STUDY ON NEUROLOGICAL SOFT SIGNS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER

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CERTIFICATE

This is to certify that the dissertation titled, **"STUDY ON NEUROLOGICAL SOFT SIGNS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER"**, submitted by **Dr.ARUL JAYENDRA PRADEEP.V,** in partial fulfillment for the award of the **MD degree in Psychiatry** by the Tamil Nadu Dr. M. G. R. Medical University, Chennai, is a bonafide record of the work done by him in the Institute of Mental Health, Madras Medical College during the academic years 2010 – 2013.

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DECLARATION

I, **Dr. Arul Jayendra Pradeep V.** solemnly declare that the dissertation titled, **"STUDY ON NEUROLOGICAL SOFT SIGNS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER"** has been prepared by me, under the guidance and supervision of **Dr. R. JEYAPRAKASH** M.D., D.P.M., Professor of Psychiatry, Madras Medical College. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad. This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree **Branch – XVIII (Psychiatry)** to be held in April 2013.

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LIST OF ABBREVATIONS USED

OCD	-	OBSESSIVE COMPULSIVE DISORDER
NSS	-	NEUROLOGICAL SOFT SIGNS
SNS	-	SOFT NEUROLOGICAL SIGNS
NES	-	NEUROLOGICAL EVALUATION SCALE
PANESS	-	PHYSICAL AND NEUROLOGICAL EXAMINATION FOR SOFT SIGNS
CNI	-	CAMBRIDGE NEUROLOGICAL INVENTORY
YBOCS	-	YALE BROWN OBSESSIVE COMPULSIVE SCALE
QNI	-	QUANTIFIED NEUROLOGICAL INSTRUMENT
GAD	-	GENERALIZED ANXIETY DISORDER
ICD-10	-	INTERNATIONAL CLASSIFICATION OF DISEASES
PET	-	POSITRON EMMISON TOMOGRAPHY
MRI	-	MAGNETIC RESONANCE IMAGING
CT	-	COMPUTERIZED TOMOGRAPHY
SSRIS	-	SELECTIVE SEROTONIN REUPTAKE INHIBITORS
IMH	-	INSTITUTE OFF MENTAL HEALTH,CHENNAI
rCBF	-	REGIONAL CEREBRAL BLOOD FLOW

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INTRODUCTION

In the era of expanding recent advancements and progress made in the field of neuro psychiatry , a relatively neglected aspect is complete neurological examination which is non invasive, easy to administer and provides wealth of information regarding the various aspects of the disease. Impaired neurological performance has been documented in various psychiatric conditions and the concept of neurological examination in psychiatry ,a time old concept whose significance has gained importance with blurring of the thin line between neurology and psychiatry leading to the concept of neuropsychiatry. Neuro biological underpinnings of psychiatric conditions further propelled the significance of neurological examination in psychiatry.

Neurological examination in psychiatry, particularly has two general aspects

1] Examination for ‘hard signs’ or ‘major signs’ or ‘localizable signs’ such as cranial nerve lesion, motor deficit, sensory impairment, reflex asymmetry which reflects presence or absence of neuropathology and a localizing lesion.

2] Evaluation of performance decrements in neurological domains without any identifiable neurological lesion or disorder (Sanders & Keshavan, 1998).

As mentioned above these decrements in neurological domains mainly includes the concept of our focus "NEUROLOGICAL SOFT SIGNS" or "SOFT NEUROLOGICAL SIGNS".(Sanders & Keshavan, 1998)

NEUROLOGICAL SOFT SIGNS

Dr. Loretta Bender ,a pioneer in neuro psychiatric aspects of childhood disorders introduced the concept of neurological soft signs in 1947 in reference to non diagnostic neurological abnormalities seen in children with schizophrenia .(Sadock, Benjamin James., Sadock, 2007)

DEFINITION

NSS are defined by Shaffer and O'connor as

" *Non normative performance (s) on a motor or sensory test(s) which would be identical or akin to test(s) of traditional neurological examination, but elicited from an individual who shows none of the features of fixed or transient neurological disorder* "

Shaffer et al also proposed that to consider a sign as an NSS it should have following features

1] No association should exist between an observed behaviour and a positive history of neurological disease or trauma

2] It should not be a pathognomonic sign of any neurologic disease or encephalopathy

3] It should not be indicate any specific CNS pathology

Thus the NSS are minor neurological deviation in motor and sensory function that are not localized to any specific area of the brain and not characteristic of any specific neurological condition ,mostly indicating diffuse cerebral dysfunction.

Ever since they have been introduced they were termed as ‘soft signs’, ‘non focal signs’, ‘diffuse signs’, ‘minimal brain damage syndrome’ due to their lack of specificity ,validity or localization at that time. The term ‘soft’ also signifies the nature of wide but blurred boundaries of varying domains like EEG findings ,behaviour disturbance, learning disorders, neurological functions that were considered under the umbrella of soft signs.(Sanders & Keshavan, 1998)

The initial focus of these NSS remained mainly in the field of child psychiatry with description of concepts of 'Minimal Brain Damage' in children with hyperactivity, impulsivity and with no demonstrable neurological lesion. Later from 1990 with quantification of validated and standardised instruments for assessment of these signs, the focus shifted to major psychiatric conditions leading to exhaustive research in the subject which provided significant understanding of the neurobiology, neuro anatomical correlates, genetic underpinnings , neuro developmental basis, endophenotypic markers and predictors of neuropsychological dysfunction in certain psychiatric conditions.

With this brief introduction about the neurological soft signs ,we now focus on existing documented literature that has changed the concept of these NSS, their significance in psychiatric conditions and the various aspects of their relation to Obsessive compulsive disorder which is the main focus of our study.

REVIEW OF LITERATURE

Ever since being introduced in medical literature, the concepts regarding NSS has undergone gradual changes from classifying and quantifying them with validated instruments ,to identification of anatomical correlates to these signs, understanding the genetic basis, neuropsychological dysfunction of the disorder related to it and their role in various aspects of the disorder studied.

CLASSIFICATION OF NEUROLOGICAL SOFT SIGNS

Various neurological domains have been considered as soft signs which may refer to

1] Behavioural symptoms like impulsivity, hyperactivity

2] Physical findings like contra lateral overflow movements

3] Variety of non focal signs like mild chorieoform movements, poor balance, mild incoordination, nystagmus, gait asymmetry, persistence of infantile reflexes(Sadock, Benjamin James., Sadock, 2007).

Till late 1980s these soft signs were evaluated under various clinical examination schedule like Isle of Wight Neurological Examination, Non Focal Neurological Sign examination, National Collaborative Perinatal Project neurological items [NCPP], Neurological Examination for Subtle Signs revised(Shaffer, D., O'connor, P.A., 1983) . In general these soft

signs can be divided into those that were normal in a young child but become abnormal when they persist in older child and those that were abnormal at any age. In 1989, Heinrich and Buchanan made a landmark contribution by analysing existing literature, considering various soft signs documented in the literature and finally categorising them to three major sub divisions namely

1] Integrative sensory function

2] Motor coordination function

3] Complex motor sequencing.

Each subset has various items to be tested and a subset for other signs including primitive reflexes, eye movement abnormalities which are not grouped under above sub groups were also included. From this division they formulated the NES-Neurological Evaluation Scale(Buchanan & Heinrichs, 1989).Later other structured scales were proposed which included various neurological domains under them. One such scale is Cambridge Neurological Inventory [CNI] a brief inventory consisting of motor coordination, sensory integration, primitive reflexes .It is a scale with well validated soft signs items to be studied in psychiatric conditions(Chen et al., 1995).The following table is a condensed format of various NSS and how they have been grouped into various scales.

S.NO	*SOFT SIGNS DOMAIN*	**NES SCALE [Buchanan & Heinrichs, 1989]**	**CNI [chen ea al., 1995]**	**QNS [Convict.,A.,volava., 1994]**	**PANESS [werry / Aman.,1976]**
I	***MOTOR***				
	Casual Gait	---	+	+	---
	Stressed gait	---	---	---	+
	Tandem walk	---	+	+	+
	Hopping	+	---	+	+
	Romberg Test	+	+	+	---
II	***COMPLEX MOTOR SEQUENCING***				
	Fist Ring test				
	Fist Edge Palm test	+	---	+	---
	Alternating Fist Palm	+	+	+	---
	test	+	+	+	---
	Diadochokinesis				
	Finger Thumb	+	+	---	---
	Opposition	+	+	+	---
	Rhythm Tapping	---	+	---	+
	Synchronous Tapping	+	---	---	+
III	**EXTRA OCULAR MOVEMENTS**				
	Convergence	---	+	---	+
	Gaze Persistence	+	---	---	---
	Visual Tracking	+	+	---	---
	SENSORY				
	Audio-Visual Integration	+	---	---	---
	Stereo gnosis	+	+	+	+
	Graphesthesia	+	+	+	+
	Extinction	+	+	+	+
	Two point				
	Discrimination	---	+	---	+
	Right Left Orientation				
		+	---	+	---

Table showing standardised version of scales with soft sign

S.NO	SOFT SIGNS DOMAIN	NES SCALE	CNI	QNI	PANESS
V	***PRIMITIVE REFLEX***				
	Grasp Reflex	+	+	---	---
	Suck Reflex	+	---	---	---
	Palmomental	---	+	---	---
	Glabellar	+	+	---	---
	Snout	+	+	---	---
VI	***OTHER DOMAINS***				
	Drift	---	+	---	---
	Motor Persistence	---	+	---	+
	Finger Nose Test	+	+	---	+
	Heel Shin Test	---	---	---	+
	Muscle Tone	---	---	+	---
	Mirror Movements	+	+	+	---
	Synkinesis	+	+	---	---
	Tremor	+	+	---	---
	Chorieoathetotic Movement	+	+	---	---

+ = DOMAIN INCLUDED --- = NOT INCLUDED

NES = NEUROLOGICAL EVALUATION SCALE

PANESS=Physical and Neurological Examination for Soft Signs

CNI = Cambridge Neurological Inventory QNI =Quantified Neurological Examination

CHANGING CONCEPTS OF NEUROLOGICAL SOFT SIGNS

Even though proposed to be non specific, non localizable abnormalities initially, with progress of time and with many advancements in imaging techniques neuro dysfunctional concept of these soft signs changed slowly but in steady and convincing manner from being non specific signs to signs that were attributable to various neuro anatomical correlates in subsequent literature(King, Wilson, Cooper, & Waddington, 1991; Mouchet-Mages et al., 2011).

The following concepts have been found from various studies done so far

1] Sensory integration abnormality is associated with volume reduction in grey matter of right pre central gyrus, defect in superior temporal volume (Dazzan et al., 2004) and smaller volume in hetero modal association cortex(Keshavan et al., 2003).

2] Motor coordination abnormalities are associated with smaller caudate and putamen volume, larger internal capsule volume and smaller cerebellum volume (Dazzan et al., 2004; Keshavan et al., 2003)

3] Impaired motor sequencing is associated with a cluster of grey matter reduction in left putamen and defect in frontal lobe function(Dazzan et al., 2004)

4] Abnormalities in eye movements and developmental reflexes suggest signs of frontal release (Bombin et al., 2005)

It was found that as a whole the NSS reflects failure in sensory and motor integration suggesting disturbed cortical- sub cortical connectivity and cortical -cortical inter neuronal connections which were also evident from reduced sub cortical and cortical structural volume (Bombin, Arango, & Buchanan, 2005; Buchanan & Heinrichs, 1989; Mouchet-Mages et al., 2011; Sanders & Keshavan, 1998).Thus Henrich and Buchannan's initial statement which meant

"*the fact that the meaning of neurological soft sign is uncertain reflects not unreality of the findings but limitation in our knowledge*" turned out to be true which also rightly coincides with Ingram's statement that "*use of the term soft sign is diagnostic only of our soft thinking*"(Sanders & Keshavan, 1998)

NSS IN PSYCHIATRIC DISORDERS

High prevalence of NSS in comparison to healthy controls is documented in

-Schizophrenia

-ADHD and learning disorders

-First episode psychosis

-Bipolar disorder

-Obsessive compulsive disorder

-Post traumatic stress disorder

Apart from ADHD, PDD, learning disorders(Halayem et al., 2010; Vitiello, Stoff, Atkins, & Mahoney, 1990; Werry & Aman, 1976) increased soft signs have been documented in individuals with low IQ, low birth weight, cognitive impairment.(Agarwal, Das, Agarwal, Upadhyay, & Mishra, 1989; Pine et al., 1996; Shaffer, D., O'connor, P.A., 1983) Even though the initial focus of NSS has been in field of child psychiatry later a substantial amount of research is on NSS has been done in patients diagnosed of schizophrenia.

In systematic reviews it has been concluded that NSS occurred in majority of patients with schizophrenia when compared to normal controls(Bombin et al., 2005; Ganesan Venkatasubramanian, Jayakumar, Gangadhar, & Keshavan, 2008).Studies have found the prevalence of NSS in patients with schizophrenia tends to be in the range of 50%-65%, compared to prevalence of 5% in healthy controls (Buchanan & Heinrichs, 1989) .Patients with schizophrenia when compared to healthy controls in aggregate measure of NSS perform 73% outside the normal range of healthy subjects.(Chan, Xu, Heinrichs, Yu, & Wang, 2010)

High rates of NSS has been reported both in drug naïve and patients on neuroleptic medications and found to be independent of age , sex, demographic status(Chan & Gottesman, 2008; Dazzan & Murray, 2002; Sanders, Keshavan, & Schooler, 1994; G Venkatasubramanian et al., 2003). Studies have reported these NSS to have significant association with negative symptoms and cognitive impairment(Bombin et al., 2005; Ganesan Venkatasubramanian et al., 2008).Relatives of patients with schizophrenia have also been found to have significantly greater NSS than healthy controls although lesser than patients suggesting a familial basis for NSS in schizophrenic subjects leading to consideration of these NSS as

potential endo phenotype marker of schizophrenia.(Chan & Gottesman, 2008)

Even though the studies are not as exhaustive as in schizophrenia ,in bipolar disorder also a significant association has been observed in NSS score when compared to normal controls in certain studies and their relation to neuro cognitive impairment has also been documented.(Goswami et al., 2006; Negash et al., 2004)

Apart from these ,in literature there exists further evidence for high NSS in

- Post traumatic stress disorder(Southwick et al., 2000)

- Substance dependence(Dervaux, Bourdel, Laqueille, & Krebs, 2010; Keenan, O'Donnell, Sinanan, & O'Callaghan, 1997)

- First episode psychosis (Dazzan & Murray, 2002; Dazzan et al., 2004; Sanders et al., 1994)

-Borderline personality disorder(De La Fuente et al., 2006)

-Schizotypal personality(Theleritis et al., 2012)

NEUROLOGICAL SOFT SIGNS AND OCD

Having seen the brief overview of NSS in various psychiatric conditions, studies pertaining to OCD are considered in detail. The studies on NSS in anxiety disorders spectrum are relatively few when compared to those on NSS in patients with schizophrenia, learning disorders and ADHD.Among the anxiety disorder spectrum, OCD has been researched well for its relation to NSS.

OBSESSIVE COMPULSIVE DISORDER-A BRIEF OVERVIEW

OCD remains as one of the most intriguing and disabling illness characterised by presence of obsessions and compulsions which constitute the core clinical feature of OCD. Obsessions are characterised by "recurrent and persistent thoughts, images or impulses that are perceived as intrusive, inappropriate which the patient usually admit as irrational, excessive, unwanted and product of their own mind and not imposed from without". Compulsions are defined as "repetitive behaviour or mental acts that the person feels driven to perform in response to an obsession or accounting to certain rule that must be applied rigidly and usually aimed at preventing or reducing the distress"(Khanna , 1991) .

CLINICAL PRESENTATION OF OCD

Quantifying the above mentioned concept of obsession and compulsion into an acceptable classification based on clinical presentation eluded consensus. Later from factor analytic approach of various epidemiological studies in Indian population obsessions and compulsions have been quantified as follows(Girishchandra & Khanna, 2001; Jaisoorya TS., Janarthan reddy YC., 2003) which shares similarity with YBOCS symptom checklist(Goodman et al., 1989; Scale, 2000; Sulkowski et al., 2008).

