 17 individual scores) representing these cognitive domains are selected based on the applicability, feasibility to our native population. All the tests were administered to 15 people before administering them to study subjects.

Patient displayed significant differences on measures of Attention as measured by Digit Vigilance Test. Error scores in this test also reached statistical significance when compared with controls. (Similar to results by Mirskey et al, 1992, Servan-Schreiber et al, 1996, Bilder et al 2000, Joyce et al, 1999). On tests of Psychomotor Speed and Scanning Ability (DSST and Color Trails 1 & 2 respectively) patient displayed significant differences from normal controls.

(virtuski et al, Braff et al). Together scores in these three groups of tests, Sustained Attention (DVT), Psychomotor Speed (DSST), Visual Scanning, Speed Of Processing, Mental Flexibility And Set Shifting (Color Trails 1 & 2) significantly differentiates cases from controls and can be considered The Core Cognitive Deficit of Schizophrenia. Not surprisingly the scores on these three groups of tests in connection with Executive Dysfunction correlates significantly with the measures of Social Competence, Social Cue Perception And Community Role Playing as measured by SFI reaching to the conclusion that Attentional disturbance can be the cause for Social Cue Misperception and Executive dysfunction may be the basis for inappropriate response selection in social situations.

On tests of Verbal Working Memory, (measured by Digit Sequencing) patient displayed significant impairment when compared to controls. The performance between the patient and controls were indistinguishable when length of the strings <3. But increasing the number of digits clearly brings out the deficit in patient population. Patients also exhibit more vulnerability to external interference than controls. PET study (carter et al 1996) reveals that activation of right DLPFC and Posterior Parietal Cortex is less in patients on comparison with controls in a test of 2 back vs. 1 back test. Striking finding is also the significant positive correlation between Working Memory deficits and Negative score on PANSS. (Similar to carter et al 1996, Graham et al 1996, Keefe et al 1997, Mohammed et al 2001, Bilder et al 2000). Similarly Working Memory deficits are consistently correlated with poor Socio Community functioning as measured by

SFI. As both Negative symptoms and Social Functioning are correlated significantly, Working Memory deficits leading to poor community functioning and repeated failures (because of Working Memory deficit) may lead to amotivation and consequently Negative symptoms.

Performance of cases on the tests of Visual Working Memory (assessed by DOT test) displayed significant differences when compared to controls. (Keefe et al 1996, Park and Holzman 1992, Salame et al 1998, Spinder et al 1997). Visual Working Memory and Digit Vigilance tests are markers of Schizophrenic Cognitive Dysfunction when compared to controls. Tests of Visual Working Memory also has significant correlations with Community Functioning (SFI) leading to the speculation that Working Memory Deficit (Visual) may be the basis for impaired Affect Perception and Working Memory Deficit (Verbal) may be the basis for impaired Social Cue Recognition leading to failure in Social Role Playing and Community Functioning. Tests findings do not reveal an association between Visual Working Memory and Negative symptoms.

Patient scores on Controlled Oral Word Association tests, Category (fluency) Tests, Frontal Assessment Battery displayed significant differences when compared to controls. (Similar to results by Welsch et al 1990, Joyce et al 1996, Spreen and Strauss et al 1998). Performance on Color Trails 1 depends on the efficiency of Visual Scanning and Psychomotor Speed. Trails 2 require Executive Control and Flexibility of thinking in addition to the above. Performance on these tests reached statistical significance ($P<0.01$) when compared with controls.

(Similar to the findings of Braff et al, Franke et al, Bilder et al, Joyce et al). Color trails 2 and Category Fluency correlated significantly with Negative symptoms (Bulter et al, Cappleton et al, Bermar et al, Possie et al). In contrast test findings show only modest association between COWAT and Negative symptoms. More importantly many Executive measures (COWAT, CAT, Color Trials 2 and Raven's) have significant correlation with Social Functioning Index. Clearly indicating the bulk of deficit in Social Functioning is due to deficits in Working Memory (Verbal & Visual) and Executive Dysfunctions (Green et al, Mueser et al, Brekke et al, Lysaker et al).

In tests of New Learning Ability (as measured by Rey's Auditory Verbal Learning Tests) it was noted that patient lacked a proper strategy, classification and groupings to remember categorization of words when compared to controls. They tend to repeat in the same order it was presented and repeated trials has no correlation with number of words remembered. Both Immediate and Delayed Recall correlated significantly with Educational status. In symptom dimension, negative correlation was observed with Anergia. Visual Learning tests also indicates that patients give more importance to minute details ignoring the over all shape distortion. Poor response selection (in method adopted in drawing) and longer time needed to copying are also noted in patients than controls. Ultimately these reflect in poor scores when compared to controls. Significant positive correlation was noted between Visual Learning and patient's Educational status and Social Functioning index. Review by Green indicates that Verbal Working

memory and Visuospatial Perception determines success in Psychosocial Rehabilitation program.

Social Functioning Index is a composite measure including Social Competence, Social Status, Social Adjustment, Social Role Playing and Social Support. Factor Analytic studies reveal that Speed of Processing and Sustained Attention consistently determines all aspects of Social Functioning. Results show that DSST, (Mental Speed) have Negative correlation with Social Function index where as positive correlation with Digit Vigilance test (measure of Sustained Attention) is observed. Significant positive correlation is also noted between Working Memory (Verbal) and Executive Functions.

It is common for patients with schizophrenia to perform poorly on a wide range of cognitive tests, with this fact recognized for the past 50 years. Patients with more severe cognitive impairments are more likely to have more severe negative symptoms and deficits in adaptive functioning. Overall outcome is also correlated with cognitive impairments, patients with a chronic course of illness more likely to perform poorly on cognitive tests than patients with more episodic illnesses. This relationship is also present on a longitudinal, predictive basis, in that more severe cognitive impairment early in the course of illness predicts a more adverse outcome over time. Thus, cognitive functioning is an intrinsic part of schizophrenia, endogenous to the illness, and is not completely accounted for by correlates of schizophrenia or its treatment. Its measurement and characterization is first of the many steps in establishing an effective treatment

strategy for its improvement. Such a novel therapeutic procedure will have impact on socio- community functioning, vocational functioning, quality of life and long term outcome leading to change the status of schizophrenia from a lifetime sentence to treatable and conquerable diagnosis.

