Relationship between neuropsychological performance and soft neurological indications in individuals with schizophrenia

Mathumai Thiyahendran

Ranil Prasad Thilakaratne

Abstract

Neurological soft signs (NSS) are mild motor and sensory abnormalities that are often detected in a variety of mental diseases, including schizophrenia. These deficiencies can be found in people who have the disorder. NSS are commonly related with a decline in cognitive capacities and a worsening of neuropsychological function in patients with schizophrenia (NP). Our goal was to investigate whether or if there is a connection between the NSS and NP in people who have schizophrenia. The inclusion and exclusion criteria were used to select sixty people for the study, thirty of whom had schizophrenia based on the International Classification of Diseases, 10th Revision, and the remaining thirty were matched controls. In addition to gathering demographic and clinical information, tests for determining neuropsychological status and neurosocial functioning (NSS) were given to the patient. A comparison was carried out between the two groups using the results that were obtained on these scales. Results showed that individuals with schizophrenia had a prevalence of NSS of one hundred percent, while only 16.775% of controls in the control group had NSS. In terms of neuropsychological evaluation, there was a difference that might be considered statistically significant between the two groups. Within Group 1, the NSS demonstrated a statistically significant inverse connection with the Tower of London, the Stroop Color Word Test, the Digit Vigilance Test, and the Digit Symbol Substitution Test. On the other hand, there was no connection found between NP and NSS in Group 2. NSS were found to be significantly higher in patients diagnosed with schizophrenia compared to healthy normal controls. In addition, in contrast to the group serving as a control, those who have schizophrenia have an inverse relationship between NSS and NP. It is possible for us to draw the conclusion that the existence of NSS not only predicts a low NP but also adds to the low cognitive abilities of those who have schizophrenia. Tower of London, motor sequencing, the Digit Symbol Substitution Test, neurological performance, neuropsychological evaluation, and the Stroop test are some of the keywords that might be associated with this article.

INTRODUCTION

Schizophrenia is a clinical syndrome that is quite complex. Both the presentation and the psychopathology might range from cognitive to emotional to perceptual to a wide variety of behavioral features. After more than a century has passed since Emil Kraepelin first identified dementia praecox in 1896, the underlying etiopathology of the condition is still not fully understood.

Over the course of the past three decades, several ideas on its etiopathogenesis have been proposed. The neurodevelopmental theory is one of those that has been shown to have the greatest validity. Multiple longterm outcome studies indicated that great recovery was well within the confines of schizophrenia. This also made the neurodevelopmental theory more agreeable than the neurodegenerative hypothesis, which was the alternative. The existence of neurological soft signs (NSS), minor physical abnormalities, and cognitive neuropsychological deficiencies are all pieces of evidence that lend credence to the theory that schizophrenia has its roots in the

neurodevelopmental process. The term "NSS" is often used to refer to clinically apparent and elicitable neurological abnormalities that are present in people with schizophrenia.[1]–[5]

These are anomalous motor or sensory findings that can include involuntary movements, a variant of dyspraxia, difficulty in completing fast alternating motions, difficulties in two point discrimination, and graphesthesia in a person who does not have a neurological illness that can be established to be its focus. When there is no matching pathological lesion, a soft lesion will be described as such using the term soft. Neurological abnormalities in schizophrenia appear to be limited to three primary neurological domains, despite the fact that the classification of NSS as "soft" (for example, frontal release and cerebellar signals) and the batteries used to test them have changed.[6]–[8]

Functions of the senses that are integrated • Coordination of the muscles • Sequencing of the muscles

Patients with schizophrenia have a greater rate of bilateral extinction, reduced audiovisual integration, agraphesthesia, and astereognosis, all of which provide credence to the idea that they have a deficiency in integrative sensory functioning [9], [10]. Tests of overall coordination, intention tremor, finger thumb opposition, stability, and gait have all indicated deficiencies in a subject's motor coordination. Lastly, poor performance in complex motor tasks has been reported in tests that involve repetitive alternating hand positions. These tests include the fist edge palm test, the fist ring test, and the Ozeretski test. This poor performance in complex motor tasks may be the result of a dysfunction in the frontal basal ganglia circuit.[11]–[14]

Eye movements (both pursuit and saccadic motions) and developmental reflexes, in particular signals of frontal release, have also been shown to be abnormal in patients with this condition. Other dysfunctions, such as those of basic sensory function, have been documented a lot less frequently. Schizophrenia is characterized by deficiencies in a wide variety of cognitive skills, including attention, abstraction, executive function, learning, and memory, as has been empirically proven.

When compared to healthy controls, meta-analytic studies suggest that those diagnosed with schizophrenia have moderate to severe impairments in the attention domain. Patients diagnosed with schizophrenia had the highest and most consistent rate of reporting set shifting abnormalities in their performance on the Wisconsin Card Sorting Test (WCST). Weickert et al. 2000 conducted a meta-analysis, and their findings showed that people with schizophrenia had significant WCST score impairments when compared to healthy controls. According to the findings of some studies, patients with schizophrenia do not have an increased interference time when performing the Stroop paradigm (a test for response inhibition). According to the findings of two meta-analyses, patients diagnosed with schizophrenia have a significantly increased interference effect when compared with healthy controls. Patients with schizophrenia have been shown in multiple studies to have poor decision making performance when measured by gambling tasks in comparison to healthy control subjects[8], [15]–[17].