OBSESSION		COMPULSION	
FEAR OF CONTAMINATION	61%	CLEANING &WASHING	50%
AGGRESSIVE OBSESSIONS	43%	ORDERING	41%
NEED FOR SYMMETRY	35%	REPEATING	38%
SEXUAL OBSESSION	31%	CHECKING	18%
RELIGIOUS OBSESSION	30%	HOARDING	7%
PATHOLOGICAL DOUBT	21%	MISCELLANEOUS	41%
MISCELLANEOUS	40%		

With its varying presentation under two broad entity, OCD usually begins in adolescence with nearly 65% having their onset before 25 years of age. In Indian sample onset of age is before 18 years(Jaisoorya TS.,

Janarthan reddy YC., 2003).Findings from various studies suggest that about 25% of patient recover completely and 15% tend to have detoriating course with rest of them having symptom fluctuation without clear remission and detoriation(Eisen et al., 1999; Skoog & Skoog, 1999).Usually presentation in male to females is in ratio of 1:1.5 with reverse male predominance in adolescence.

The significance of OCD resurged with Epidemiological Catchment Area study which concluded OCD to be fourth common psychiatric disorder.(Karno, Golding, Sorenson, & Burnam, 1988)The prevalence of OCD in the community from various data combined was found to be 2% being more prevalent than schizophrenia and BPAD but less reported out earlier making it seemingly less prevalent(Guruswamy, Relan, & Khanna, 2002; Khanna, n.d.; Reddy, Rao, & Khanna, 2010).

CO MORBIDITY IN OCD

OCD usually would be associated with one or other psychiatric conditions mainly depressive disorders and anxiety disorders. The most common psychiatric disorder is major depression[30-55%],social phobia[11-23%],GAD[18-20%],simple phobia[7-21%],panic disorder[6-

12%],eating disorder[8-15%], tic disorder[5-8%],Toilettes syndrome[5%]. (Khanna, 1991; Reddy et al., 2010).

In Epidemiological Catchment Area study, it was found that two thirds of patients with OCD had co morbid psychiatric illness.(Karno et al., 1988).similarly in cross national epidemiological study anxiety[24-70%] and depression[12-60%] had greater co presentation.(Horwath & Weissman, 2000)

There have been certain shared conditions rather than to be said as co morbidity which have similar presentation as OCD by phenomenology, treatment response and patho physiology.These conditions include tricho tillomania, Body dysmorphobia,hypochondriasis, anorexia nervosa, Touretts syndrome, binge eating, kleptomania ,pathological mania and sexual compulsions.(Bienvenu et al., 2000; E Hollander & Rosen, 2000; Eric Hollander, Kim, Khanna, & Pallanti, 2007; Jaisoorya TS., Janarthan reddy YC., 2003).They have been termed the ***OCD spectrum disorders*** which further add to the view of significant neurobiological consideration of OCD.

NEUROBIOLOGY OF OCD

Being a time old concept OCD traversed the path of various explanations from spirituality to fixation at oral stage by Freud due to complexity and heterogeneous presentation and finally ended in neurobiological under pinnings. Earlier concepts of neurological assessment in OCD patients made the significant path in shifting the focus to neurobiology(E Hollander et al., 1990; Stein et al., 1993) ,followed by neuropsychological studies and then towards imaging techniques which has focussed the neuro biological concept around the circuit of thalamus, caudate nucleus, orbito frontal cortex suggesting a frontal-subcortical basal ganglia circuit dysfunction(Eric Hollander et al., 2007; Khanna, n.d.; Modell, Mountz, Curtis, & Greden, 1989; Stein, 2000).Serotonergic imbalance with involvement of strial-thalamic-cortical strial circuit evident by high signal intensities in left caudate and putamen in functional imaging and high intensity rCBF in orbito frontal cortex in PET studies as suggested by Baxter points to perturbed functioning of the circuit involving frontal and sub cortical basal ganglia circuit(Compulsive & Working, 1997; Khanna, 1999; Khanna, Sumant.,venkatasubramanian G., 2003; Leckman et al., 2005; Rauch SL., cora-Locatelli G., n.d.; Stein, 2000).

As it passed through various explanation with progress of time these NSS played a significant role in establishing the neuropsychological dysfunction and to putative localization areas in brain(E Hollander & Rosen, 2000).With many advanced imaging techniques a significant increase in activity in frontal lobe, caudate nucleus and cingulum is found (Bolton, Raven, Madronal-Luque, & Marks, 2000; Eric Hollander et al., 2007; Reddy et al., 2010; Sadock, Benjamin James., Sadock, 2007; Van Den Heuvel et al., 2011).MRI imaging also quantified bilaterally smaller caudate nucleus and treatment responsiveness with brain stimulation methods in anterior capsule and ventral striatum have also given indirect evidence to underpin the neurobiology of OCD (Baxter, 1992; Sadock, Benjamin James., Sadock, 2007; Saxena & Rauch, 2000)but only in few sample of studies due to lack of availability, invasiveness and other reasons .In this context NSS played a significant role as being a simple ,non invasive easy to administer tests but giving strong supportive evidence for putative localization of neuro biological dysfunction in the illness. Studies reporting their prevalence in drug naïve patients ,not influenced by drugs, state of the disease, also significantly associated in first degree relatives when proved conclusively will strongly back the neuro developmental hypothesis and endo phenotype marker for OCD.

NSS have also been a focus of controversy ,since studies from 1990 to till 2011 have supported and disapproved their significance in OCD(N Jaafari et al., 2012). In OCD various studies have explored the neurological soft signs but the results have been variable and eluded definitive conclusions. Existing literature on assessing Neurological soft signs in patients with OCD have focussed on following domains:

1] Studies comparing NSS in patients with OCD in comparison to matched normal controls.

2] Studies assessing severity of NSS to symptom severity.

3] Studies assessing the relation of NSS to neuro cognitive impairment.

4] Studies comparing NSS severity in relation to insight of the illness.

5] Studies assessing NSS severity with treatment response.

NEUROLOGICAL SOFT SIGNS IN PATIENTS WITH OCD

The available literature has focussed on studying the occurrence of NSS in patients with OCD comparing them with normal controls and by some studies comparing them with patients with other illness like schizophrenia.

A significant difference in NSS in patients with OCD has been reported when compared to normal controls in total score and all sub domains in some studies. Few studies have reported significant difference in total score but not in certain individual sub scores and some studies have reported no significant difference in NSS in patients with OCD when compared to normal controls.

Hollander et al, on comparing 41 medication free patients of OCD with 20 normal controls matched for age, gender and handedness found significant difference in the domain of motor coordination, involuntary movements, mirror movements, visuo spatial function on left half of the body .The NSS are significantly correlated with severity of obsession. No significant difference was observed in the sensory integration domain.(E Hollander et al., 1990)

In another study a significant difference in NSS score in patients with OCD when compared to controls is found with no significant difference was noted in relation to medication status of the patient.(Bihari et al, 1991).In some studies which focussed on obsessional slowness initially found generalized non specific impairment in frontal basal ganglia loop by significant indication of impairment in the presence of soft signs associated with it(Lees, Hymans, Bolton, Epps, & Head, 1991)

David Mataix ,on comparing 30 patients with primary OCD and normal matched controls using Cambridge Neurological Inventory found significantly high score on NSS in patients with OCD and significant relation to non verbal memory performance, but primitive frontal release reflexes didn't have any significant variation among both groups.(Mataix-Cols et al., 2003)

In another study on comparing 30 patients with OCD and 30 normal matched controls using PANESS scale a significant difference in total score and in graphesthesia and two point discrimination domain was found. No significant difference was found in other domain of motor coordination and motor movements.(Guz & Aygun et al, 2004)

Salma et al 2008 found that patients with OCD had significantly higher NSS score than controls in total score and domains of motor coordination, balance, graphesthesia with significant correlation between NSS score, symptom severity and poor insight.(Salama HM,Saad Allah HM, 2008)

In Indian studies, Summant Khanna on comparing thirty seven drug free OCD subjects and 20 normal healthy volunteers found significantly more total NSS score compared to controls using NES scale.(Khanna, 1991; Reddy, Rao, & Khanna, 2010) .A few studies have also reported the neuro cognitive impairment being linked to presence of severity of NSS. In follow up cases of juvenile OCD with co morbid features have reported high NSS in patients with OCD.(Jaisoorya TS., Janarthan reddy YC., 2003; Khanna, n.d.).A significant proportion of Indian research being contributed by Summant Khanna et al.,channabasavanna et al.,Janarthan reddy et al.,has focussed on epidemiology(Khanna, 1999),classification of clinical profile(Girishchandra & Khanna, 2001),studying on course(Bienvenu et al., 2000),neurobiology ,neuroimaging, cognition, and treatment strategies(Guruswamy et al., 2002; Reddy et al., 2010)

On other hand in the available literature, Stein et al ,found that on comparing patients with OCD, trichotillomania and normal controls there

is no significant difference in total scores and in individual subscale domains on soft signs battery.(Stein et al., 1994)

Jaafari et al on comparing 162 subjects including 54 OCD patients, 54 patients of schizophrenia and 54 normal controls in three different groups found that there has been no significant difference between soft signs score in patients with OCD when compared with normal controls and significantly reduced in patients with OCD when compared to schizophrenia patients using krebs scale for NSS.(Nematollah Jaafari et al., 2011)

Apart from these , some studies have compared patients of OCD with schizophrenia patients and normal controls for soft signs using CNI found patients with OCD had higher significant higher rates of NSS than normal controls.(Bolton et al., 1998; Sevincok, Akoglu, & Arslantas, 2006)

Poyurovsky et al ,on comparing patients with pure OCD, schizophrenia with obsessive symptoms and without obsessive symptoms along with normal controls for NSS using NES scale found that patients with OCD had significantly higher NSS than controls ,equally significant with no major difference in schizophrenia patients with and without OCD

.higher scores on motor sequencing tests were also noticed in patients with OCD than all other groups.(Poyurovsky et al., 2007)

ASSESSMENT OF NEUROLOGICAL SOFT SIGNS

Even though various studies have been conducted involving NSS in various psychiatric conditions, the main lag initially was in using a validated and standardized instrument for assessment of NSS as mentioned earlier.

Initially scheduled clinical examinations were followed along with introduction of PANESS in children(Werry & Aman, 1976).Later it was mainly Henrich and Buchannan who combined the existing literature regarding the documented neurological domains in schizophrenia and formulated a standardized and validated scale termed the neurological evaluation scale-NES scale for assessment of neurological soft signs in schizophrenic patients (Buchanan & Heinrichs, 1989) where in they quantified the soft signs to occur in three basic domains as mentioned earlier .Since then NES scale has become the most commonly used scale for assessment of soft signs along with Cambridge neurological inventory, Heidelberg scale in all other psychiatric conditions(Dazzan & Murray, 2002).

Of the existing studies assessing NSS in OCD patients nearly 50% studies combinely used NES and CNI. Nearly 30 %of rest of the studies employed structured clinical examination. CNI and NES scale has been equally employed in many studies as both of them were standardized and well validated(N Jaafari et al., 2012).Certain other aspects have been found to influence NSS with conflicting reports which should be focussed

NEUROLOGICAL SOFT SIGNS AND MEDICATION EFFECT

There has been a controversy for long time regarding the effect of medication use in neurological soft signs whether these signs precede the onset of illness or could be even a part of the side effects or performance being influenced by medication effects or a consequence of disease per se.This debate also made a road block in considering these NSS as predictors or risk factor for the onset of illness. Comparison of drug naïve patients of OCD with normal controls have yielded significantly higher level of NSS in patients suggesting the presence of NSS even before medication use.(Hollander et al., 1990; N Jaafari et al., 2012;

Khanna, 1991)

In studies involving comparison of OCD patients with medication and without medication ,no significant difference is observed in inter

group comparison with no possible effect of medication particularly SSRI in NSS score. (Bihari et al, 1991; N Jaafari et al., 2012; Karadag et al., 2011)

About the use of anti psychotics ,various studies in schizophrenic subjects have found that medication effect could not explain the NSS in patients even after controlling by using extra pyramidal symptom scale, akathisia scale (Gupta et al., 1995; Sanders et al., 1994; Varambally, Venkatasubramanian, Thirthalli, Janakiramaiah, & Gangadhar, 2006;)

NEUROLOGICAL SOFT SIGNS AND LATERALITY

Till date there has been no convincing report suggesting any particular laterality or cerebral dominance in NSS in patients with schizophrenia, OCD or other disorders. Even though there exists conflicting report like more soft signs over left half of the body(Mataix-Cols et al., 2003), the significant evidence stems from Heinrich and Buchannan who on standardizing and validating neurological evaluation scale concluded there has been no significant difference in observation of NSS in both half of the body.(Buchanan & Heinrichs, 1989)Jaffari and Fernandez de la Cruz et al in their empirical studies and meta analysis

also reported there has been no significant difference in right sided and left sided total NSS score.

NEUROLOGICAL SOFT SIGNS ,SYMPTOM SEVERITY AND INSIGHT

Studies have reported a significant correlation between NSS score and OCD symptom severity (Salama HM,Saad Allah HM, 2008) with a significant correlation between YBOCS score and total NSS score along with age of onset and insight to the illness. On the other end most of the studies found no significant difference between OCD symptom severity and NSS score suggesting them to be a trait marker of the disease rather than a state marker(N Jaafari et al., 2012; Nematollah Jaafari et al., 2011; Karadag et al., 2011; Sevincok et al., 2006; Stein et al., 1994).In the some of the studies they found that patients with higher score on NSS relatively had poor insight sub type of OCD, which was statistically significant and provides insight to formulate treatment based on NSS.

(Karadag et al., 2011; Salama HM,Saad Allah HM, 2008)

OTHER FACTORS INFLUENCING OCD

None of the other potential moderating variables like sex,intelligence , age of onset of illness have been significantly associated with NSS in

OCD and schizophrenia which has been confirmed by various studies and meta analysis(Chan et al., 2010; Dazzan & Murray, 2002; N Jaafari et al., 2012).Till date even though definitive conclusion has not been reached regarding their significance studies which reported significant relation have taken a further step even in analysing the relation of their severity to SSRI treatment response eliciting a poor response in patients scoring high on NSS(Eric Hollander et al., 2005)

To conclude from the existing pool of literature regarding NSS in OCD, it is found that

1] Majority of studies have reported high NSS in patients with OCD but contradictory reports of no significant results of high NSS in patients with OCD compared to normal controls have also been documented.

2] Among the published data one Indian study by Summant Khanna has found high NSS in patients with OCD.

3] About 45% of published studies have employed standardized instruments like NES scale for adults in assessing NSS with most of the studies being un blinded and a vast group of studies employing non validated clinical examination schedule.

4] Medication use has been found to have no significant effect on NSS score with conflicting reports in few studies.

5] In relation to OCD symptom severity though initial studies have reported significant correlation, subsequent studies and review has found no significant influence of disease severity to NSS score.

With scanty literature on Indian studies, slight inconsistency in the existing literature and less focus on laterality effect from the available evidence we took the first step of studying the neurological soft sign in patients with OCD using standardised instrument and compared it to age, sex, handedness matched controls so that it would a foundation for understanding the further significance of NSS in OCD .

AIM OF THE STUDY

AIM

To study about the neurological soft signs in patients with Obsessive Compulsive Disorder compared to normal controls

OBJECTIVES

1] To compare the Neurological Soft Signs assessed by Neurological Evaluation Scale in patients with Obsessive compulsive disorder in comparison with normal matched controls.

2] To compare the individual Neurological Soft Signs in patients with OCD and normal matched controls.

2] To compare the total NSS score and individual sub scale score for NSS between patients with OCD and control group

3] To compare the mean NSS score and individual subscale score between patients on medications and drug naïve patients

NULL HYPOTHESIS

1] There is no significant difference in NSS assessed by Neurological evaluation scale [NES] in patients with OCD compared to normal controls.

2] There is no significant difference in mean NSS score between patients suffering from OCD and normal controls

3] There is no significant difference in mean sensory integration sub score and individual items under the subscale between patients suffering from OCD and normal controls

4] There is no significant difference in mean motor coordination sub score and individual domains under the subscale between patients suffering from OCD and normal controls.

5] There is no significant difference in mean complex motor sequencing sub score and individual domains under the subscale between patients suffering from OCD and normal controls.

6] There is no significant difference in soft signs under other domains in NES scale including primitive reflexes, eye movement abnormalities between patients suffering from OCD and normal controls.

7] There is no significant difference in mean NSS score and individual mean subscale score between drug naïve patients and patients on medication.

8] There is no significant difference in individual NSS between patients on medication and medication free patients.

METHODOLOGY

STUDY SETTING

The study was conducted over a period of 6 months from June 2012 to November 2012 at the Institute of Mental Health, Chennai and the Psychiatric OPD, Madras Medical College, Chennai.