CONCLUSION

1. I episode psychosis (schizophrenia spectrum) displayed significant cognitive impairment in all tests when compared to controls.
2. Educational status correlated significantly with tests of Mental Speed, Working Memory, Executive Functions and New Learning Ability.
3. Social Functioning correlated significantly with tests of Mental Speed, Sustained Attention, Working Memory, Executive Functions and New Learning Visual.
4. Positive symptoms correlated significantly with Mental Speed, Sustained Attention, Verbal Working Memory and Mental Flexibility.
5. Negative symptoms correlated significantly with Mental Speed, Sustained Attention, Verbal Working Memory and Lexical Fluency.
6. Anergia correlated significantly with Mental Speed, Sustained Attention Verbal Working Memory, Lexical Fluency, Mental Flexibility and New Learning Verbal.

LIMITATIONS

1. Estimation of premorbid I.Q is difficult due to the lack of standardized test in our population.

2. Overlap of various Cognitive functions particularly Executive Functions makes the interpretation speculative.

3. Neuropsychological assessments help us understand the biological underpinnings and neuroanatomical substrates, boundaries of specific neurocognitive functions are blurred.

4. Prospective comparative studies, after clinical stabilization, remission with and without drugs will throw light on state / trait nature of cognitive disturbances.

RERFERENCES

1. Addington, J. & Addington, D. (1999) Neurocognitive and social functioning in **schizophrenia**. ***Schizophrenia*** *Bulletin*, **25**, 173–182.
2. Addington, J. and Addington, D. (1991) Positive and negative symptoms of schizophrenia: their course and relationship over time. Schizophrenia Research, 5, 51-59.
3. Allen, H. (1990) Cognitive processing and its relationship to symptoms and social functioning in schizophrenia. British Journal of Psychiatry, 156, 201-203.
4. Andreasen, N.C. and Olsen, S. (1982) Negative versue positive schizophrenia: definition and validation. Archives of General Psychiatry, 39, 789-794.
5. Andreasen, N.C., O'leary, D.S., Flaum, M., Nopoulos, P., Watkins, G.L., Boles Ponto, L.L. and Hichwa, R.D. (1997) Hypofrontality in schizophrenia: distributed dysfunctional circuits in neuroleptic-naïve patients. Lancet, 349, 1730-1734.
6. Andreasen, N.C., Paradiso, S. and O'Leary, D.S. (1998) 'Cognitive dysmetria' as an integrative theory of schizophrenia: a dysfunction in cortical-subcortical-cerebellar circuitry. Schizophrenia Bulletin, 24, 203-218.
7. Andreasen, N.C., Rezai, K., Alliger, R., Swayze. V.W., Flaum, M., Kirchner, P. et al. (1992) Hypofrontality in neuroleptic-naïve patients and in patients with chronic schizophrenia assessment with Xenon 133 single-photon emission computed tomography and the Tower of London. Archives of General Psychiatry, 49, 943-958.
8. Archer, J. and Hay, D.C. (1992) Face processing in psychiatric conditions. British Journal of Clinical Psychology, 31, 45-61.
9. Arnold, S.E., Franz, B.R., Gur, R.C., Gur, R.E., Shapiro, R.M., Moberg, P.J. and Trojanowski, J.Q. (1995) Smaller neuron size in schizophrenia in hippocampal subfields that mediate cortical-hippocampal interactions. American Journal of Psychiatry, 152, 738-748.
10. Baxter, R. D. & Liddle, P. F. (1998) Neuropsychological deficits associated with schizophrenic syndromes. ***Schizophrenia*** *Research*, **30**, 239–249.
11. Bellack, A.S., Sayers, M., Mueser, K.T. and Bennett, M. (1994) An evaluation of social problem solving in schizophrenia. Journal of Abnormal Psychology, 103, 371-378.
12. Berman, I., Viegner, B., Merson, A., Allan, E., pappas, D. and Green, A.I. (1997) Differential relationships between positive and negative symptoms and neuropsychological deficits in schizophrenia. Schizophrenia Research, 25, 1-10.

13. Bilder, R.M., Mukherjees, Rider, R.O. and Pandurangi, A.K. (1985) Symptomatic and neuropsychological component of defect states. Schizophrenia Bulletin, 11, 409-419.
14. Blanchard, J. J. & Neale, J. M. (1994) The neuropsychological signature of **schizophrenia**: generalized or differential deficit? *American Journal of Psychiatry*, **151**, 40–48.
15. Borod, J.C., Martin, C.C., Alpert, M., Brozgold, A. and Welkowitz, J. (1993) Perception of facial emotion in schizophrenic and right brain-damaged patients. Journal of Nervous and Mental Disease, 181, 494-502.
16. Braff, D.L. (1989) Sensory input deficits and negative symptoms in schizophrenic patients. American Journal of Psychiatry, 146, 1006-1011.
17. Braff, D.L. (1993) Information processing and attention dysfunctions in schizophrenia. Schizophrenia Bulletin, 19, 233-259.
18. Braff, D.L. and Geyer, M.A. (1990) Sensorimotor gating and schizophrenia. Human and animal model studies (see comments). Archives of General Psychiatry, 47, 181-188.
19. Breier, A. (1999) Cognitive deficit in **schizophrenia** and its neurochemical basis. *British Journal of Psychiatry*, **174** (suppl. 37), 16–18.
20. Brekke, J.S. Raine, A., Ansel, M., Lenez, T. and Bird, L. (1997) Neuropsychological and psychophysiological correlates of psychosocial functioning in schizophrenia. Schizophrenia Bulletin, 23, 19-28.
21. Buchanan, R.W., Kirkpatrick, B., Heinrichs, D.W. and Carpenter, W.T. (1990) Clinical correlates of the deficit syndrome of schizophrenia. American Journal of Psychiatry, 147, 290-294.
22. Buchanan, R.W., Strauss, M.E., Breier, A., Kirkpatrick, B. and Carpenter, W.T. (1997) Attentional impairments in deficit and nondeficit forms of schizophrenia. American Journal of Psychiatry, 154, 363-370.
23. Buchanan, R.W., Strauss, M.E., Kirkatrick, B., C., Breier, A. and Carpenter. W.T., Jr (1997) Attentional impairments in deficit and nondeficit forms of schizophrenia. American Journal of Psychiatry, 154, 363-370.
24. Buchanan, R.W., Strauss, M.E., Kirkatrick, B., Holstein, C., Breier, A. and Carpenter. W.T., Jr (1994) Neuropsychological impairments in deficit vs nondeficit forms of schizophrenia. Archives of General Psychiatry, 51, 804-811.
25. Buchanan, R.W., Strauss, M.E., Kirkpatrick, B., Holstein, C., Breier, A. and Carpenter, W.T., Jr (1994) Neuropsychological impairments in deficit vs non-deficit forms of schizophrenia. Archives of General Psychiatry, 51, 804-811.