SUBJECTS

The subjects of this study were patients suffering from obsessive compulsive disorder and normal age, gender, handedness matched controls. Thirty consecutive patients diagnosed to be suffering from Obsessive Compulsive Disorder attending new case OPD , in IMH and Psychiatric OPD in Madras Medical College were selected.

Thirty Normal controls were selected from the relatives of patients attending general medicine department OPD, Madras Medical College .

CASES

INCLUSION CRITERIA

1] Patients meeting ICD-10 diagnostic criteria [clinical description and diagnostic guidelines-CDDG] for OCD

2] Patients in age group 15-45 years

EXCLUSION CRITERIA

1] Presence of any neurological disorder including seizure and focal neurological deficit

2] History of psychosis in past or present

3] History of any other psychiatric disorder in past or present

3] Family history of psychiatric illness in first degree relative

CONTROLS

INCLUSION CRITERIA :

1] Relatives of patients attending medicine OPD for minor ailments.

2] Normal individuals matched to age, gender, handedness and educational status with the patients

EXCLUSION CRITERIA:

1] Presence of any neurological disorder including seizure, focal neurological deficit

2] Presence of any psychiatric disorder in present or past

3] Family history of psychiatric illness in first degree relative

TOOLS EMPLOYED:

1] ICD -10 diagnostic criteria [Clinical Description and Diagnostic Guidelines] for OCD

2] The **NEUROLOGICAL EVALUATION SCALE –NES** for assessment of presence of neurological soft signs and scoring each item

3] YBOCS symptom checklist and YBOCS scale as part of routine assessment to study symptom profile in patients

4] Semi structured pro forma to collect information regarding socio demographic profile in both study groups

NEUROLOGICAL EVALUATION SCALE:

NES is a structured instrument for assessment of neurological soft signs devised by Robert W. Buchanan and Douglas W. Heinrichs in 1988.It is a standardized and validated instrument initially proposed for assessment of NSS in patients with Schizophrenia with good inter rater reliability.It consists of a battery of 26 items grouped into 3 major domains namely sensory integration, motor coordination, complex motor sequencing and a 4 th division which has other signs including eye

movement abnormalities and frontal release signs.A fixed order of administration and standardized way of assessing each sign and scoring them is provided by the authors.

Each item is scored in a 3 point scale

0=No abnormality

1=mild, but definitive impairment

2=marked impairment

Except for snout and suck reflex which are scored either as 0-present or 2-absent.The scale also includes guidelines for assessment of cerebral dominance.

Of the total 26 items, 14 signs are tested and scored separately for right and left sides of the body. Descriptive guidelines are given for each score to facilitate standardized judgements by the authors themselves. Neurological evaluation scale tends to be one of the most commonly used structured scale for assessment of neurological soft signs in psychiatric conditions. Even though initially devised for assessment in schizophrenic patients it has been widely used in existing studies assessing NSS in

patients with OCD (N Jaafari et al., 2012; Karadag et al., 2011; Mataix-Cols et al., 2003; Poyurovsky et al., 2007).

Of the existing studies nearly 50% have employed structured instrument for assessment of NSS in patients with OCD of which 20% of studies have employed NES with rest of the studies using CNI, PANESS, QNI,Kerbs scale.(N Jaafari et al., 2012) .

METHODOLOGY:

The study got the approval of Institutional Ethics Committee of Madras Medical College. Study details were explained to participants in both study groups meeting the above criteria and members who gave consent to participate in the study were only enrolled into the study and written consent obtained from study participants.

30 consecutive patients meeting ICD-10 diagnosis of OCD and above mentioned inclusion and exclusion criteria were selected from new case OPD in IMH, Rajiv Gandhi Government General Hospital and special clinic in IMH. Diagnosis of all new cases was confirmed by respective unit consultants apart from assessing them individually for the study.

Among the cases selected from Special Clinic consecutive patients were selected, their initial diagnosis was verified from documentation in case sheets and again screened for symptoms before enrolment in the study. Clinical symptom profile of the cases were documented from YBOCS Symptom Check list for obsession and compulsion. YBOCS scale was administered to patients as part of routine assessment.

A thorough neurological examination was done and clear history was obtained from patients and relatives to rule out any neurological illness. Past history of any psychiatric treatment, any history suggestive of the same, substance dependence pattern, family history of psychiatric illness in first degree relative was clearly questioned and subjects were included only after strictly meeting the inclusion and exclusion criteria. Patients were also screened for presence of co morbidity in which except for associated depressive feature which would be part of illness, presence of other co morbidity were excluded. Presence of oblivious neurological co morbidity like tics were also excluded.

Neurological Evaluation Scale was administered to all selected cases and controls for assessment of NSS and scoring was done individually as per the standardized instructions given by the authors who devised the scale. In case of doubtfulness opinion of a senior resident was

sought. Handedness of both groups were assessed by handedness questionnaire in NES scale. In the initial few cases and controls procedure of administration was supervised by a senior resident. Every possibility was taken into account to avoid rater bias as blinding was not done due to methodological constraints.

STATISTICS AND DATA ANALYSIS

A Statistician was consulted prior to onset of study to decide on sample size.

1] Chi-square test was administered to find the significance of proportion of occurrence of individual signs in NES [as their occurrence was marked as absent, minimal impairment, marked impairment]between cases and controls

2] Independent sample t test was administered to find significance in mean total NES score and individual subscale score between patients and controls. As the sample size is 30 ,as per Normality Theorem data would follow normal distribution which was verified by Kolmogorov-Smirnov (K-S) test in SPSS software

3] As patient's age and education were recorded in years of schooling [continuous variable] independent sample t test was employed to compare significance in them between the two groups

4] Gender and socio economic status were recorded as discrete variables and hence Chi square test was employed to test significance.

5] All tests were done in SPSS software version 20 with the help of the statistician and results were tabulated.

RESULTS

TABLE 1

COMPARISON OF AGE, EDUCATIONAL STATUS OF THE PATIENT AND CONTROL GROUP

Variables	GROUP	N	Mean	Std. Deviation	P-Value
AGE (YEARS)	Cases	30	31.40	5.386	0.761
	Controls	30	30.97	5.617	
EDUCATION (YEARS)	Cases	30	10.20	5.281	0.827
	Controls	30	10.47	4.032	

P value -0.05 significant

As seen in the Table-1 total number of cases and controls included in the study were 30 respectively. Among the cases the gender distribution is 19 females [63%] and 11 males [37%] and in the control group 17 females [57%] and 13 males [43%] were present[shown in chart 1 and 2].The mean age of patients with OCD was 31.4 years [SD-5.386] and the mean age of control group was 30.9 years[SD-5.617].The mean duration of education was 10.2 years in cases and 10.47 years in controls. No significant difference is observed in age[p-0.761] and educational status[p-0.827] of the study group.

TABLE 2

COMPARISON OF GENDER, SOCIO ECONOMIC STATUS OF THE PATIENT AND CONTROL GROUP

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
SEX	Male	11	36.7	13	43.3	24	40.0	0.598
	Female	19	63.3	17	56.7	36	60.0	
SOCIO ECONOMIC STATUS	LSES	19	63.3	20	66.7	39	65.0	0.787
	MSES	11	36.7	10	33.3	21	35.0	
MARITAL STATUS	Married	14	46.7	13	43.3	27	45	0.625
	unmarried	16	53.3	17	56.7	33	55	

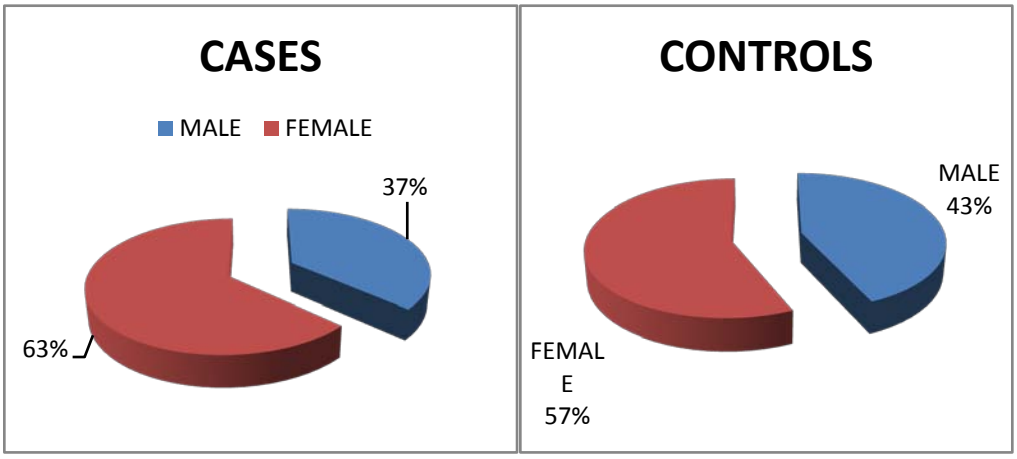
P value <0.05 significant **MSES-middle socio economic status**

LSES-low socioeconomic status

.No statistically significant difference is observed in gender[p-0.59] , educational status [p-0.82] and socio economic status [p-o.78] of both groups as seen in Table-2.[p>0.05].As patient's age and education are measured in years [continuo variable] independent t test was used to compare the mean value between cases and controls whereas socioeconomic status is a categorical variable ,hence chi square test was employed to asses statistical significance .

CHART-1

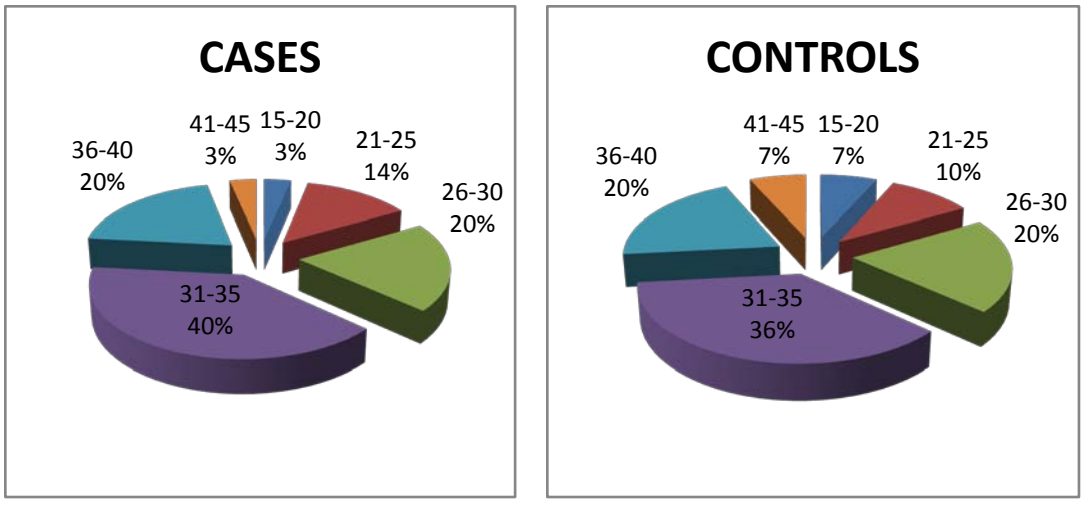
REPRESENTATION OF GENDER DISTRIBUTION IN STUDY GROUPS



1[A] -CASES **1[B]-CONTROLS**

CHART-2

REPRESENTATION OF AGE DISTRIBUTION IN STUDY GROUPS [AGE REPRESENTED IN YEARS]



2[A] -CASES **2[B]-CONTROLS**

TABLE-3

CLINICAL SYMPTOM ANALYSIS AMONG THE PATIENTS

OBSESSIONS	PATIENTS PRESENTING	COMPULSIONS	PATIENTS PRESENTING
CONTAMINATION OBSESSIONS	**47%**	**CLEANING /WASHING COMPULSION**	**47%**
SEXUAL OBSESSIONS	**23%**	**CHECKING COMPULSION**	**20%**
RELIGIOUS OBSESSIONS	**20%**	**COUNTING COMPULSION**	**20%**
OBSESSION WITH EXACTNESS	**13%**	**REPEATING COMPULSION**	**6%**
MISCELLANEOUS	**6%**	**MISCELLANEOUS**	**6%**

In patients symptoms were quantified by YBOCS Symptom Checklist as a part of routine assessment. Most common obsessions among the patients were fear of contamination [47%] , followed by sexual obsessions(sexual thoughts) which was seen almost only in males. No hoarding obsession was noticed among the patient group. ***Most of the patients presented with multiple obsession [63%]*** with combination of contamination obsession and obsession for exactness being more common. As seen in the table -3 ,the most common compulsive symptom was hand washing [47%] followed by checking and counting compulsions.

TABLE-4

ILLNESS VARIABLE IN PATIENTS WITH OCD

MEAN AGE OF PATIENTS	**31.2 YEARS**
MEAN AGE OF ONSET OF ILLNESS	**22.4 YEARS**
YBOCS SCORE [MEAN]	
OBSESSIONS	**12.86**
COMPULSIONS	**12.3**
TOTAL SCORE [MEAN]	**25.16**

TABLE-5

HANDEDNESS AND MEDICATION STATUS IN PATIENT GROUP

	HANDEDNESS				**MEDICATION**			
	RIGHT		**LEFT**		**PRESENT**		**ABSENT**	
STUDY GROUP	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
PATIENTS	**30**	**100**	**0**	**0**	**17**	**57**	**13**	**43**
CONTROLS	**30**	**100**	**0**	**0**	**--**	**---**	**---**	**----**

N-number of sample

As seen in the Table- 5 among the cases and controls ***all members were right handed individual*** as assessed by the Handedness Questionnaire in NES scale.

Among the patients 13 cases [43%] were newly diagnosed cases who were not on any medications. The rest 17 cases [57%] were cases who were on previous treatment .All cases were on SSRI and 3 cases [10%] were also on a antipsychotic medication . YBOCS score was administered as a part of routine assessment and average score is 25.16 with obsessions score 12.8 and compulsion score of 12.3 suggesting the patients clinical profile to be predominantly mixed obsession and compulsion.[as seen in Table-4]

TABLE -6

COMPARISON OF NEUROLOGICAL SOFT SIGN SCORE BETWEEN PATIENTS AND CONTROLS

[TOTAL NES SCORE AND INDIVIDUAL SUB SCALE SCORE]

[Independent sample t test to compare mean of two groups]

NES DOMAIN	GROUP	N	MEAN	SD	P-value
SENSORY INTEGRATION SUB SCORE	Cases	30	2.60	1.958	<0.001*
	Controls	30	0.77	0.898	
MOTOR COORDINATION SUB SCORE	Cases	30	2.97	2.109	<0.001*
	Controls	30	1.10	1.269	
COMPLEX MOTOR SEQUENCING SCORE	Cases	30	4.50	2.301	<0.001*
	Controls	30	1.17	1.802	
TOTAL NES SCORE	Cases	30	13.97	5.887	<0.001*
	controls	30	4.33	3.651	

P value <0.05 –significant *-P value significant

As mentioned NES scale was administered to patients and controls and items were scored exactly as per the instruction given by the authors.[appendix-I]

Total NSS mean score by NES in cases was 13.97 [SD+5.9] and mean NSS score in controls was 4.33[SD+3.7].Mean score in sensory integration, motor coordination, motor sequencing with SD has been mentioned in Table- 6 which was found to be statistically significant on comparing the mean between the two independent samples by independent sample t test[$p<0.01$ in all items].

[also Represented in charts 3,4,5,6]

Taking into account presence of one or more of the soft sign as markedly impaired [maximum score of 2] about 57% of patients had presence of at least one soft sign in contrast to 10 % of control group. On including minimal impairment but definitely present[score of 1] in to consideration about 67% of patients and 16% of controls reported positive soft sign overall.

"TOTAL NES SCORE WHICH GIVES PRESENCE OF NSS IS HIGHLY SIGNIFICANT IN CASES COMPARED TO CONTROLS [P<0.01]"

CHART-3

COMPARISON OF TOTAL MEAN NES SCORE AMONG PATIENTS AND CONTROL GROUP

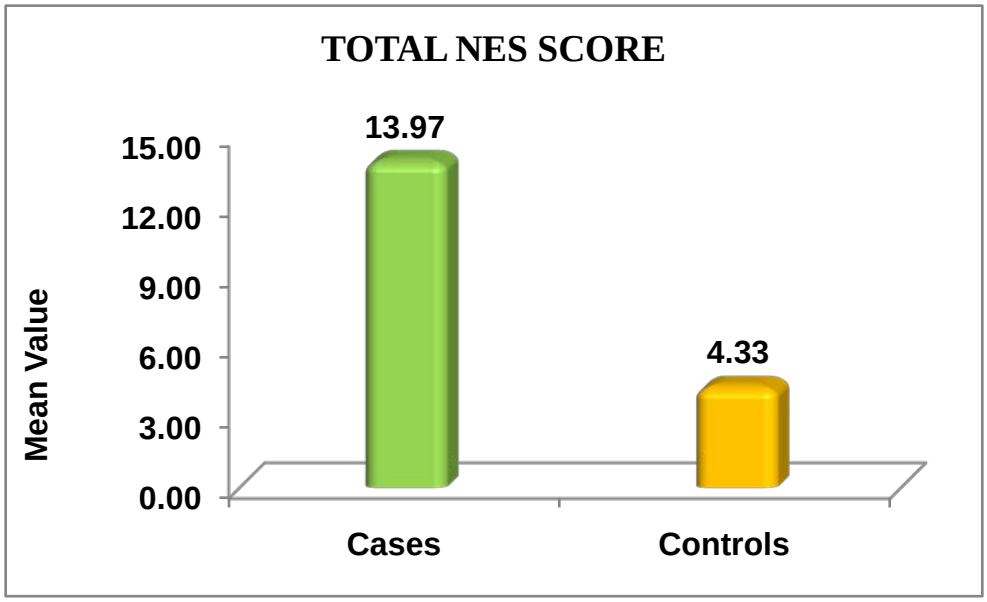
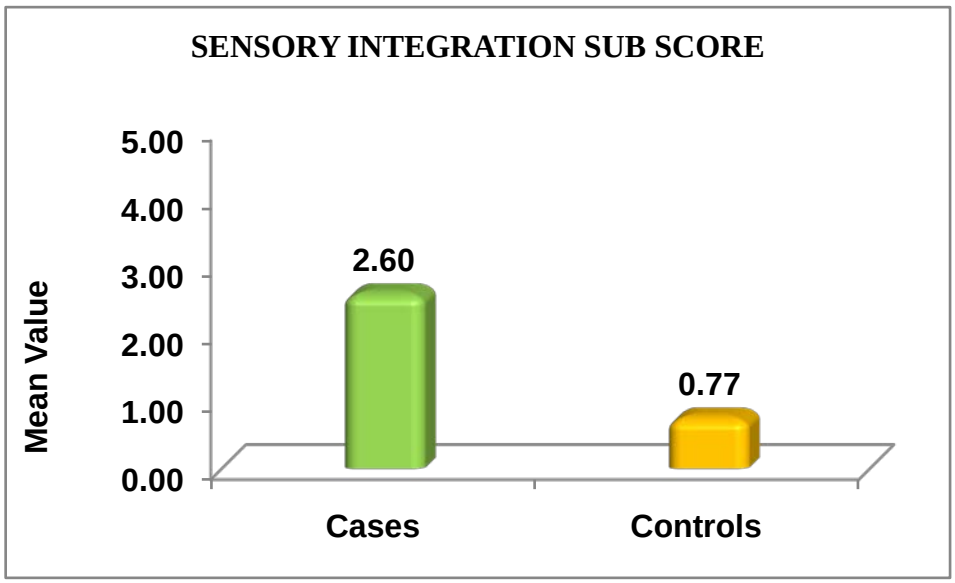


CHART-4

COMPARISON OF MEAN SENSORY INTEGRATION SUBSCORE BETWEEN PATIENTS AND CONTROLS



*-values represent score in NES scale. Mean of total score was represented

CHART-5

COMPARISON OF MEAN SCORE IN MOTOR COORDINATION DOMAIN*

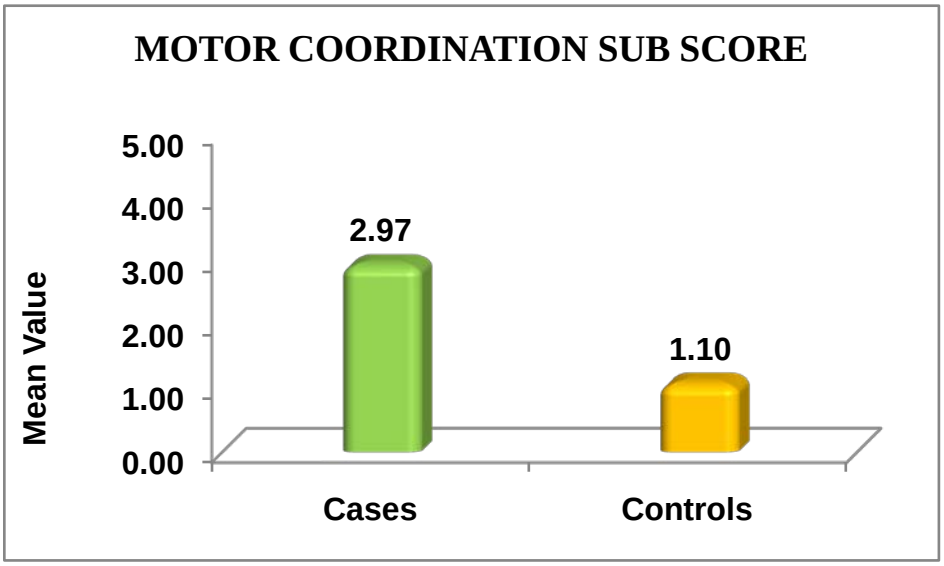
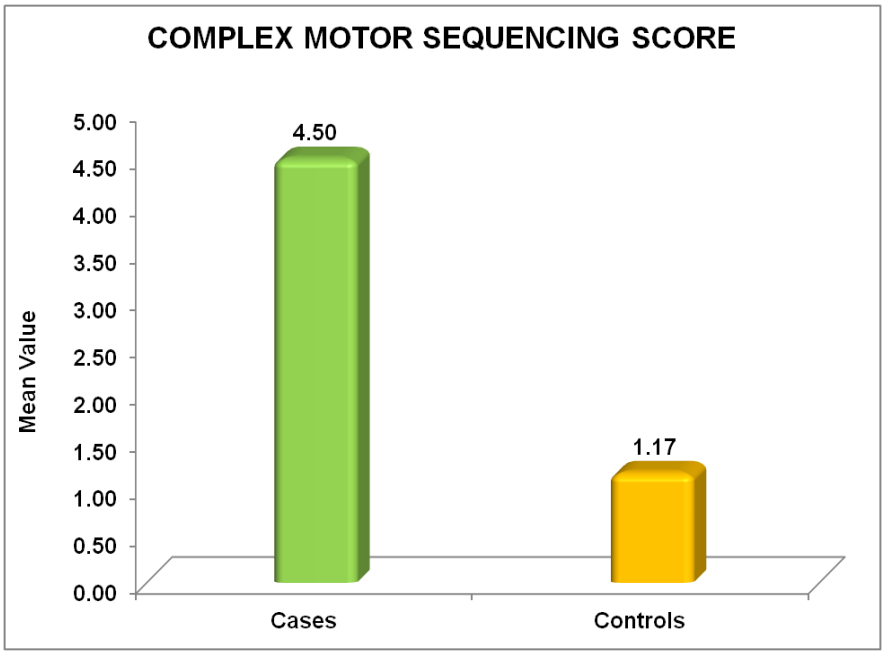


CHART-6

COMPARISON OF MEAN SCORE IN COMPLEX MOTOR SEQUENCING DOMAIN*



***Values represent score in NES scale items. Mean of total score was represented**

TABLE -7

COMPARISON OF SENSORY INTEGRATION DOMAINS BETWEEN PATIENTS AND CONTROLS

SENSORY INTEGRATION DOMAIN		GROUPS				TOTAL		P-VALUE
		CASES		CONTROLS				
		N	%	N	%	N	%	
AUDIO-VISUAL INTEGRATION	A	11	36.7	23	76.7	34	56.7	<0.001*
	B	4	13.3	5	16.7	9	15.0	
	C	15	50.0	2	6.7	17	28.3	
STEREO GNOSIS: RIGHT	A	27	90.0	29	96.7	56	93.3	0.612
	B	3	10.0	1	3.3	4	6.7	
STEREO GNOSIS: LEFT	A	27	90.0	29	96.7	56	93.3	0.612
	B	3	10.0	1	3.3	4	6.7	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **P<0.05 significant** ***-P value significant**

In sensory integration domain, out of the 5 items in NES scale (appendix-I) stereo gnosis, graphesthesia were assessed in both sides of the body and scored.

As noticed in the Table -7 no statistically significant difference was observed in impairment in stereo gnosis [p-0.612] In audio visual integration [p-0.022] statistically significant difference was noticed in impairment in cases compared to controls.

TABLE -8

COMPARISON OF SENSORY INTEGRATION SIGNS BETWEEN PATIENTS AND CONTROLS

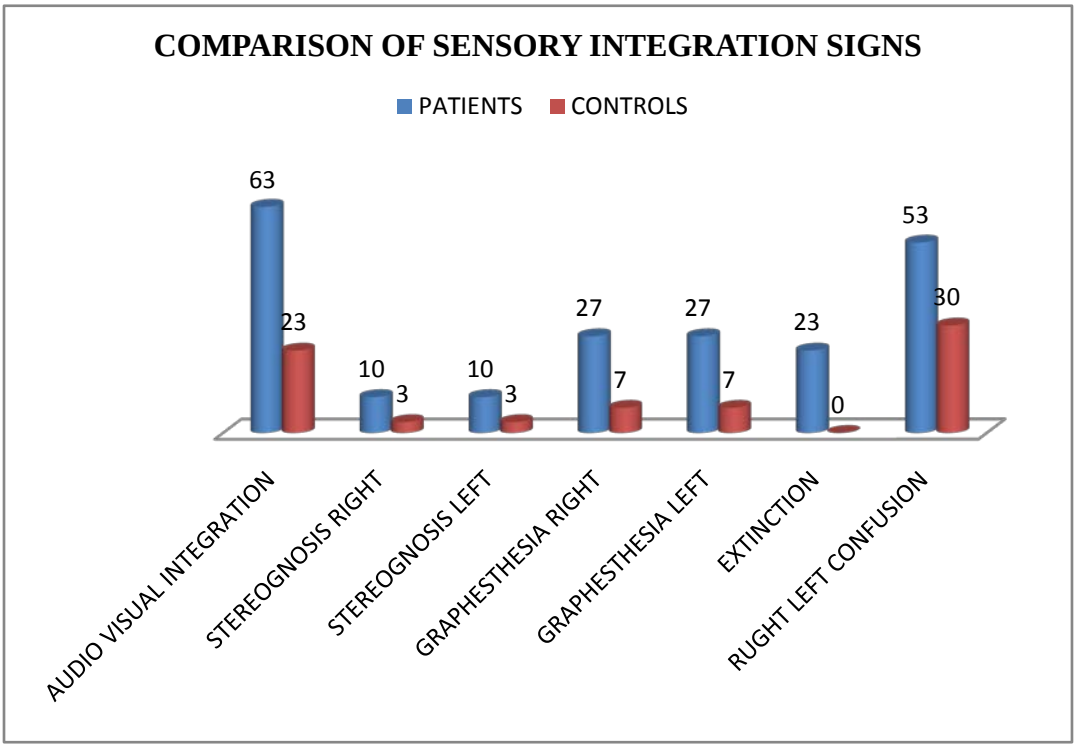
		GROUPS				TOTAL		P-VALUE
		CASES		CONTROLS				
		N	%	N	%	N	%	
GRAPHESTHESIA: RIGHT	A	22	73.3	28	93.3	50	83.3	0.022*
	B	4	13.3	2	6.7	6	10.0	
	C	4	13.3	0	0.0	4	6.7	
GRAPHESTHESIA: LEFT	A	22	73.3	28	93.3	50	83.3	0.022*
	B	4	13.3	2	6.7	6	10.0	
	C	4	13.3	0	0.0	4	6.7	
EXTINCTION	A	23	76.7	30	100.0	53	88.3	0.011*
	B	7	23.3	0	0.0	7	11.7	
Rt-Lt CONFUSION	A	14	46.7	21	70.0	35	58.3	0.160*
	B	10	33.3	7	23.3	17	28.3	
	C	6	20.0	2	6.7	8	13.3	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **p<0.05 significant** ***-significant**

As seen in the table 8 ,in testing of right left disorientation there was no significant difference[p-0.160] in impairment in cases compared to controls. In the signs of graphesthesia [0.022] and sensory extinction [0.011] ,significant impairment was seen in cases with OCD compared to controls.

CHART-7

REPRESENTATION OF IMPAIRMENT IN SENSORY INTEGRATIVE SIGNS IN PATIENTS AND CONTROLS



Numbers denoting the columns were percentage of patients and controls showing impairment in particular sign [both definitive and marked impairment].

No significant difference was observed in the effect of laterality on presence of soft signs. In patients 63% had impairment in audio visual integration with 50% having marked impairment compared to 23% having impairment in controls with 7% having marked impairment.

As shown in the chart-7, percentage of cases and controls with impairment in individual signs were as follows

In graphesthesia similar result was found on both sides with 26% of patients showing impairment compared to 7% in controls.

In sensory extinction 7% of cases had impairment compared to no impairment being found in controls.

In stereo gnosis even though no significant difference is observed 10% of cases had impairment compared to 3% in controls

In right left confusion both patients and controls had impairment with 53% in cases and 30% in controls

TABLE-9

COMPARISON OF MOTOR COORDINATION DOMAIN BETWEEN PATIENTS AND CONTROLS

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
TANDEM WALK	A	14	46.7	20	66.7	34	56.7	0.045*
	B	11	36.7	10	33.3	21	35.0	
	C	5	16.7	0	0.0	5	8.3	
RAPID ALTERNATING MOVEMENTS: RIGHT	A	12	40.0	22	73.3	34	56.7	0.003*
	B	12	40.0	8	26.7	20	33.3	
	C	6	20.0	0	0.0	6	10.0	
RAPID ALTERNATING MOVEMENTS: LEFT	A	9	30.0	22	73.3	31	51.7	<0.001*
	B	15	50.0	8	26.7	23	38.3	
	C	6	20.0	0	0.0	6	10.0	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **p<0.05 --significant** ***-significant P value**

TABLE-10

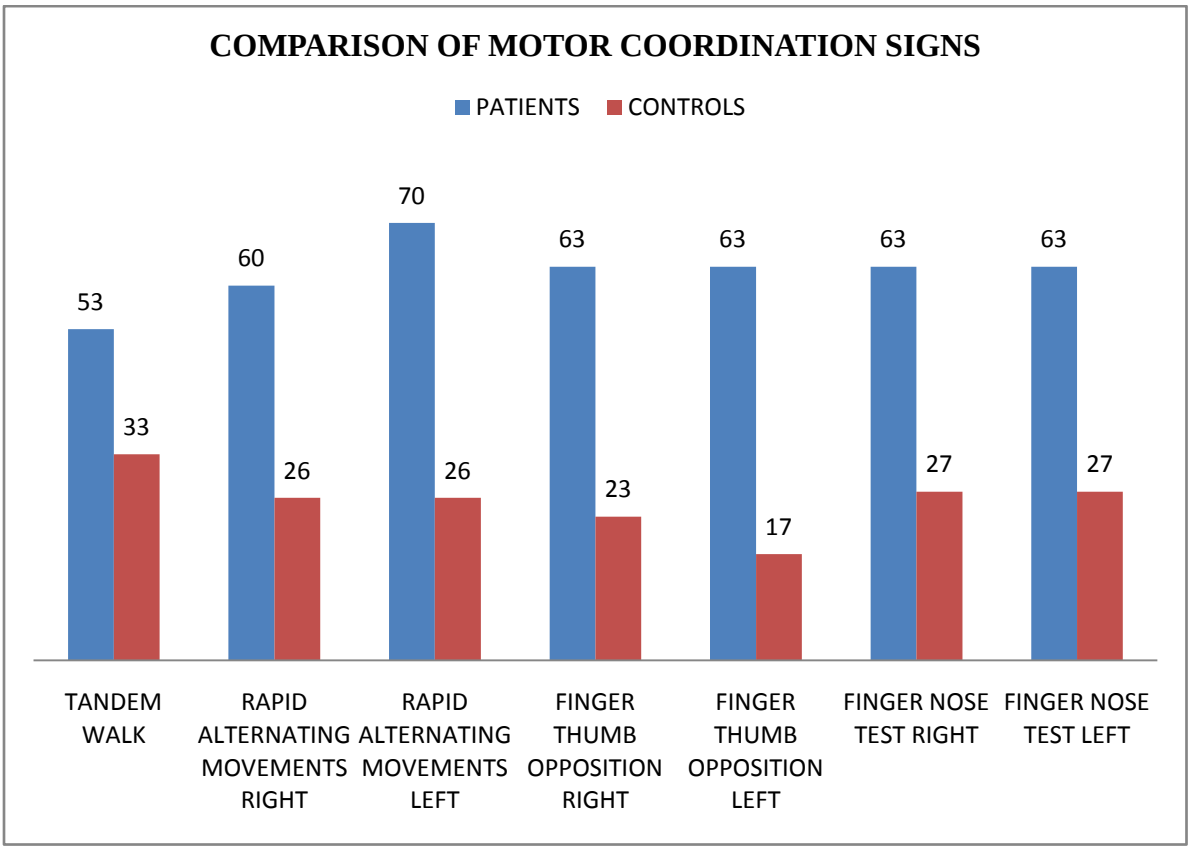
COMPARISON OF MOTOR COORDINATION SIGNS BETWEEN PATIENTS AND CONTROLS

		GROUPS				TOTAL		P-VALUE
		CASES		CONTROLS				
		N	%	N	%	N	%	
FINGER THUMB OPPOSITION: RIGHT	A	11	36.7	23	76.7	34	56.7	0.002
	B	16	53.3	7	23.3	23	38.3	
	C	3	10.0	0	0.0	3	5.0	
FINGER THUMB OPPOSITION: LEFT	A	11	36.7	25	83.3	36	60.0	<0.001
	B	14	46.7	5	16.7	19	31.7	
	C	5	16.7	0	0.0	5	8.3	
FINGER NOSE TEST: RIGHT	A	11	36.7	22	73.3	33	55.0	0.004
	B	16	53.3	8	26.7	24	40.0	
	C	3	10.0	0	0.0	3	5.0	
FINGER NOSE TEST: LEFT	A	11	36.7	22	73.3	33	55.0	0.004
	B	16	53.3	8	26.7	24	40.0	
	C	3	10.0	0	0.0	3	5.0	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **p<0.05 significant** ***-P value significant**