26. Buchsbaum, M. S. (1990) Frontal lobes, basal ganglia, temporal lobes – three sites for **schizophrenia**? ***Schizophrenia*** *Bulletin*, **16**, 377–378.
27. Cadenhead, K., Geyer, M. and Braff, D. (1993) Impaired startle prepulse inhibition and habituation in schizotypal personality disordered patients. American Journal of Psychiatry, 150, 1862-1867.
28. Carter, C., Robertson, L., Nordahl, T., Chaderjian, M., Kraft, L. and O'Shora-Celaya, L. (1996) Spatial working memory deficits and their relationship to negative symptoms in unmedicated schizophrenia patients. Biological Psychiatry, 40, 930-932.
29. Carter, C.S., Mintun, M., Nichols, T. and Cohen, J.D. (1997) Anterior cingulated gyrus dysfunction and selective attention deficits in schizophrenia: [^{15}O]H_2O PET study during single-trial Stroop task performance. American Journal of Psychiatry, 154, 1670-1675.
30. Carter, C.S., Perlstein, E., Ganguli, R., Brar, J., Mintun, M. and Cohen, J.D. (1998) Functional hypofrontality and working memory dysfunction in schizophrenia. American Journal of Psychiatry, 155, 1285-1287.
31. Castellon, S.A., Asarnow, R.F., Goldstein, M.J. and Marder, S.R. (1994) Persisting negative symptoms and information-processing deficits in schizophrenia. Archives of General Psychiatry, 50, 825-831.
32. Corrigan, P.W. and Toomey, R. (1995) Interpersonal problem-solving and information processing in schizophrenia. Schizophrenia Bulletin, 21, 395-403.
33. Corrigan, P.W. and Toomey, R. (1995) Interpersonal problem-solving and information processing in schizophrenia. Schizophrenia Bulletin, 21m 395-403.
34. Corrigan, P.W., Green, M.F. and Toomey, R. (1994a) Cognitive correlates to social cue perception in schizophrenia. Psychiatry Research, 53, 141-151.
35. Corrigan, P.W., Wallace, C.J. and Green, M.F. (1992) Deficits in social schemata in schizophrenia. Schizophrenia Research, 8, 129-135.
36. Crespo-Facorro, B., Paradiso, S., Andreasen, N.C., O'Leary, D.S., Watkins, L., Boles Pinto, L.L. and Hichwa, R.D. (1999) Recalling word lists reveals 'cognitive dysmetria' in schizophrenia: a positron emission tomography study. American Journal of Psychiatry 156, 386-392.
37. Crosson, B. and Hughes, C.W. (1987) Role of the thalamus in language: is it related to schizophrenic thought disorder? Schizophrenia Bulletin, 13, 605-621.
38. Cummings, J.L. (1993) Frontal-subcortical circuits and human behavior. Archives of Neurology, 50, 1380-1382.

39. Dickerson, F., Boronow, J.J., Tringel, N. and Parente, F. (1996) Neurocognitive deficits and social functioning in outpatients with schizophrenia. Schizophrenia Research, 21, 75-83.
40. Dworkin, R.H. (1990) Patterns of sex differences in negative symptoms and social functioning consistent with separate dimensions of schizophrenic psychopathology. American Journal of Psychiatry, 147, 347-349.
41. Feinberg, T.E., Rifkin, A., Schaffer, C. and Walker, E. (1986) Facial discrimination and emotional recognition in schizophrenia and affective disorders. Archives of General Psychiatry, 43, 276-279.
42. Fenton, W.S. and McGlashan, T.H. (1992) Testing systems for assessment of negative symptoms in schizophrenia. Archives of General Psychiatry, 49, 179-184.
43. Fletcher, P.C., McKenna, P.J., Frith, C.D., Grasby, P.M., Friston, K.J. and Dolan, R.J. (1998) Brain activations in schizophrenia during a graded memory task studied with functional neuroimaging. Archives of General Psychiatry, 55, 1001-1008.
44. Gold, J.M., Carpenter, C., Randolph, C., Goldberg, T.E., and Weinberger, D.R., (1997) Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. Archives of General Psychiatry, 54, 159-165.
45. Goldberg TE, Ragland DR, Gold J, Bigelow LB, Torrey EF, Weinberger DR: Neuropsychological assessment of monozygotic twins discordant for schizophrenia. Arch Gen Psychiatry 1990; 147:1066–1072.
46. Goldberg, T. E., Greenberg, R. D., Griffin, S. J., *et al* (1993) The effect of clozapine on **cognition** and psychiatric symptoms in patients with **schizophrenia**. *British Journal of Psychiatry*, **162**, 43–48.
47. Goldberg, T.E., Greenberg, R.D., Griffin, S.J., Gold, J.M., Kleinman, J.E., Pickar, D., Schulz, S.C. and Weinberger, D.R. (1993) The effects of clozapine on cognition and psychiatric symptoms in patients with schizophrenia. British Journal of Psychiatry, 162, 43-48.
48. Goldberg, T.E., Karson, C.N., Leleszi, J.P. and Weinberger, D.R. (1988a) Intellectual impairment in adolescent psychosis: a controlled psychometric study. Schizophrenia Research, 1, 261-266.
49. Goldman-Rakic PS: Working memory dysfunction in schizophrenia. J Neuropsychiatry Clin Neurosci 1994; 6:348–357
50. Goldman-Rakic, P.S. (1994) Working memory dysfunction in schizophrenia. Journal of Neuropsychiatry, 6, 348-357.