CHART-8

REPRESENTATION OF IMPAIRMENT IN MOTOR COORDINATION SIGNS BETWEEN PATIENTS AND CONTROLS



Numbers indicate percentage of impairment in patients and controls in total for individual signs

Among the 4 signs in the motor coordination sub group, rapid alternating movements, finger thumb opposition, finger nose test were assessed on both sides of the body. As seen in the above table -9, statistically significant difference was found in presence of impairment in signs of tandem walk[p-0.045] and rapid alternating movements[p-0.003].In rapid alternating movements even though difference has been noticed in scoring over both half of body, no significance could be found in impairment over both half of the body .

As seen in above table -10 and chart- 8 a significant difference has been observed in the impairment of finger nose test[p -0.004 &p-0.004] and in finger thumb opposition[p-0.002 & p<0.001] with impairment in both sides having equally significant difference in cases compared to controls

In tandem walk test, 44% of patients had positive sign when compared to 33% of controls with no marked impairment in any of them. In rapid alternating movements, about 70 % of patients had impairment with 20 % having marked impairment compared to 27 % in control group among which none of them had marked impairment.[chart-8]

In finger nose test ,63% of patients had positive sign as opposed to 27 % in controls with 10% of cases having marked impairment in performance compared to controls. In finger thumb opposition, 64% patients had positive sign with 17 % having marked impairment compared to 17 % minimal presence in controls.

TABLE-11

COMPARISON OF COMPLEX MOTOR SEQUENCING DOMAINS BETWEEN PATIENTS AND CONTROLS

		GROUPS				TOTAL		P-VALUE
		CASES		CONTROLS				
		N	%	N	%	N	%	
OZERETSKI TEST	A	8	26.7	24	80.0	32	53.3	<0.001*
	B	11	36.7	4	13.3	15	25.0	
	C	11	36.7	2	6.7	13	21.7	
RHYTHM TAPPING TEST B	A	16	53.3	25	83.3	41	68.3	0.004*
	B	7	23.3	5	16.7	12	20.0	
	C	7	23.3	0	0.0	7	11.7	

A=no abnormality[score-0] B=mild but definite impairment [score-1]
C=marked impairment [score-2] P<0.05 significant *-P value significant

TABLE-12

COMPARISON OF COMPLEX MOTOR SEQUENCING DOMAIN BETWEEN PATIENTS AND CONTROLS

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
FIST RING TEST: RIGHT	A	8	26.7	21	70.0	29	48.3	<0.001 *
	B	5	16.7	7	23.3	12	20.0	
	C	17	56.7	2	6.7	19	31.7	
FIST RING TEST: LEFT	A	9	30.0	21	70.0	30	50.0	<0.001 *
	B	3	10.0	5	16.7	8	13.3	
	C	18	60.0	4	13.3	22	36.7	
FIST EDGE PALM: RIGHT	A	7	23.3	21	70.0	28	46.7	<0.001 *
	B	4	13.3	7	23.3	11	18.3	
	C	19	63.3	2	6.7	21	35.0	
FIST EDGE PALM: LEFT	A	7	23.3	19	63.3	26	43.3	<0.001 *
	B	4	13.3	8	26.7	12	20.0	
	C	19	63.3	3	10.0	22	36.7	

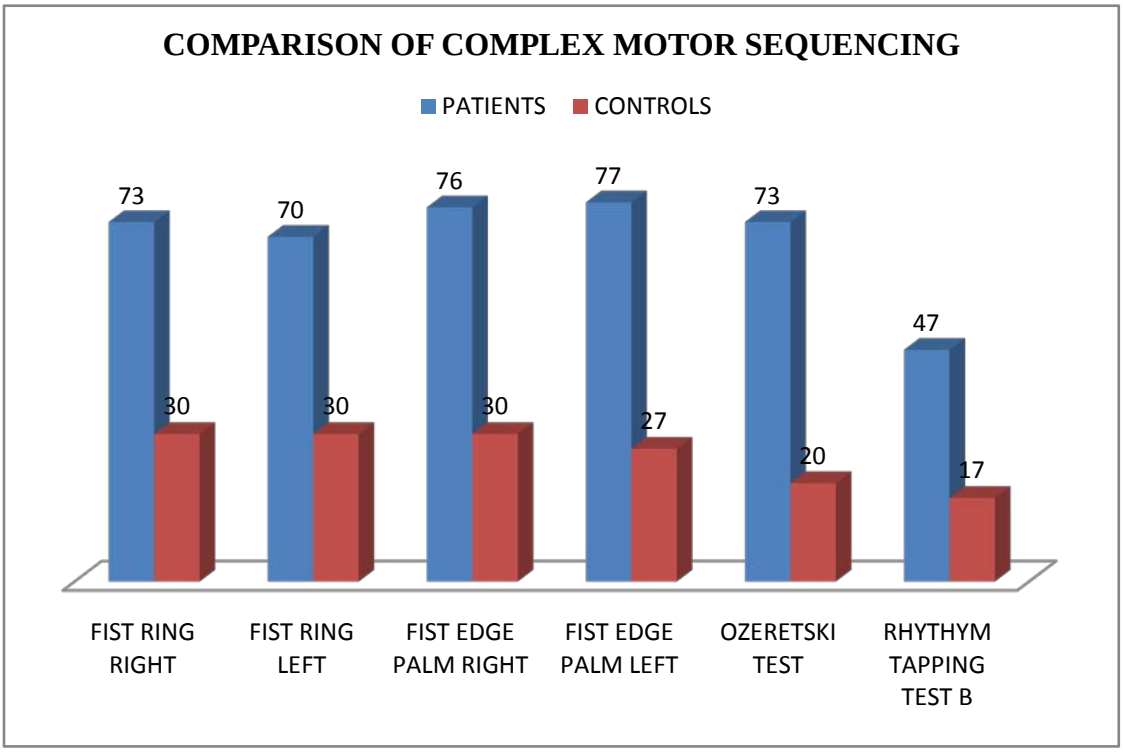
A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **P<0.05 significant** ***-P value significant**

Among the soft signs under the motor sequencing sub score, fist ring test and fist edge palm test as noticed in the table-11 above , a statistically significant impairment is observed in cases compared to controls [$p<0.001$ in both signs]

In fist ring test and fist edge palm test which were tested separately in both half of the body , significant difference was observed in both sides even though slight variation is observed in scoring and degree of impairment. As seen in the above table-12 in both Ozeretski Test[$p<0.001$] and Rhythm Tapping test B [p-0.004] significant .[as seen in table-12]In fist- ring test 73% of patients had impairment with a high rate of 56% having marked impairment compared to 30% positivity in controls with 7% having maximum impairment In fist edge palm 76% of patients had impairment of which 63% having severe impairment compared to 30% and 7% in controls. In ozeretski test 73% of patients had impairment of which 37% had severe impairment compared to 20% and 7% in controls.In rhythm tapping test B 46% of patients had impairment of which 23 % had severe impairment compared to 17% in controls with none of them having severe impairment. Representation of impairment in individual signs is shown in the chart – 9 below. No significant difference observed in lateralisation of the soft signs under this domain

CHART-9

REPRESENTATION OF IMPAIRMENT IN MOTOR SEQUENCING DOMAIN IN PATIENTS AND CONTROLS



Numbers indicate percentage of impairment in individual signs in patients and controls

TABLE-13

COMPARISON OF OTHER DOMAINS IN NES SCALE BETWEEN PATIENTS AND CONTROLS

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
ADVENTITIOUS OVERFLOW: RIGHT	A	24	80.0	27	90.0	51	85.0	0.213
	B	3	10.0	3	10.0	6	10.0	
	C	3	10.0	0	0.0	3	5.0	
ADVENTITIOUS OVERFLOW: LEFT	A	24	80.0	27	90.0	51	85.0	0.213
	B	3	10.0	3	10.0	6	10.0	
	C	3	10.0	0	0.0	3	5.0	
ROMBERG TEST	A	25	83.3	29	96.7	54	90.0	0.138
	B	3	10.0	1	3.3	4	6.7	
	C	2	6.7	0	0.0	2	3.3	
TREMOR: RIGHT	A	26	86.7	29	96.7	55	91.7	0.353
	B	4	13.3	1	3.3	5	8.3	
TREMOR: LEFT	A	26	86.7	29	96.7	55	91.7	0.353
	B	4	13.3	1	3.3	5	8.3	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **$p<0.05$ significant**

TABLE-14

COMPARISON OF OTHER DOMAINS IN NES SCALE BETWEEN PATIENTS AND CONTROLS

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
MEMORY	A	13	43.3	23	76.7	36	60	0.006*
	B	13	43.3	7	23.3	20	33.3	
	C	4	13.3	0	0.0	4	6.7	
RHYTHM TAPPING TEST A	A	16	53.3	26	86.7	42	70.0	0.007*
	B	12	40.0	4	13.3	16	26.7	
	C	2	6.7	0	0.0	2	3.3	
MIRROR MOVEMENTS: RIGHT	A	14	46.7	26	86.7	40	66.7	<0.001*
	B	9	30.0	4	13.3	13	21.7	
	C	7	23.3	0	0.0	7	11.7	
MIRROR MOVEMENTS: LEFT	A	15	50.0	25	83.3	40	66.7	0.003*
	B	9	30.0	5	16.7	14	23.3	
	C	6	20.0	0	0.0	6	10.0	

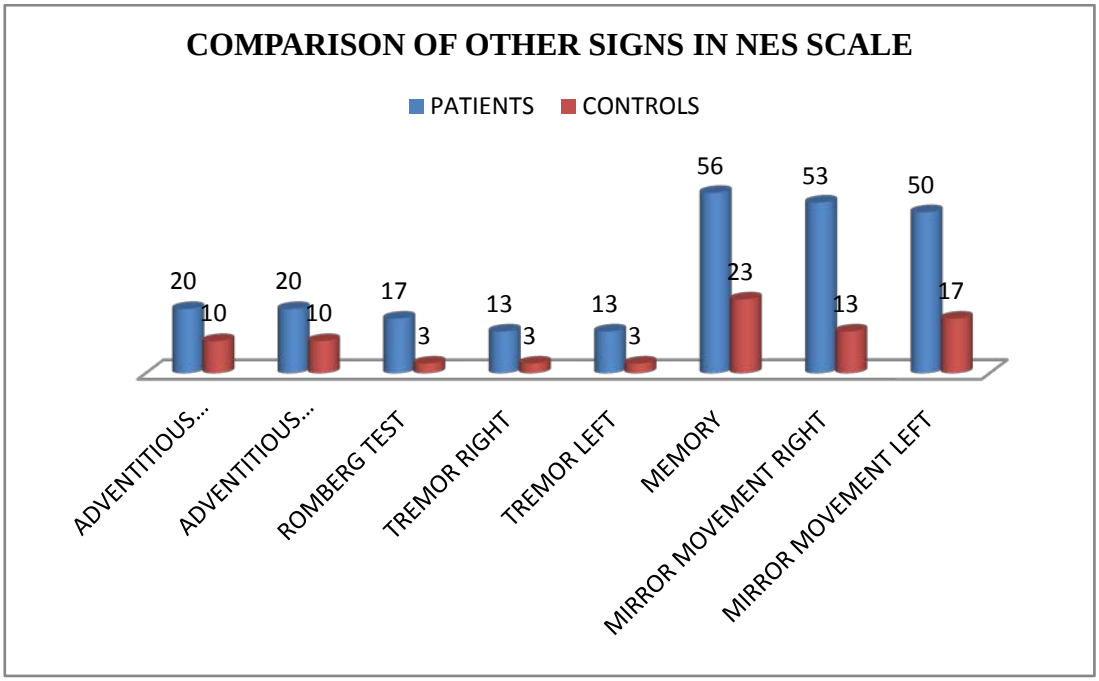
A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **p<0.05 significant** ***-P value significant**

As seen in the above table-13, in adventitious overflow[P-0.213 in both side],Romberg test[0.138],tremor [p-0.353 both sides] was greater than 0.05 and no statistical significance could be found.

As seen in the above table-14 impairment of memory[p-0.06] ,rhythm tapping test A [p-0.007] and mirror movements[p-0.001] has statistical significance. From the above tables-13 and 14 and chart– 10, we could find that Romberg test was positive in 17% of cases compared to 3% in controls. In adventitious overflow 20% of patients and 10% controls had positive sign. Tremors were noticed in 13% of cases compared to 3% in controls over both arms. Significant memory impairment is observed in 56% of cases compared to 23% in controls. Mirror movements were observed in marked level in 53% in right side and 50% in left side of cases compared to 13% in normal controls with marked impairment in 20% of cases and none with severe impairment in controls.

CHART-10

REPRESENTATION OF IMPAIRMENT IN OTHER SIGNS IN PATIENTS AND CONTROLS



Percentage of impairment and presence of soft signs denoted as corresponding number

TABLE – 15

COMPARISON OF EYE MOVEMENT ABNORMALITIES SIGN BETWEEN PATIENTS AND CONTROLS

		GROUPS				Total		P-Value
		Cases		Controls				
		N	%	N	%	N	%	
SYNKINESIS :RIGHT	A	15	50.0	25	83.3	40	66.7	0.001*
	B	3	10.0	5	16.7	8	13.3	
	C	12	40.0	0	0.0	12	20.0	
SYNKINESIS :LEFT	A	15	50.0	24	80.0	39	65.0	0.005*
	B	5	16.7	5	16.7	10	16.7	
	C	10	33.3	1	3.3	11	18.3	
CONVERGENCE RIGHT	A	18	60.0	25	83.3	43	71.7	0.065*
	B	11	36.7	5	16.7	16	26.7	
	C	1	3.3	0	3.3	1	1.7	
CONVERGENCE LEFT	A	18	60.0	25	83.3	43	71.7	0.147*
	B	11	36.7	4	13.3	15	25.0	
	C	1	3.3	1	3.3	2	3.3	
GAZE IMPERSISTANCE: RIGHT	A	17	56.7	27	90.0	44	73.3	0.004*
	B	10	33.3	3	10.0	13	21.7	
	C	3	10.0	0	0.0	3	5.0	
GAZE IMPERSISTANCE LEFT	A	17	56.7	26	86.7	43	71.7	0.010*
	B	10	33.3	4	13.3	14	23.3	
	C	3	10.0	0	0.0	3	5.0	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**

C=marked impairment [score-2] **P<0.05 significant** ***-P significant**

TABLE-16

COMPARISON OF PRIMITIVE REFLEX BETWEEN PATIENTS AND CONTROLS

		GROUPS				TOTAL		P-VALUE
		CASES		CONTROLS				
		N	%	N	%	N	%	
GLABELLAR REFLEX	A	28	93.3	27	90.0	55	91.7	0.999
	B	2	6.7	3	10.0	5	8.3	
SNOUT REFLEX	A1	27	90.0	30	100.0	57	95.0	0.078
	B1	3	10.0	0	0.0	3	5.0	
GRASP REFLEX: RIGHT	A	25	83.3	29	96.7	54	90.0	0.052
	B	0	0.0	1	3.3	1	1.7	
	C	5	16.7	0	0.0	5	8.3	
GRASP REFLEX: LEFT	A	25	83.3	29	96.7	54	90.0	0.052
	B	0	0.0	1	3.3	1	1.7	
	C	5	0.0	1	3.3	1	1.7	
SUCK REFLEX	A1	28	93.3	29	96.7	57	95.0	0.999
	B1	2	6.7	1	3.3	3	5.0	

A=no abnormality[score-0] **B=mild but definite impairment [score-1]**
C=marked impairment [score-2] **A1=absent [score-0]** **B1=present[score-2]**
p<0.05 significant ***-P significant**

In the eye movement abnormalities division, as seen in table-15 three signs namely synkinesis, convergence, gaze impersistence were included all of which were assessed on both sides. No statistically significant difference was observed[p-0.065,0.147] in presence of convergence of eye movement sign in cases compared to controls.