51. Goldstein, G. and Shemansky, W.J. (1995) Influences on cognitive heterogeneity in schizophrenia. Schizophrenia Research, 18, 59-69.
52. Green, M. F. (1996) What are the functional consequences of neurocognitive deficits in **schizophrenia**? *American Journal of Psychiatry*, **153**, 321–330.
53. Green, M. F., Marshall, B. D., Jr., Wirshing, W. C., *et al* (1997) Does risperidone improve verbal working memory in treatment-resistant **schizophrenia**? *American Journal of Psychiatry*, **154**, 799–804.
54. Green, M.F. (1996) What are the functional consequences of neurocognitive deficits in schizophrenia? American Journal of Psychiatry, 153, 321-330.
55. Green, M.F., Marshall, B.D., Wrishing, W.C., Ames, D., Marder, S.R., McGurk, S. Kern, R.S. and Mintz, J. (1997) Does risperidone improve verbal working memory in treatment-resistant schizophrenia? American Journal of Psychiatry, 154, 799-804.
56. Green, M.F., Nuechterlein, K.H. and Breitmeyer, B. (1997) Backward masking performance in unaffected siblings of schizophrenia patients: evidence for a vulnerability indicator. Archives of General Psychiatry, 54, 465-472.
57. Green, M.F., SAatz, P., Ganzell, S. and Vaclav, J.F. (1992) Wisconsin Card Sorting Test performance in schizophrenia: remediation of a stubborn deficit. American Journal of Psychiatry, 149, 62-67.
58. Harvey, P.D., Howanitz, E., Parrella, M., White, L., Davidson, M., Mohs, R.C., Hoblyn, J. and Davis, K.L. (1998) Symptoms, cognitive functioning, and adaptive skills in geriatric patients with lifelong schizophrenia: a comparison across treatment sites. American Journal of Psychiatry, 155, 1080-1086.
59. Harvy, P.D., Howanitz, E., Parrella, M., White, L., Davidson, M., Mohs, R.S., Hoblyn, J. and Davis, K.L. (1998) Symptoms, cognitive functioning, and adaptive skills in geriatric patients with lifelong schizophrenia: a comparison across treatment sites. American Journal of Psychiatry, 155, 1080-1086.
60. Keefe, R.S., Silverman, J.M., Mohs, R.C., Siever, L.J., Harvey, P.D., Friedman, L. et al. (1997) Eye tracking, attention, and schizotypal symptoms in nonpsychotic relatives of patients with schizophrenia. Archives of General Psychiatry, 54, 169-176.
61. Keefe, R.S.E., Silverman, J., Mohs, R.C., Siever, L.J., Harvey, P.D., Friedman, L. et al. (1997) Eye tracking, attention, and schizotypal personality symptoms in nonpschotic relatives of patients with schizophrenia. Archives of General Psychiatry, 54, 169-177.

62. Kerr, S.L. and Neale, J.M. (1993) Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance? Journal of Abnormal Psychology, 102, 312-318.
63. Klapow, J.C., Evans, J., Patterson, T.L., Heaton, R.K., Koch, W.L. and Jeste, D.V. (1997) Direct assessment of functional status in older patients with schizophrenia. American Journal of Psychiatry, 154, 1022-1024.
64. Lee, M.A., Thompson. P.A. and Meltzer, H.Y. (1994) Effects of clozapine on cognitive function in schizophrenia. Journal of Clinical Psychiatry, 55, 82-87.
65. Liddle, P.F. (1987) schizophrenic syndromes, cognitive performance and neurological dysfunction. Psychological Medicine, 16, 49-57.
66. Liddle, P.F. (1987a) The symproms of chronic schizophrenia: a re-examination of the positive and negative dichotomy. British Journal of Psychiatry, 151, 145-151.
67. Liddle, P.F. and Morris, D.L. (1991) schizophrenia syndromes and frontal lobe performance. British Journal of Psychiatry, 158, 340-345.
68. Lysaker, P. and Bell, M. (1994) Insight and cognitive impairment in schizophrenia. Performance on repeated administrations of the Wisconsin Card Sorting Test. Journal of Nervous and Mental Disease, 182, 656-660.
69. Lysaker, P. and Bell, M. (1995) Work rehabilitation and improvements in insight in schizophrenia. Journal of Nervous and Mental Disease, 183, 103-106.
70. Lysaker, P.H., Bell, M.D. and Goulet, J.L. (1995a) The Wisconsin Card Sorting Test and work performance in schizophrenia. Schizophrenia Research, 11, 45-51.
71. Lysaker, P.H., Bell, M.D., Zito, W.S. and Bioty, S.M. (1995b) Social skills at work: Deficits and predictors of improvement in schizophrenia. Journal of Nervous and Mental Disease, 183, 688-692.
72. McEvoy, J.P., Hartman, M., Gottlieb, D., Godwin, S., Apperson, L.J. and Wilson, W. (1996) Common sense, insight, and neuropsychological test performance in schizophrenia patients. Schizophrenia Bulletin, 22, 653-641.
73. Meltzer, H.Y. and McGurk, S.R. (1999) The effects of neuroleptics, and olanzapine on cognitive function in schizophrenia. Schizophrenia Bulletin, 251, 233-255.
74. Mueser, K.T., Bellack, A.S., Douglas, M.S. and Wade, J.H. (1991) Prediction of social skill acquisition in schizophrenic and major affective disorder patients from memory and symptomatology. Psychiatry Research, 37, 281-296.

75. Mueser, K.T., Donnan, R., Penn, D.L., Blanchard, J.J., Bellack, A.S., Nishith, P. and deLeon, J. (1996) Emotion recognition and social competence in chronic schizophrenia. Journal of Abnormal Psychology, 105, 271-275.
76. Mueser, K.T., Doonan, R., Penn, D.L., Blanchard, J.J., Bellack, A.S., Nishith, P. and deLeon, J. (1996) Emotion recognition and social competence in chronic schizophrenia. Journal of Abnormal Psychology, 105, 271-275.
77. Penn, D.L., Mueser, K.T., Spaulding, W., Hope, D.A. and Reed, D. (1995a) Information processing and social competence in chronic schizophrenia. Schizophrenia Bulletin, 21, 269-281.
78. Penn, D.L., Mueser, K.T., Spaulding, W., Hope, D.A. and Reed, D. (1995) Information processing and social competence in chronic schizophrenia. Schizophrenia Bulletin, 21, 269-281.
79. Penn, D.L., Spaulding, W., Reed, D. and Sullivan, M. (1996) The relationship of social cognition to ward behavior in chronic schizophrenia. Schizophrenia Research, 20, 327-335.
80. Saykin AJ, Gur RC, Gur RE, Mozley LH, Resnick SM, Kester DB, Statiniak P: Neuropsychological function in schizophrenia: selective impairment in memory and learning. Arch Gen Psychiatry 1991; 48:141–162.
81. Saykin, A.J., Shtasel, D.L., Gur, R.E., Kester, D.B., Mozley, L.H., Stafiniak, P. and Gur, R.C. (1994) Neuropsychological deficits in neuroleptic naïve patients with first-episode schizophrenia. Archives of General Psychiatry, 51, 124-131.
82. Schneider, F., Gur, R.C., Gur, R.E. and Shtasel, D.L. (1995) Emotional processing in schizophrenia: neurobehavioral probes in relation to psychopathology. Schizophrenia Research, 17, 67-75.
83. Strandburg, R.J., Marsh, J.T., Brown, W.S., Asarnow, R.F. and Guthrie, D. (1994) Information-processing deficits across childhood and adult onset schizophrenia. Schizophrenia Bulletin, 20, 685-695.
84. Strauss, M.E. (1993) Relations of symptoms to cognitive deficits in schizophrenia. Schizophrenia Bulletin, 19, 215-231.
85. Suddath RL, Christison GW, Torrey EF, Weinberger DR: Cerebral anatomical abnormalities in monozygotic twins discordant for schizophrenia. N Engl J Med 1990; 322:789–794.
86. Taylor, M.A. and Abrams, R. (1984) Cognitive impairment in schizophrenia. American Journal of Psychiatry, 141, 196-201.

87. Walker, E. (1981) Attention and neuromotor functions of schizophrenic, schizoaffectives and patients with other affective disorders. Archives of General Psychiatry, 38, 1355-1358.
88. Weinberger DR, Berman KF, Zec RF: Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia, I: regional cerebral blood flow evidence. Arch Gen Psychiatry 1986; 43:114– 124.

APPENDIX

1**. DIGIT SYMBOL SUBSTITUTION TEST**:

The digit symbol substitution test [weschler, 1981]is test of visuomotor coordination ,motor persistence ,sustained attention and response speed, Rapid information processing is required in order to substitute the symbols accurately and quickly. The test consists of a sheet in which numbers 1-9 are randomly arranged in 4 rows of 25 squares each. The subject substitutes each number with a symbol using a number symbol key given on a top on a page.

2. **COLOR TRAILS TEST:**

The color test Trails test [D Elia,Satz , Uchiyama &White ,1996] was developed by the W.H.O as part of a multi center study on HIV infection. The test is an analogue of the trial making test is considered to be free from the influence of language .It has two parts. Part 1 requires sustained attention, perceptual tracking and simple sequencing, while part 2 requires mental flexibility in addition to the above. The test is considered as a measure of focused attention because in both parts of the test, the subject has no ignore irrelevant

numbers while scanning for the number which is the next in sequence, In each part a practice form precedes the test.

3**. DIGIT VIGILANCE TEST**:

The digit vigilance test [Lezak ,1995]consist of numbers 1-9 randomly ordered and placed in rows on a page. There are 30 digits per row and 50 rows on the sheet. The digits are closely

packed on the sheet. The same level of mental effort or attention deployment is required over a period of time, The subject has to focus on the target digits i,e 6and 9 amongst other distracter digits. Inability to sustain and focus attention leads to both increased time to complete the test as well as errors.

Score- there are two scores:

1. The time taken to complete the test.

2. Error score-sum total of the number of omissions i.e. the number of 6and 9 which have not been crossed and commissions i,e the number of digits other than the target digits which have been cancelled.

4. **CONTROLLED ORAL WORD ASSOCIATION TEST**:

The controlled Oral word Association test [Benton &Hamsher, 1989] is a measure of phonemic fluency. The subject generates words based on the phonetic similarity of words. The subject generates words beginning with the letters F, A, S. Proper nouns and names of numbers should be excluded. The same word should not be repeated with a different suffix. In our adaptation, the subjects who do not know the English language are asked to generate words in their mother tongue, commencing with the consonants 'KA' PA''. MA''

Score: The total number of acceptable new words produced in one minute is noted down for each trial. The average new words generated over 3 trials forms the score.

5. **CATEGORY FLUENCY:**

Category fluency is another form of fluency. In category fluency, unlike in phonemic fluency, it is the content of the words, rather than the phonetic similarity of the words, that is regulated. In a test, which measures category fluency, the subject generates words, which belong to a particular semantic category. The Animal names test [Lezak, 1995] requires the generate names of animals for the one minute.