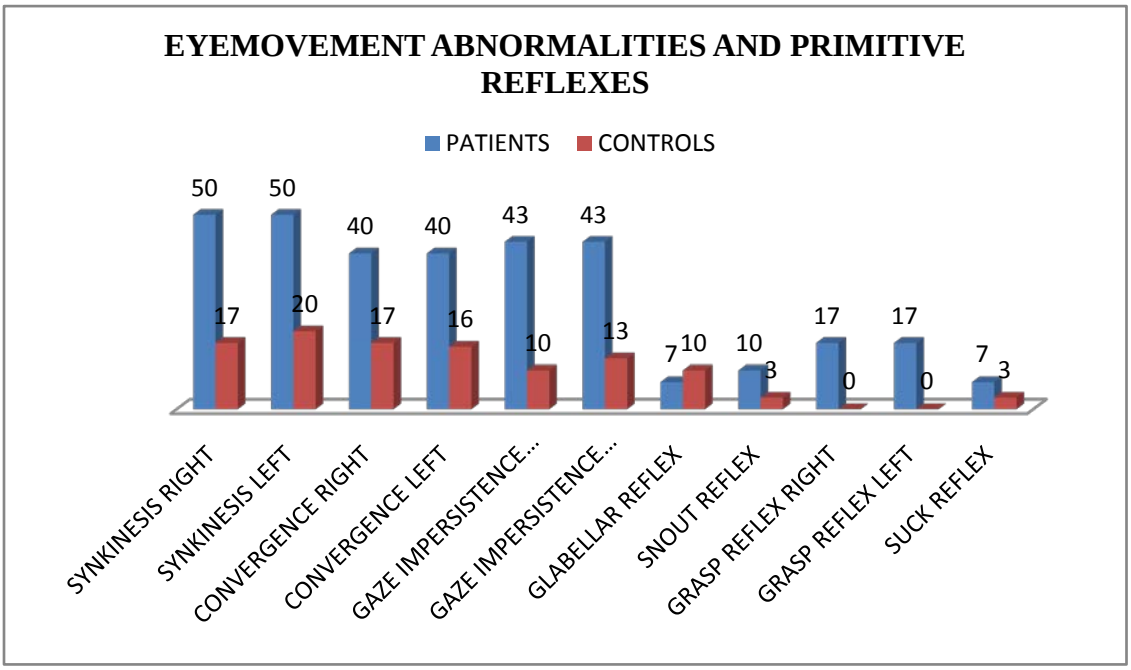
Synkinesis and gaze impersistence were noted to have slight variation over both sides but this was insignificant statistically. significant difference was observed in impairment in cases compared to controls.[refer table 15]A slight variation has been noticed in presence of convergence of eye movements in scoring and presence in both side of the body both of which were not found to have significant difference when compared to controls.

As seen in table-16 glabellar reflex and primitive reflexes like grasp, snout, suck reflexes grasp reflex is scored on both sides in 3 point scale whereas other two reflexes are scored as present or absent. Statistically significant difference was not observed in all 4 reflexes on comparing between cases and controls as mentioned Glabellar reflex[p-0.99] ,snout reflex[p-0.078] and suck reflex [0.99] were not found to have definitive statistical significance. However in grasp reflex p value of 0.052 in both sides should be carefully interpretated as technically speaking it

doesn’t have significance ,it could possibly be on either side and could be due to moderator effect. Among the controls 3% had positive suck reflex and grasp reflex ,7% had positive glabellar reflex and none of them had positive snout reflex whereas in cases 6% had positive glabellar reflex, 10% had snout reflex, 17% had grasp reflex and 7% had positive suck reflex both on comparison did not yield any significance. [chart-11]

CHART-11

REPRESENTATION OF IMPAIRMENT IN EYE MOVEMENT ABNORMALITIES AND PRIMITIVE REFLEXES IN STUDY GROUP



Numbers denote impairment in percentage in individual signs in cases and controls

TABLE-17

COMPARISON OF TOTAL NES SCORE AND INDIVIDUAL SUB SCALE SCORE BETWEEN PATIENTS ON MEDICATION AND DRUG NAÏVE PATIENTS

	ON SSRI	N	Mean	Std. Deviation	P-Value
SENSORY INTEGRATION SUB SCORE	No Drugs	13	1.92	1.656	0.098
	On Drugs	17	3.12	2.058	
MOTOR COORDINATION SUB SCORE	No Drugs	13	2.38	1.557	0.191
	On Drugs	17	3.41	2.399	
COMPLEX MOTOR SEQUENCING SCORE	No Drugs	13	4.38	2.468	0.815
	On Drugs	17	4.59	2.238	
TOTAL NES SCORE	No Drugs	13	12.69	4.461	0.308
	On Drugs	17	14.94	6.750	

P value < 0.05 significant

Among the cases as mentioned in the table , 17 cases were on medication ,mostly on SSRI and rest of the 13 cases were not on any treatment at the time of assessment. In order to rule out the possibility of

drugs being influencing the presence of NSS, an inter group comparison was made in performance of NES scale by independent sample t test.

In summarizing the results as mentioned in table-17 in the mean of total NES score [p-0.308],mean of sensory integration sub score[p-0.098],mean of motor coordination sub score[p-0.191]no statistically significant difference was noted among the NSS domains between drug naïve patients and patients on medications to suggest any possibility of NSS being influenced by the drug intake.[refer chart-5,6,7,8]

CHART-12

COMPARISON OF TOTAL MEAN NES SCORE BETWEEN DRUG NAÏVE PATIENTS AND PATIENTS ON MEDICATION

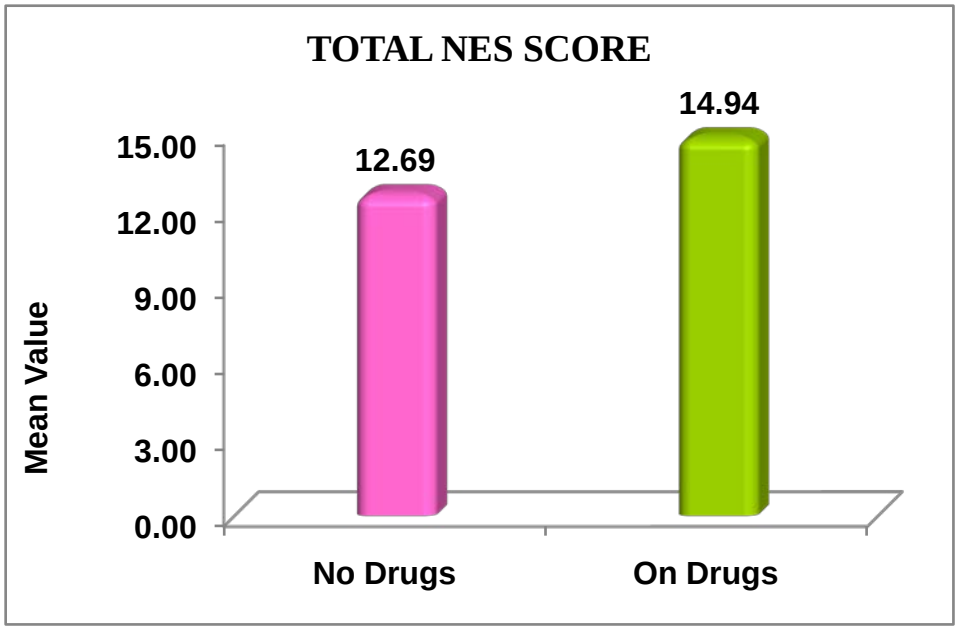
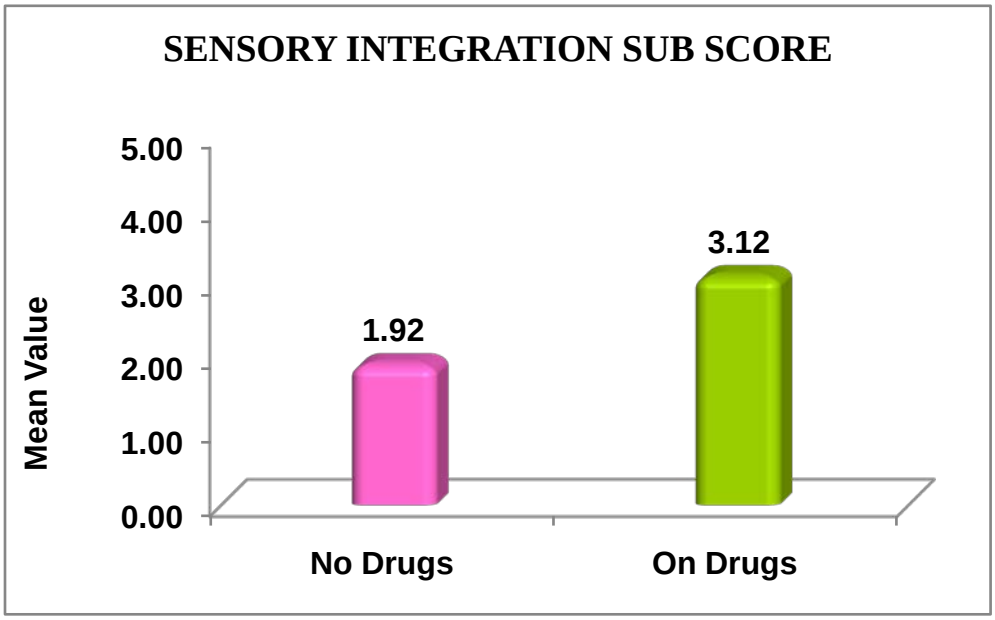


CHART-13

COMPARISON OF TOTAL MEAN SENSORY INTEGRATION SCORE BETWEEN TWO PATIENT GROUPS*



*¬ patients on medication and drug naïve patients

CHART-14

COMPARISON OF TOTAL MEAN MOTOR COORDINATION SUB SCORE BETWEEN TWO PATIENT GROUPS*

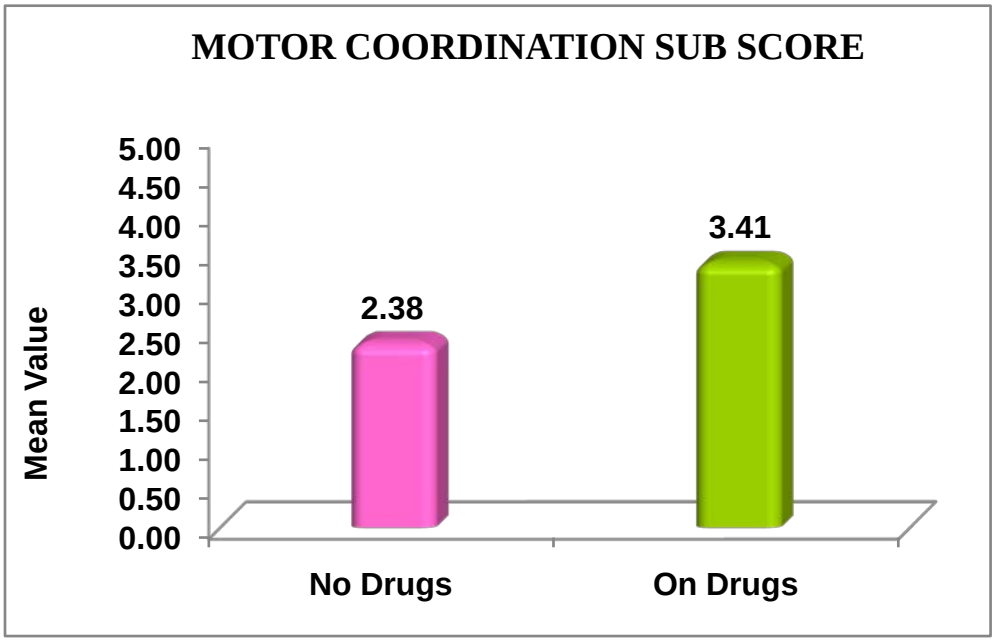
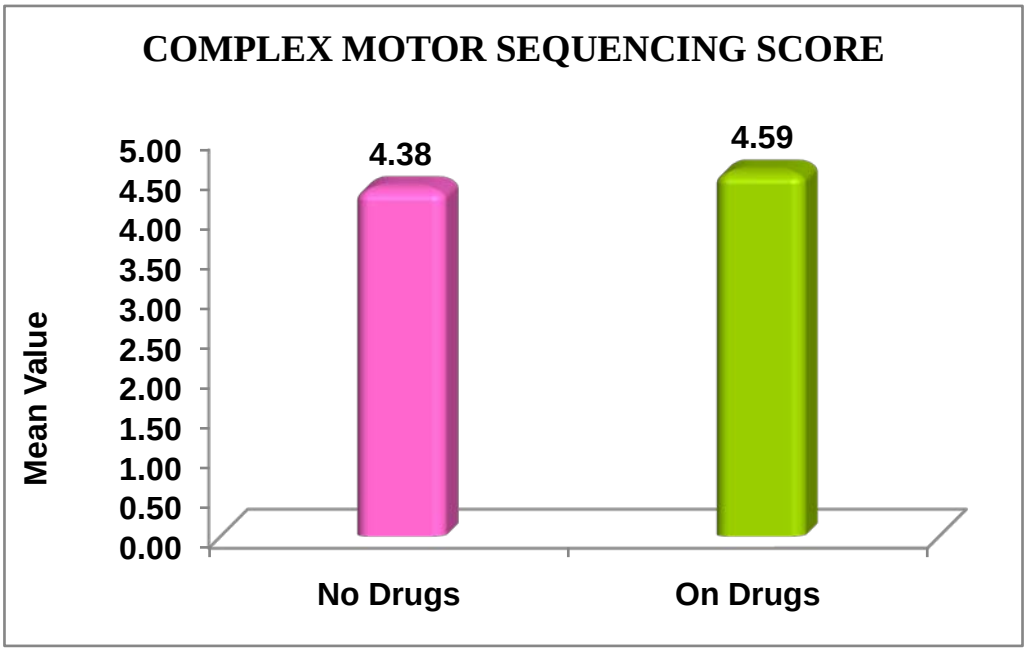


CHART-15

COMPARISON OF TOTAL MEAN COMPLEX MOTOR SEQUENCING SCORE BETWEEN TWO PATIENT GROUPS



DISCUSSION

Neurological Soft Signs [NSS] are one particular entity in which enormous studies have been done in relation to psychiatric disorders. As mentioned earlier they have undergone drastic change in their concept particularly with their study in schizophrenia .The concept of non specific, non localizable signs and use of the term ‘soft’ appears to be be a misnomer indicating only our soft thinking in completely understanding their presence.

Many studies have set the platform in establishing their role in understanding hereditary basis in certain psychiatric conditions, linking to structural correlates in brain with imaging techniques, correlating to neurobiological and neuro cognitive impairment and as a predictor of treatment response and prognosis.