Score: The total number of new words generated forms the score.

6**. REY'S AUDITORY VERBAL LEARNING TEST:**

The Rey's Auditory Verbal Leaning Test (AVLT) [Schmidt, 1996] adapted different cultures by WHO [Maj et al, 1994] was adopted to suit conditions in India. Rey originally developed the test in 1964. It consists of words designating familiar objects like vehicles, tools, animals and body parts. There are two lists A and B, with 15 different words in each list. The words were translated into the Indian language of Tamil. Words in List A are presented at rate of one word per second during 5 successive trials. The words are presented in the same order in every trial. Each trial consists of the presentation of all 15 words, immediately followed by recall of the same. In each trial, after the presentation the subject is asked to recall the words but no cues are given. 30 minutes later recall of the words presented was scored.

7**. DIGIT SEQUENCING TASK:**

Patients are presented with clusters of numbers of increasing length. They are asked to tell the experimenter the numbers in order, from lowest to highest. The trials are of increasing difficulty. The outcome measure is the total number of correct items.

8. **DOT TEST:**

'Dot test' [Keefe et al,. 1995,1997],For the no –delay trials of this task ,subjects were presented with a solid black dot.0.5cm in diameter ,on a piece of standard white paper. Simultaneously, they were given an entirely blank sheet of paper and were instructed to copy the dot on the blank paper in the location as the dot they saw on the stimulus page. No delay performance for each trial was calculated by measuring the distance between the actual dot and the subject's mark. For the delayed recall trials, the procedure described above was repeated with the following the 5s presentation of the dot, subjects were presented with a list of words to read aloud in order inhibit verbal meditation of stimulus location memory during the delay period; after delay period subjects were asked to make a mark where they remembered the dot to have been. Over two separate studies, delay periods of 10,20 and 30s were used.

9. **REY COMPLEX FIGURE TEST:**

The visuo constructive ability was tested using the Rey ‘s complex Figure test [Meyers&Meyers,1995]. Rey developed the test in 1941.The test consists of a complex design which is abstract in nature and cannot be named easily. .It has an overall structure and multiple subcomponents within it.

Procedure ;- An 8.5 inch by 11 inch card containing the complex figure is placed in front of the subject. A paper of same size of the complex figure card is placed in front of the subjects. The patient has to copy the figure the paper. The patient is not allowed to use rulers to use rulers to draw lines, but rather has to draw to freehand. An eraser may be used.

10. **VISUAL MEMORY:**

Procedure: The complex figure is recalled by drawing it from memory. The subject is asked to recall figure twice; the first time is an immediate recall three minutes after the copying is completed, and the second time is a delayed recall 30 minutes later. For the intervening three minutes, after the patient finishes copying the design and before the immediate recall, another task such as one measuring verbal fluency may be given to the subject or the examiner may engage the subject in a brief clinical interview. After the lapse of three minutes another sheet of paper, the size of the complex figure card, is placed in front of the subject and the subject is asked, the size of the complex figure card, on placed in front of the subject and the subject is asked to draw the design again. Following this, during the thirty minutes before the second, delayed recall is given; the subject is given another task he\ she is not told that the design has to be drawn after this delay period. After thirty minutes have elapsed, another sheet of paper, once again the size of the complex figure card is placed in front of the subject and the subject and the subject is again asked to draw the same design from memory. The subject is not allowed to use rulers to draw lines, but has to draw it freehand. Erasers may be used. The complex is figure is exposed to the subject only initial copying, It is not exposed before immediate recall or delayed recall.

11**. Frontal assessment battery (Dubois’ 2000):**

This is a recently validated instrument for assessing the frontal lobe functions. As we know that frontal lobes control conceptualization and abstract reasoning, mental flexibility, motor programming and executive control of action, resistance to interference, self regulation, inhibitory control, and environmental autonomy functions that are mediated by the prefrontal cortex and is essential for adapting the subjects response to new or challenging situations.

It consists of six subtests, each scoring from 0 to 3. Performance of the six subtests of the FAB can give a composite score which evaluates the severity of the dysexecutive syndrome and an descriptive pattern of executive dysfunction in a given patient.The six subtests are:

1. **Similarities (**Conceptualization): Subjects have to conceptualize the links between two objects from the same category. Patient may be unable to establish an abstract link between the items, adhering to the concrete aspects of the objects or may be unable to establish a link of similarity.
2. **Lexical fluency (**mental flexibility): Tests the ability to self organize cognitive strategies and revival from semantic memory.
3. **Motor series** (programming): Requires temporal organization, maintenance and execution of successive actions.
4. **Conflicting instructions** (Sensitivity to interference): Deficits in behavioral self regulation may be observed in tasks in which verbal commands conflict with sensory information. Here the subject must provide a response which is opposite to the alternating signal. Thus the subject should obey verbal commands and refrain from following what they see. Subjects with frontal dysfunction will have echopractic tendency imitating the examiner.
5. **Go-No-Go (Inhibitory control):** Withholding a response may be difficult for some one who have dysfunction of ventral part of the frontal lobes. This can be assessed by go-no-go paradigm in which the subjects must inhibit a response that was previously given to the same stimulus.

6. **Prehension behaviour (Environmental autonomy):** Here the response to external cues and whether he conceives the sight of movement as an order to imitate (imitating behaviour) or the sight of an object implying an order to use it (utilization behaviour) is noted.

SOCIAL FUNCTIONING INDEX

(rating options are given below each question)

I. Self Concern

a. Self Care

Q. Are you (is he/she) concerned about keeping clean?

1. Totally unconcerned
2. Rarely concerned
3. Occasional lapses in concern
4. Usually concerned
5. Always concerned

b. Personal belongings and personal space

Q. Are you (is he/she) concerned about your (his/her) personal belongings?

1. Totally concerned
2. Rarely concerned
3. Occasional lapses in concern
4. Usually concerned
5. Always concerned

c. Eating Practices

Q. Are you (is he/she) concerned about eating the right food?

1. Totally concerned
2. Rarely concerned
3. Occasional lapses in concern
4. Usually concerned
5. Always concerned

d. Health Care

1. Totally concerned
2. Rarely concerned
3. Occasional lapses in concern
4. Usually concerned

5. Always concerned

II. Occupational role

a. Regularity in occupational functioning

Q. Are you (is he/she) employed?

1. Unemployed
2. Regular unjustified absences
3. Occasional absences
4. Occasional justified absences
5. Volunteers for overtime

b. Quality of occupation

Q. Are you (is he/she) employed?

1. Unemployed
2. House wives/ students / retired pensioners
3. Unskilled and skilled labourers
4. Holds a white collared job
5. Is a professional, businessman, etc.

c. Quality of performance

Q. How is your (his/she) performance at work/home/college?

1. Unemployed
2. Barely holding on to the job
3. Occasional lapses in performance
4. Satisfactory performance
5. Superior performance recognized

d. Occupational Interests

Q. Are you (is he/she) actively looking for a job?

1. Shows no interest in occupation
2. Occasional applications made but no interest in follow up
3. Active applications made but no interest in follow up
4. Active applications with active follow up

5. Employed

Rate 3 for Housewives/students/retired pensioners in this sub-section

III. Role in the family

a. Marital Role

Q. How do you (does he/she) get along with the spouse?

1. Repeated separations
2. Repeated arguments but with no separations
3. Affectionate relationship but with regular arguments
4. Affectionate relationship with infrequent arguments
5. Stable affectionate relationship

b. Role as a child

Q. How do you (does he/she) get along with your (his/her) parents?

1. Repeated separations
2. Repeated arguments but with no separations
3. Affectionate relationship but with regular arguments
4. Affectionate relationship with infrequent arguments
5. Stable affectionate relationship

c. Role as a parent

Q. How do you (does he/she) get along with the children?

1. Physically abusive and assaultive
2. Phychologically abusive and assaultive
3. Unconcerned
4. Affectionate with occasional inconsistencies
5. Stable affectionate relationship

d. Family Relationships

Q. How do you (he/she) get along with other family members living in the same home?

1. Total lack of contact

2. Lack of affectionate relationship, but with no arguments

3. Affectionate relationship with regular arguments

4. Affectionate relationship with infrequent arguments

5. Stable affectionate relationship

Rate 9 when not applicable in this sect

IV. Other social roles (Rate 9 where not applicable)

a. Relationship with family members not living in the same home

Q. How do you (does he/she) get along with other family members not living with you (him/her)?

1. Frequent arguments and frictions

2. Occasional arguments

3. No interaction /no contact

4. Warm relationship with no participation in group gatherings

5. Warm relationship with participation in group gatherings

b. Relationship with friends

Q. How do you (does he/she) get along with friends?

1. No friends at all

2. Transient unstable friendships

3. Has stable friendships with repeated arguments

4. Atleast one stable friendship

5. More than one stable friendship

c. Relationship with Neighbours

Q. How do you (does he/she) get along with neighbours?

1. Frequent arguments and frictions

2. Occasional arguments

3. No interaction

4. Warm relationship with no participation in group gatherings

5. Warm relationship with participation in group gatherings

d. Colleagues at place of work

Q. How do you (does he/she) get along with colleagues at place of work?

1. Frequent arguments and frictions
2. Occasional arguments
3. No interaction
4. Warm relationship with no participation in group gatherings
5. Warm relationship with participation in group gatherings

e. Social Activity Groups

Q. How do you (does he/she) involve in social activities?

1. No involvement at all
2. Passive attendance with no active involvement
3. Occasional involvement
4. Regular involvement in atleast one activity group
5. Regular involvement in several activity groups

Social functioning index – Scoring Sheet

1. Person interviewed subject / informant
2. Name:
3. Age: 4. Sex:
5. Marital Status: 6. Education:
7. Religion:
8. Informant's relationship to client:

SSSFI

I.	a_____	II.	a_____
	b_____		b_____
	c_____		c_____
	d_____		d_____
III.	a_____	IV.	a_____
	b_____		b_____

c_____ c_____

d_____ d_____

Global Impression: Mild

Moderate

Severe

Positive and Negative Syndrome Scale (PANSS) Rating Form[1,2]:

Instructions: Circle the appropriate rating for each dimension following the specified clinical interview. Refer to the rating manual for item definitions, description of anchoring points, scoring procedure and norms.

Patients Name :_____

Age: _____ Sex: _____

Study: _____ Observation Period: _____

Diagnosis: _____ Years since first hosp: _____

Ward/Location: _____ Date:_____ Rater:_____

		ABS	MIN	MILD	MOD	SEV	SEV	EXT
POSITIVE SCALE								
P1. Delusions	P1.	1	2	3	4	5	6	7
P2. Conceptual disorganization	P2.	1	2	3	4	5	6	7
P3. Hallucinatory behaviour	P3.	1	2	3	4	5	6	7
P4. Excitement	P4.	1	2	3	4	5	6	7
P5. Grandiosity	P5.	1	2	3	4	5	6	7
P6. Suspiciousness persecution	P6.	1	2	3	4	5	6	7
P7. Hostility	P7.	1	2	3	4	5	6	7
NEGATIVE SCALE								
N1. Blunted affect	N1.	1	2	3	4	5	6	7
N2. Emotional withdrawal	N2.	1	2	3	4	5	6	7
N3. Poor rapport	N3.	1	2	3	4	5	6	7
N4. Passive /apathetic social withdrawal	N4.	1	2	3	4	5	6	7
N5. Difficulty in abstract thinking	N5.	1	2	3	4	5	6	7
N6. Lack of spontan eity and flow of conversation	N6.	1	2	3	4	5	6	7
N7. Stereotyped thinking	N7.	1	2	3	4	5	6	7
GENERAL PSYCHOPATHOLOGY SCALE								
G1. Somatic Concern	G1.	1	2	3	4	5	6	7
G2. Anxiety	G2.	1	2	3	4	5	6	7
G3. Guilt feling	G3.	1	2	3	4	5	6	7