In spite of such huge change in their basic concept ,in anxiety spectrum disorders NSS has received less focus when compared to psychosis spectrum and Child Psychiatry. OCD leads the way in anxiety spectrum disorders in studying their relation to NSS .Studies have focused on various aspects from establishing the significant relation of NSS in

patients to the extent of predicting treatment response and prognosis as mentioned earlier.(Eric Hollander et al., 2005)

Existing literature is also not as uniform and as convincing as they are established in schizophrenia. (Bombin et al., 2005)The initial step of identifying significance in the presence of NSS in OCD patients compared to normal controls is supported by various studies(Bolton et al., 2000; Guz & Aygun, 2004; E Hollander et al., 1990; Mataix-Cols et al., 2003; Poyurovsky et al., 2007),still there eludes a clear consensus as varying reports have been documented till date supporting the other side of the debate also.(Nematollah Jaafari et al., 2011; Stein et al., 1994)

The main objective of the study is to take the first step in knowing about the presence of neurological soft signs in patients with OCD compared to normal matched controls .As mentioned by Jaafari et al, most of the studies involving NSS in OCD have taken into account only clinical examination schedule. To avoid such discrepancies standardised and well validated Neurological Evaluation Scale was advocated in this study which gives clear guiding instruction to record abnormality and score them. Patients were selected strictly on the basis of ICD-10 diagnostic criteria and they were screened to exclude other psychiatric co morbidities like psychosis, substance dependence pattern and severe depression that

would have become a confounding factor in influencing the results. As NSS are reported to be significantly associated with first degree relatives of patients with psychosis(Dazzan & Murray, 2002) , those with family history of psychosis were also excluded. Considering the fact the fact that NSS are relatively increased in children which would disappear by age (Vitiello et al., 1990)and reports of higher incidence in old age both groups were excluded from the study.

It was found that patients with OCD differ significantly from normal , age, sex. and handedness matched controls on total score and the three subscale scores. This is consistent with previous studies in finding a significant difference in total score.(Bolton et al., 1998; Chen et al., 1995; Guz & Aygun, 2004; E Hollander et al., 1990; Mataix-Cols et al., 2003; Salama HM,Saad Allah HM, 2008)

It is in contrary to few studies that have reported no significant difference(Nematollah Jaafari et al., 2011; Stein et al., 1994) which could be due to some studies employing only clinical schedule, some using other scale like PANESS which includes comparatively less domains of soft signs except for one study that employed NES in which the study included OCD, schizophrenia ,normal control groups and found patients with OCD

had no significant difference in NSS compared to controls(Nematollah Jaafari et al., 2011)

Among the subscale score ,in the domain of sensory integration signs , result of the current study is similar to previous studies as most of the studies which found significant relation for total NSS score also reported significant relation to sensory integration sub score.(Bolton et al., 1998; Guz & Aygun, 2004; E Hollander & Rosen, 2000)

In motor coordination signs, result of the current study differs from few studies that found no significant presence of impaired motor coordination(Guz & Aygun, 2004; Sevincok et al., 2006; Stein et al., 1994) . This could be possibly due to scale used as current study employed NES scale whereas rest of the studies used PANESS and clinical schedule. Studies which employed NES and other commonly used validated CNI have found significant impairment in motor coordination (Mataix-Cols et al., 2003)similar to the current study as both these scales include most of the documented soft signs after careful research. Result of the current study is also similar to many studies reporting significant difference in motor coordination(E Hollander et al., 1990; Lees et al., 1991; Salama HM,Saad Allah HM, 2008). In complex motor sequencing domain, the finding of higher statistical significance was similar to results

of poyurovsky et al and other studies(Karadag et al., 2011; Mataix-Cols et al., 2003; Salama HM,Saad Allah HM, 2008).

TABLE-18

TABLE SHOWING SIGNIFICANT DIFFERENCE IN INDIVIDUAL SIGNS IN THE STUDY

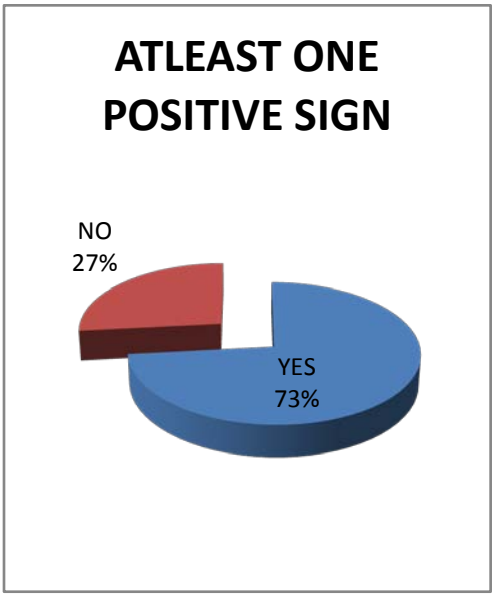
Individual signs that had significant difference in cases of OCD	***Individual signs with no significant difference***
1] Audio-Visual Integration	1] Stereo gnosis*
2]Graphesthesia*	2] Right-Left Confusion
3] Extinction	3] Tremors*
4] Right Left Confusion	4] Romberg Test
5] Tandem Walk	5] Adventitious Overflow*
6] Rapid Alternating Movements*	6] Glabellar Reflex
7] Finger Thumb Opposition*	7] Suck Reflex
8] Fist Ring Test*	8] Snout Reflex
9] Fist Edge Palm Test*	9] Grasp Reflex**
10] Ozeretski Test	10] Convergence
11] Rhythm Tapping Test A	
12] Rhythm Tapping Test B	
13] Memory Impairment	
14] Synkinesis*	
15] Gaze Impersistence*	
16] Finger Nose Test*	

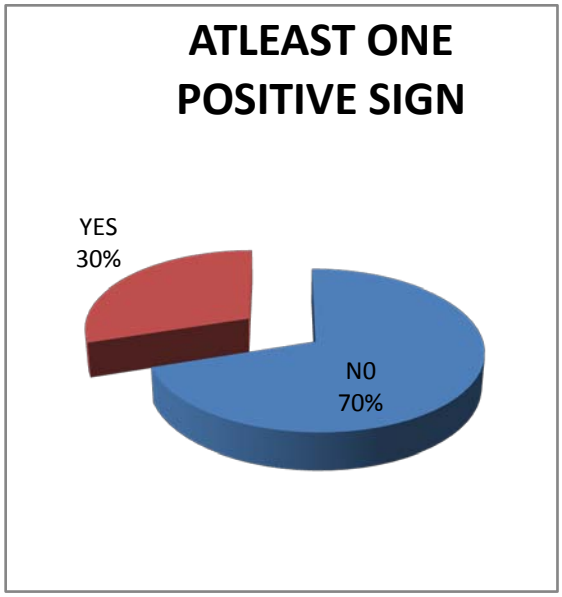
P value<0.05 is significant *-tested over both sides of body

**-p-0.052 has to be cautiously interpreted

CHART-16

REPRESENTATION OF NSS IN PATIENTS AND CONTROLS

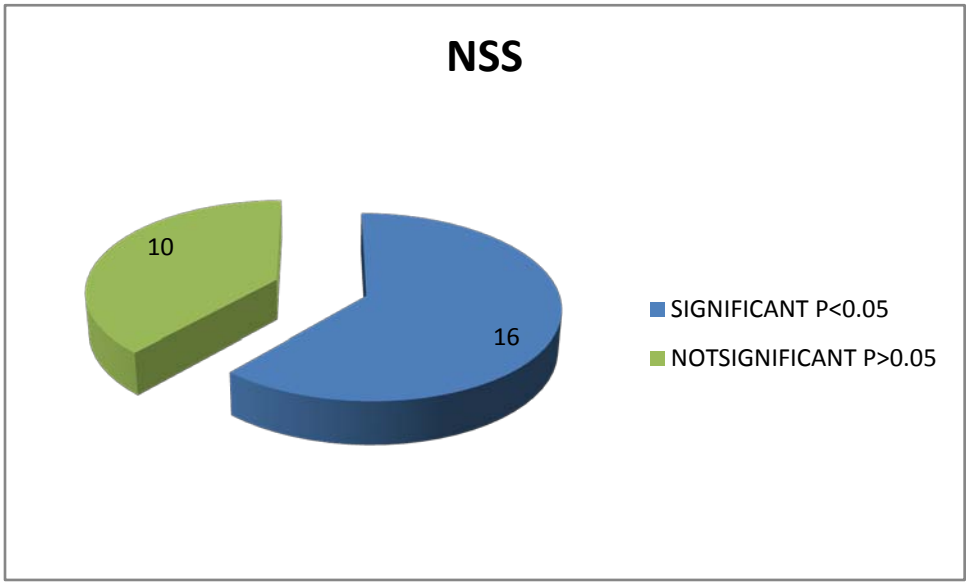




[A] -CASES **[B] –CONTROLS**

CHART-17

REPRESENTATION OF NSS IN PATIENTS



16 out of total 26 signs is significantly present in patients compared to controls

Apart from these results, percentage of OCD patients having a positive sign is higher than for controls on all 41 items measured with difference being significant in 25 items. When combining the signs measured in both sides into one single entity ,in 16 out of the 26 items a significant difference is observed as mentioned in the above table- and chart -16 and 17 . Taking into account presence of one or more of the soft sign in maximum score as positive about 57% of patients had soft sign in contrast to 10 % of control group. On including minimal impairment into consideration about 73% of patients and 30% of controls reported positive soft sign. In normal controls about 5% prevalence has been observed and about 50% in schizophrenia (Buchanan & Heinrichs, 1989).Studies have found NSS to be lower when compared to schizophrenia(Bolton et al., 1998; Poyurovsky et al., 2007; Sevincok et al., 2006) which is against the current result. This has to be carefully assessed as sample size might be the reason for such varying presentation or over representation in current sample

With regards to individual items data of only few studies have mentioned about score and positivity in individual items. The significant difference observed in graphesthesia, tandem walk, all tests of motor sequencing, mirror movements, eye movement abnormalities is similar to

previous studies. Guz et al reported significant association in sensory integration particularly with graphesthesia and not in stereo gnosis which has been found in the current study also.(Guz & Aygun, 2004)

Another contradicting finding from other studies is arriving at a conclusion of no significant difference in occurrence of primitive reflex as most studies have found significant difference.(Bolton et al., 1998; Chan & Gottesman, 2008; Karadag et al., 2011; Mergl R, 2005; Salama HM,Saad Allah HM, 2008).Only few studies have mentioned about lack of significant difference(Mataix-Cols et al., 2003).This could be due to strict criteria in assessment in NES scale and small representation of OCD sample

Regarding eye movement abnormalities lack of significance in convergence is similar to finding of the previous study which have concluded only mild impairment in smooth pursuit movement not as significant as they are considered in schizophrenia. Inconsistencies have been noticed in existing studies but they have concluded eye movement abnormalities not to be as significant needing further research. In similar view current study also concludes in arriving at significance in 2 out of 3 domains(Jaafari N, Rigalleau F, 2011; Nickoloff, Radant, Reichler, & Hommer, 1991)

These fact that total score and individual sub score being highly significant but ten of the individual sign found to have no significant difference could be due to following reasons:

1] High scoring in the motor sequencing tests to the level of maximum impairment could have influenced overall total score. Considering the performance of motor sequencing and other motor domains could be influenced by the distress associated with disease per se ,either assessing them in follow up or comparing them with patient having remitted of symptoms would have explained the fact clearly. Neuro cognitive impairment mainly in executive dysfunction has been well documented ,which favours the finding of significant high scoring in this domain in current study.

2] The other possibility could be the lack of blinding of the rater to the study groups. Meta analysis revealing only very few studies having been done with blinding, even though significant result have been shown in studies with strict criteria supports this current study .As overall

subscale score being significant and individual functioning domain is also significant ,the individual items that are found to have no significant

difference could not be neglected altogether considering the limitation of the studies particularly blinding being not done.

On comparing with studies done with validated instruments our finding of significant total score is similar to most of the studies differing only from Jaffari et al. In the domain of sub scale analysis finding of significant difference in all subscales in patients with OCD has been reported exactly in certain previous studies. Overall results of this study is similar to majority of available literature with slight inconsistency in certain aspects of soft signs but not in soft signs as a whole. This could be due to inter-rater variation, different scales being used, heterogenicity of the OCD disease per se and the study being a cross sectional rather than a follow up study, as some study patients who scored highly could be a forerunner for psychosis.

In laterality of soft signs this study is consistent with previous studies majority of which found no significant difference in lateralisation of soft signs(Bolton et al., 1998; Buchanan & Heinrichs, 1989; Guz & Aygun, 2004).Certain difference is noticed only in scoring the signs rather than overall presence which could be due to rater bias and could have been clarified with inter -rater validity.

Regarding the debate of whether the soft signs are due to effect of medication adverse effects or influenced by medication effect or present independently of medication status ,this study supports the third hypothesis as do the majority of previous study.(Bihari K,Pato MT,Hill JL, 1991; Karadag et al., 2011; Khanna, 1991; Salama HM,Saad Allah HM, 2008)A strict protocol of employing mean daily dosage of drugs, duration of intake ,including individual drugs in future study will refine the result further. As noticed in the results section none of the individual signs had significant difference in patients taking medication and drug naïve patients. Other factors which were initially considered to influence NSS like sociodemographic profile, sex, age, educational status has been found not to have any significant difference in both study groups.

Bombin et al in systematic review suggested the putative localization for these signs .Sensory integrative signs represents parietal lobe functions, which hosts primary sensory functions .Motor coordination sings represents frontal lobe and cerebellar function. Complex motor sequencing acts represents pre frontal lobe function and primitive reflexes localizable to frontal area(Bombin et al., 2005).Eye movement function point towards frontal cortical basal ganglia function(Jaafari N, Rigalleau F, 2011; Mataix-Cols et al., 2003).Extinction, mirror movements,

impaired motor coordination have also sub cortical and thalamus localization.

A validated clinical examination scale in this current study, revealed impairment in all these domains in patients with OCD .When extra-polated to findings by Bombin et al and others, a frontal-sub cortical-thalamus loop dysfunction could be found which is the basis for neurobiological dysfunction in OCD as evident in current literature. NSS could be taken further to relate to exact localization and structural correlates. NSS being one aspect that has been taking the disorder close to neuro developmental hypothesis from this point it should be taken for further research in understanding the neurobiology of illness and its various aspects. This has to be taken into account carefully considering the limitations as although our primary objective goes with existing literature ,other subscale analysis still eludes clarity .

LIMITATIONS

Even though every possible attempt is made to make the methodology reasonable and flawless, each study has its own limitation

1] First, the rating of Neurological Evaluation Scale is done without blinding for the study groups(cases and controls) which would contribute to administrator /rater bias. Every effort was made to avoid any bias and the guidelines were followed strictly.

2] A sample size of 30 is taken considering the statistical power and past studies. But the samples are representative of both new cases and cases on treatment, with more representation of the latter. An equal representation of both groups would have been useful in assessing the influence of drug intake on NSS

3] OCD as well known is a heterogenous disorder with varying presentation. Considering all patients of OCD into a single group could have been avoided .

4]Rating scale was administered once and no follow up assessment was done as patient with OCD could present with psychotic feature and that will confound the result as previously it has been shown NSS are

increased in patients prone for psychosis in course of illness.(Khanna, Sumant.,venkatasubramanian G., 2003; Skoog & Skoog, 1999)

5] Depression and other co morbidity in OCD certainly has effect on certain task of NSS and cognitive assessment. Eventhough patients were thoroughly screened and patients with MDD were excluded still patients have persisting distress that will certainly have effect in testing and scoring

FUTURE RECOMMENDATIONS

The Current study is only a first step in evaluating the NSS in patients with OCD in comparison to normal controls. Further research has to be taken forward from this step .A few suggestions regarding future studies that could be done with assessment of NSS in patients with OCD are-

1] Patients with OCD could be stratified into groups based on their symptomatology ,insight, medication status and co morbidity. Relation of NSS severity with each stratified group could be assessed which gives idea about NSS in relation to the heterogenous presentation of OCD and possible impact of medication status, co morbidity in NSS score.

2] First degree relatives of patients could also be assessed for presence of NSS compared with control group to know the possibility of genetic basis of NSS, which would further take us a step closer to quantify them as endo phenotypes of OCD

3]Whether NSS precede the development of OCD or a consequence of OCD symptoms-A clear answer to this question by prospective longitudinal studies will throw light on whether NSS are neuro developmental risk factor for development of OCD

4] whether NSS are state marker or trait marker – even though existing document suggest them to be trait marker further study comparing patient fully remitted with patients having active symptoms could be done. This would also give us evidence for quantifying NSS as endo phenotypic markers in OCD

5] Effect of NSS on treatment response and effect of treatment on NSS score could be done by follow up studies .Whether NSS represents a subgroup that predicts varying treatment response would help us in deciding therapy.