G4.	Tension	G4.	1	2	3	4	5	6	7
G5.	Mannerisms and posturing	G5.	1	2	3	4	5	6	7
G6.	Anxiety	G6.	1	2	3	4	5	6	7
G7.	Motor retardation	G7.	1	2	3	4	5	6	7
G8.	Uncooperativeness	G8.	1	2	3	4	5	6	7
G9.	Unusual thought content	G9.	1	2	3	4	5	6	7
G10.	Disorientation	G10.	1	2	3	4	5	6	7
G11.	Poor attention	G11.	1	2	3	4	5	6	7
G12.	Lack of judgement and insight	G12.	1	2	3	4	5	6	7
G13.	Disturbance of volition	G13.	1	2	3	4	5	6	7
G14.	Poor impulse control	G14.	1	2	3	4	5	6	7
G15.	Preoccupation	G15.	1	2	3	4	5	6	7
G16.	Active social avoidance	G16.	1	2	3	4	5	6	7

PROFILE SUMMARY

	Raw Total	Percentile	Range
Scales*			
Positive syndrome	_____	_____	_____
Composite index	_____	_____	_____
General psychopathology	_____	_____	_____
Cluster scores**			
Anergia	_____	_____	_____
Thought disturbance	_____	_____	_____
Activation	_____	_____	_____
Paranoid/belligerence	_____	_____	_____
Depression	_____	_____	_____

*Positive syndrome	=	Sum of P1 through P7
Negative syndrome	=	Sum of N1 through N7
Composite index	=	Positive syndrome minus Negative Syndrome
General Psychopathology	=	Sum of G1 through G16
**Anergia	=	N1+N2+G7+G10
Thought disturbance	=	P2+P3+P5+G9
Activation	=	P4+G4+G5
Paranoid/belligerence	=	P6+P7+G8
Depression	=	G1+G2+G3+G6

1. Kay S.R, Opler L.A., Fiszbein A (1986), PANSS Rating Manual, Albert Einstein College of Medicine, New York.
2. Kay S.R, Fiszbein A, Opler L.A, (1987), The PANSS for Schizoprenia – Schizophrenia Bulletin 13, 261-276.

DIGIT SYMBOL SUBSTITUTION TEST

1	2	3	4	5	6	7	8	9
□	⊥	]	L	U	O	^	X	=

2	1	3	7	2	4	8	1	5	4	2	1	3	2	1	4	2	3	5	2	3	1	4	6	3

1	5	4	2	7	6	3	5	7	2	8	5	4	6	3	7	2	8	1	9	5	8	4	7	3

6	2	5	1	9	2	8	3	7	4	6	5	9	4	8	3	7	2	6	1	5	4	6	3	7

9	2	8	1	7	9	4	6	8	5	9	7	1	8	5	2	9	4	8	6	3	7	9	8	6

DIGIT VIGILANCE TEST

Serial no: Name: Age: Sex: Date:

Total time errors O C

9	5	3	6	4	7	2	8	1	9	2	8	6	2	4	1	2	4	6	8	9	7	3	5	1	8	6	4	2	9
8	4	2	1	3	5	6	1	9	7	5	6	3	8	2	3	9	7	4	1	2	3	4	5	6	7	8	9	1	2
1	7	4	8	6	3	2	9	7	1	4	3	2	5	9	5	7	8	6	3	4	5	6	1	7	2	8	3	9	4
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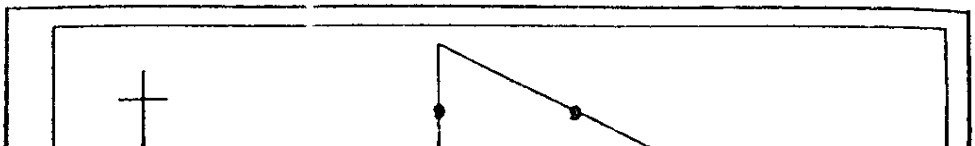

FRONTAL ASSESSMENT BATTERY (FAB)

Domain	Instructions	Score
Similarities (Concepts)	'In what way are they alike?' A banana and an apple; A table and a chair; A tulip, a rose, and a daisy	Three correct: 3 Two correct: 2 One correct: 1 None correct: 0
Lexical fluency (Mental flexibility)	'Say as many words as you can beginning with the letters 'S', except surnames or proper nouns' (If no response for 5 sec, say 'for instance, snake'; do not count repetitions, variations) – time 6 sec	>9 words: 3 6-9 words: 2 3-5 words: 1 <3 words: 0
Motor series (Programming)	'Look carefully at what I'm doing' The examiner performs 3 times the fist-palm-edge series 'Now, with your right hand, do the same series, first with me, then alone'.	6 correct consecutive series alone:3 3 correct consecutive series alone: 2 3 correct consecutive series with the examiner: 1 <3 correct consecutive series with the examiner: 0
Conflicting instructions (Sensitivity to interference)	'Tap twice when I tap once' (Make 3 trials of 1-1-1 and 2-2-2 to make sure that patient has understood) Test series: 1-1-2-1-2-2-2-1-1-2	No error: 3 1-2 errors: 2 >2 errors: 1 4 consecutive errors: 0
Go/no go (Inhibitory control)	'Tap once when I tap once, do not tap when I tap twice'. (a series of 3 trials is run with 1-1-1 and 2-2-2) Test series: 1-1-2-1-2-2-2-1-1-2	No error: 3 1-2 errors: 2 >2 errors: 1 4 consecutive errors: 0
Prehension behaviour (Environmental autonomy)	'Do not take my hands' The examiner brings his hands close to the patient's hands (that are resting palms face upwards on his knees) and touches the palms of patient's hands. Repeat instructions and try again if patient takes the hands.	Does not take the examiner's hands: 3 Hesitates and asks what he has to do:2 Takes the hands: 1 Takes the hands even after being told not to: 0