6] Since NSS are found to be higher in patients with other psychiatric conditions like schizophrenia, to identify any particular specific tendency for soft signs in OCD a comparative study with OCD and other patient group could be done

7] With advanced structural and functional neuroimaging techniques these clinical signs could be correlated with structural and functional changes in brain in drug naïve patients, first degree relatives that would support the neuro developmental etiologic hypothesis

CONCLUSION

From this study we could find that patients with OCD have significant Neurological soft signs compared to normal matched controls in total scale score and in individual group of sensory integration, motor coordination, complex motor sequencing as assessed by NES scale. Among the individual signs significant impairment /positivity is noticed in following signs: audio-visual integration, graphesthesia, tandem walk, alternating motor movements, rhythm tapping test A and B, finger nose test, fist edge palm, fist ring, ozeretski test, mirror movements, synkinesis, gaze impersistance with no lateralisation of signs and no significant difference in soft signs between patients on medications and drug naïve patients. The positive signs giving a possible link to frontal sub cortical thalamus circuit involvement ,these NSS could be taken further into various aspects of the disorder considering the limitation of the study and future recommendations suggested.

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Appendix-I

NEUROLOGICAL EVALUATION SCALE

1. Tandem Walk
Instructions: Subject to walk, in a straight line, 12 feet, heel to toe.
Assessment:
0 = no missteps after subject has completed first full step;
1 = one or twomissteps after completion of first full step;
2 = 3 or more missteps, grabbing, or falling.

2. Romberg Test
Instructions: Subject to stand with his/her feet together, eyes closed, his/her arms heldparallel to the floor, and fingers spread apart. The subject is to maintain this position for 1 min.
Assessment:
0 = relatively stable, minimal swaying;
1 = marked swaying;
2 = subject steps to maintain balance or falls.

3. Adventitious Overflow
Instructions: Same as Romberg Test.
Assessment:
0 = absence of movement of fingers, hands, or arms;
1 = irregular fluttering movement of fingers only;
2 = irregular fluttering movement extended to hands and/ or arms.

4. Tremor
Instructions: Same as Romberg Test.
Assessment:
0 = no tremor;1 = mild, fine tremor;2 = marked, fine or coarse tremor.

5. Audio-Visual Integration
Instructions: The subject is asked to match a set of tapping sounds with one of three sets ofdots presented on a 5-inch x 7-inch index card. The subject is instructed to close his/ her eyes during the tapping. Three practice trials are performed first to ensure that the subject under- stands the directions.
***Assessment*:**
0 = no error; 1 = one error; 2 = two or more errors.

6. Stereognosis
Instructions: Subject, with eyes closed, is asked to identify an object placed in his/ her hand.Subject is instructed to feel the object with one hand and to take as much time as needed. Ifsubject cannot name the object, he/she is asked to describe for what purpose the object is used.The subject starts with the dominant hand, based on the prior evaluation of handedness, or thehand with which he/she writes, if there is mixed hand dominance. The instructions are repeatedat the beginning of the second trial.
Assessment:
0 = no errors; 1 = one error; 2 = more than one error.

7. Graphesthesia

Instructions: Subject, with eyes closed, is asked to identify the number written on the tip of his/her forefinger. The order of hands is determined as with stereognosis.
Assessment:
0 = no errors;1 = one error; 2 = more than one error.

8. Fist-Ring Test
Instructions: The subject is asked to alternate placing his/her hand on the table, in theposition of a fist, with the thumb placed either over the knuckles or over the middle phalanges and placing his/ her hand, on the table, in the position of a ring, with the tips of the thumb and forefinger touching and the remaining three fingers extended. The subject is to bring his/ her arm into the upright position between each change in hand position. If the subject does not perform the movement accurately or in a manner that can be appropriately assessed, he/ she is to be stopped, to be reinstructed, and to start the test again. The subject is to repeat each set of hand position changes 15 times.
Assessment:
0 = ***no major disruption of motion after first repetition;*** errors limited toincomplete extension of fingers in ring position and no more than two hesitancies in the transition from fist to ring or vice versa and no more than one fist/ ring confusion
1 =***no majordisruption of motion*** after ***first repetition or complete breakdown of motion;*** more than two hesitancies in the transition from fist to ring, difficulty in developing and maintaining a smooth,steady flow of movement, three to four fist/ring confusions, or any total of three but not more
than four errors.
2 = ***major disruption of movement or complete breakdown of motion,*** **or** ***more than four fist Jring hesitations or confusions.***

9. Fist-Edge-Palm Test
Instructions: Ask the subject, using a smooth and steady rhythmic pattern, to touch the table with the side of his/ her fist, the edge of his/ her hand, and the palm of his/ her hand. The subject is to break contact with the surface of the table between each change in hand position, but not to bring the arm back in full flexion. The subject is to repeat this sequence of position changes 15 times.
Assessment:
0 =***no major disruption of motion afterfirst repetition;*** errors limited to no more than two hesitancies in the transition from one position to the next and no more than one mistake in hand position.
1 = ***no major disruption of motion after first repetition or completebreakdown of motion;*** more than two hesitancies in the transition from one position to another,difficulty in developing and maintaining a smooth, steady flow of movement, three to fourposition confusions, or any total of three or four errors. 2 = ***major disruption of movement or complete breakdown of motion, or more than four hesitations or position confusions.***

10. **Ozeretski Test**
Instructions: The subject is to place both hands on the table, one hand palm down and the other hand in the shape of a fist. The subject is then asked simultaneously to alternate the position of his/her hands in a smooth and steady motion. The subject is asked to repeat this motion 15 times.
Assessment:

0 = ***no major disruption of motion afterfirst repetition;*** errors limited to no more than two hesitancies in the transition from one position to the next and no more than one mistake in hand position.

1 = no major disruption of motion after first repetition or complete breakdown of motion; more than two hesitancies in the transition from one position to another,difficulty in developing and maintaining a smooth, steady flow of movement, three to four
position confusions, or any total of three, but no more than four errors.

2 = ***major disruption of movement or complete breakdown of motion, or more than four hesitations or position confusions.***

11. Memory

Instructions: Subject is told four words and is asked to repeat them immediately after they are all presented. If the subject is unable to repeat the four words correctly, they are represented.If the subject still cannot repeat the four words after a total of three presentations of the words,the test is terminated and the subject is given a score of 2 for both parts of the item. If the subject
is able to repeat the four words after the initial or two subsequent presentations, he/she is then asked to remember the words as well as possible and told that he/ she will be asked to repeat the words twice later on during the interview. The subject is then asked to recall the four words at 5 and 10 min.

Assessment:

0 = Subject remembers all words;
1 = Subject remembers three words;
2 = Subject remembers fewer than three words.

12. Rhythm Tapping Test -Part A

Instructions: Ask the subject to reproduce exactly the series of taps heard while the subjecthas eyes closed. The subject may have eyes open while reproducing series of taps.

Assessment:
0 = no errors;
1 = one error of either nondiscrimination between soft and hard sounds, rhythm, or error in number of taps;
2 = more than one error.

13.Rhythm tapping test –Part B

Part B
Instructions: Ask the subject to produce a series of taps as instructed.
Assessment:
0 = no errors; 1 = one error;2 = more than one error.

14. Rapid Alternating Movements

Instructions: Ask the subject to place his/ her hands palm down on legs. The subject is to start with his/ her dominant hand and is to slap his/ her leg distinctly with the palm and the back of his/ her hand in an alternating motion. The determination of dominance is as described above(see item 8). The subject is to perform the task 20 times, with both hands, one hand at a time.

Assessment:
0 = no major disruption of motion, hesitation, or mistake in hand placement;

I= no major disruption of motion or one to two hesitations or mistakes in hand placement;
2 =major disruption of motion or three or more hesitations or mistakes in hand placement.

15. Finger-Thumb Opposition
Instructions: Ask the subject to place both hands palm up with fingers fully extended on his/ her legs. The subject is to start with his/ her dominant hand and is to touch the tip of his/ her fingers with the tip of his/her thumb, from forefinger to pinky, returning to forefinger, for a total of IO repetitions.
Assessment:
0 = no major disruption of motion and no more than one mistake;
1 = no major disruption of motion or two to three mistakes;
2 = major disruption of motion or four or more mistakes.

16. Mirror Movements
Instructions: The subject's hand, which is not performing the Finger-Thumb Opposition Test, is observed for parallel movements of the fingers and thumb.
Assessment:
0 = no observable movements of the fingers;
I = minor, inconsistent, orrepetitive movements of the fingers;
2 = consistent, distinctive movements of the fingers.

17. Extinction (Face-Hand Test)
Instructions: The subject is seated, with hands resting palm down, on his/her knees and with eyes closed. The subject is told that he/she will be touched on either the cheek, hand, or both, and is to say where he/she has been touched. If the subject names just one touch, he/she is asked-the first time this occurs only-if he/she felt a touch anywhere else. The simultaneous touching is done in the following order: right cheek-left hand, left cheek-right hand, right cheek-right hand, left cheek-left hand, both hands, and both cheeks.
Assessment:
0 = no errors; 1 = one error; **2 =** more than one error.

18. Right/Left Confusion
Instructions: Subject is asked to point to his/her right foot, left hand; place his/her right hand to left shoulder, left hand to right ear; point to examiner's left knee, right elbow; with examiner's arms crossed, point to examiner's left hand with his/ her right hand, and with examiner recrossing arms, point to examiner's right hand with his] her left hand.
Assessment: 0 = no error: 1 = one error; 2 = two or more errors.

19. Synkinesis
Instructions: Subject is instructed to follow the cap of a pen with his/ her eyes only as it is moved between extremes of horizontal gaze. If the subject moves his/ her head, the subject is asked to keep his/ her head still and follow the cap of a pen with the eyes only.
Assessment:
0 = no movement of the head;
1 = movement of the head on first trial but not when specifically told to keep head still;

2 = movement of the head even when told to keep head still.

20. Convergence
Instructions: Subject is instructed to follow the cap of a pen with his/ her eyes as it is moved toward the subject's nose.
Assessment:
0 = both eyes converge on object;
1 = one or both eyes are unable to converge completely, but can converge more than halfway;
2= one or both eyes fail to converge more than halfway.

21. Gaze lmpersistence
Instructions: Subject is instructed to fix his/ her gaze on the cap of a pen at a 45 o angle in the horizontal plane of the right and left visual fields for 30 sec.

Assessment: 0 = no deviation from fixation; 1 = deviation from fixation after 20 set; 2 =deviation from fixation before 20 sec.

22. Finger to Nose Test
Instructions: The subject is instructed to close eyes and touch the tip of his/ her nose with the tip of his/ her index finger.
Assessment: 0 = no intention tremor or passpointing; 1 = mild intention tremor or pass-pointing; 2 = marked intention tremor or passpointing.

23. Glabellar Reflex
Instructions: Subject is instructed to fix his/ her gaze on a point across the room. The subject is approached from above the forehead outside of the visual field, and the examiner taps the glabellar region 10 times with the index finger.
Assessment: 0 = three or fewer blinks; 1 = four or five full blinks, or more than six partial or full blinks; 2 = six or more full blinks.

24. Snout Reflex
Instructions: Subject is instructed to relax, and the examiner presses his finger against the subject's philtrum.
Assessment:
0 = no contraction of the orbicularis orris (or puckering of the lips);
2 = any contraction of the orbicularis orris (or puckering of the lips).

25. Grasp Reflex
Instructions: The subject is instructed not to grab, and the examiner strokes the inside of the subject's palm between the index finger and thumb. This procedure is repeated a second time with the subject being asked to spell the word "help" backwards.
Assessment: 0 = no flexion of the subject's fingers;
1 = mild flexion of the subject's fingers on first trial or flexion of any kind on second trial;
2 = marked flexion of the subject's fingers on first trial.

26. Suck Reflex
Instructions: The examiner places the knuckle of a flexed index finger or tongue depressor between the subject's lips.

Assessment:
0 = no movement; 2 =any pursing or sucking motion by the subject's lips.

Assessment of Cerebral Dominance
Handedness
Instructions: Ask subject to demonstrate how he/ she would write, throw a ball, use a tennis racket, strike a match, use scissors, thread a needle, use a broom, use a shovel, deal cards, use a hammer, brush teeth, and unscrew the lid of a jar.
Assessment: R-Subject writes with right hand and performs at least seven other activitieswith right hand; M-Subject writes with right/left hand but performs less than seven otheractivities with right/left hand; L-Subject writes with left hand and performs at least sevenother activities with left hand.

APPENDIX -II

F42 OBSESSIVE-COMPULSIVE DISORDER

A. Either obsessions or compulsions (or both), present on most days for a period of at least two week

B. Obsessions (thoughts, ideas or images) and compulsions (acts) share the following features, all of which must be present:

(1) They are acknowledged as originating in the mind of the patient, and are not imposed by outside persons or influences.

(2) They are repetitive and unpleasant, and at least one obsession or compulsion must be present that is acknowledged as excessive or unreasonable.

(3) The subject tries to resist them (but if very long-standing, resistance to some obsessions or compulsions may be minimal). At least one obsession or compulsion must be present which is unsuccessfully resisted.

(4) Carrying out the obsessive thought or compulsive act is not in itself pleasurable. (This should be distinguished from the temporary relief of tension or anxiety).

C. The obsessions or compulsions cause distress or interfere with the subject's social or individual functioning, usually by wasting time.

D. Most commonly used exclusion criteria: not due to other mental disorders, such as schizophrenia and related disorders (F2), or mood [affective] disorders (F3).

The diagnosis may be specified by the following four character codes:

F42.0 Predominantly obsessional thoughts and ruminations

F42.1 Predominantly compulsive acts

F42.2 Mixed obsessional thoughts and acts

F42.8 Other obsessive-compulsive disorders

F42.9 Obsessive-compulsive disorder, unspecified

ஆராய்ச்சி தகவல் தாள்

1. எண்ண சுழற்ச்சி நோயினால் [Obsessive Compulsive] பாதிக்கப்பட்டவர்களில் காணப்படும் நரம்பியல் சார்ந்த அறிகுறிகளை கண்டறிய ஆராய்ச்சி மேற்கொண்டுள்ளோம்.

2. அரசு மனநல காப்பகம் கீழ்ப்பாக்கம் மற்றும் ராஜிவ் காந்தி அரசு பொது மருத்துவமணையில் உள்ள மனநோய் பிரிவில் கண்டறியப் படும் எண்ண சுழற்ச்சி நோயாளிகளிடம் இந்த ஆராய்ச்சி நடைபெற உள்ளது.

3. நரம்பியல் அறிகுறிகளை கண்டறிய எளிதில் தரக்கூடிய சில சோதனைகளை கொண்ட அங்கிகறிக்கப்பட்ட சோதனை மதிப்பீட்டு அட்டவனை பயன்படுத்தப்படும்.

4. என்ன சுழற்ச்சி நோயினால் பாதிக்கப்பட்ட தாங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க விரும்புகிறோம். மேற்கூறப்பட்டுள்ளபடி சில சோதனைகள் தங்களிடம் செய்யப்படும். அதனால் தங்களின் நோயின் சிகிச்சைக்கு பாதிப்பு ஏற்படாது என்பதை தெரிவித்துக் கொள்கிறோம்.

5. முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்பொழுது மற்றும் ஆராய்ச்சியின் பொழுதோ தங்களது பெயர் அல்லது அடையாளங்கள் வெளியிடப்பட மாட்டாது என்பதை தெரிவித்துக்கொள்கிறோம்

6. இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின்படி தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

ஆராய்ச்சி ஒப்புதல் தாள்

ஆராய்ச்சி தலைப்பு

எண்ண சுழற்ச்சி நோயினால் [Obsessive Compulsive]
காணப்படும் நரம்பியல் சார்ந்த அறிகுறிகள்

பெயர் :

தேதி :

வயது :

நோயாளி எண் :

பால் :

ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட செய்திகளை புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

என்ன சுழற்ச்சி நோயில் காணப்படும் நரம்பியல் அறிகுறிகளை கண்டறியும் சில பரிசோதனையை செய்துகொள்ள சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியின் விவரங்கள் அல்ங்கிய தகவல் தாளைப் பெற்றுக்கொண்டேன்.

நான் என்னுடைய விவரங்கள் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள சம்மதிக்கின்றேன்.

தேதி :

பங்கேற்பாளர் கையொப்பம்

STUDY ON NEUROLOGICAL SOFT SIGNS IN PATIENTS WITH OBSESSIVE COMPULSIVE DISORDER

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

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