The vast majority of the existing body of research points to the fact that the presence of NSS in schizophrenia is linked to deficient cognitive abilities. However, research emphasizing the association between NSS and neuropsychological performance (NP) in individuals with schizophrenia are rare especially so from north eastern area of Sri Lanka. The current study was designed to investigate this correlation in patients diagnosed with schizophrenia and gain a better understanding of the neurobiology underlying schizophrenia, which will ultimately assist us in developing a more effective strategy for the treatment of the mental illness.[18]–[20]

Aims and objectives

In individuals diagnosed with schizophrenia, the purpose of this research was to investigate the relationship between NSS and NP.

METHODS

Following the institution's receipt of both ethical and scientific clearance, the research was carried out in a tertiary care psychiatric teaching institute in Sri Lanka. The duration of the trial was a single year. A total of sixty people were enrolled in the study; thirty of them met the criteria for schizophrenia as outlined in the International Classification of Diseases, 10th Revision (Group 1), while the remaining thirty individuals served as matched controls (Group 2). The healthy persons who worked at the institution in a variety of roles served as the matched controls. They were comparable to one another in terms of age, gender, and the presence of comorbidities. The size of the sample was determined by taking into account the rate at which schizophrenia is diagnosed in the region as well as the number of patients who utilize the services provided by the institute's outpatient and inpatient departments.[21]–[25]

On the basis of the database, appropriate consultation with the institute's biostatistician was obtained for determining the sample size. Primary investigators were the ones responsible for recruiting individuals for the study after first obtaining their informed permission from the participants in the study. The research participants were allocated to the investigators in a random fashion to exclude any possibility of bias [26], [27]. The principal investigators used all of the scales in their unaltered forms when conducting their research. The patient was provided with an explanation of the scales in their native language. In order to examine demographic and other clinical factors, a pro forma with a semi-structured format was utilized. It was determined that the patient did not have any further mental comorbidities by using the Mini International Neuropsychiatric Interview (MINI) (after obtaining the required permission). Primary investigators who were experienced in employing MINI and interpreting its results were responsible for its application and interpretation. To determine the degree of severity of the symptoms, the Positive and Negative Syndrome Scale was utilized. After acquiring the necessary consent, the Neurological Evaluation Scale (NES) was utilized in order to perform the NSS measurement. The Annett's Handedness Questionnaire is one of the 30 questions that make up this measure. Each question receives a score between 0 and 2. It has been broken down into its component subscores, which are as follows: the subscore for sensory integration, the subscore for motor coordination (MCS), the subscore for sequential complex motor performance (SCMP), and the subscore for primitive reflex. After this, a battery of neuropsychological tests, including the Token Test (TT), the Stroop Color Word Test (SCWT), the Digit Vigilance Test (DVT), the Digit Symbol Substitution Test (DSST), and the Tower of London (TOL) test, were carried out on the subject. [28]–[30] These examinations were carried out on both the study group and the control group simultaneously. Tabulation of the data and application of relevant statistical methods, including the mean, standard deviation (SD), t test, and Pearson's correlation test, were carried out with the assistance of IBM SPSS Statistics for Windows version 22. (IBM Corp., Armonk, N.Y., USA). It was decided to employ descriptive statistics for the continuous variables, and the Chi square test was carried out in order to determine how the different variables were distributed across the two groups. It was possible to determine the frequency distribution of continuous variables as well as categorical ones by using a frequency table. The t test was used to compare the groups, and finally, the Pearson correlation test was utilized to analyze the degree to which the findings were correlated with one another (the appropriate assumptions were met in order to use a parametric test). The number of people who participated in the study was sufficient to meet the thirty-person minimum sample requirement for the test. The findings were examined in light of the prior research conducted in this field.[31]–[34]

RESULTS

Both groups had a similar mean age, which was determined to be 31.53 years; the age range of 29–38 years accounted for the greatest proportion of samples in both groups (57%). 70% of members in each of the groups were male. In a similar vein, there was not a significant difference between the two groups in any of the other sociodemographic factors that were compared. In more than half of the instances, 17 out of 30, the length of time the patient had been unwell ranged from one to four years.

Table 1: Group differences of neurological soft signs among Group 1 (study group) and Group 2 (control group)

	Mean±SD		*P*
	Group 1 (study group)	Group 2 (control group)	
NSS	32.03±5.05	0.70±1.70	<0.001
Motor sequencing	4.26±1.68	0.16±0.46	<0.001
Motor coordination	10.63±2.93	0.26±0.63	<0.001
Sensory integration	6.70±1.74	0.10±0.30	<0.001
Primitive reflex	2.70±1.68	0.13±0.34	<0.001

Table 2: Group differences in neurological performance in Group 1 (study group) and Group 2 (control group)

	Score (mean±SD)		*P*
	Group 1 (study group)	Group 2 (control group)	
Tower of London test	6.20±1.73	12.90±1.04	<0.001
Token test	22.13±3.25	32.10±2.64	<0.001
Stroop Color-Word Test	389.30±65.94	101.40±30.09	<0.001
Digit Vigilance Test	937.00±158.92	614.80±89.90	<0.001
Digit Symbol Substitution Test	563.46±117.22	352.60±44.30	<0.001

Table 3: Correlation of neurological soft signs and neurological performance in Group 1 (study group)

	Tower of London	Token test	Stroop Color-Word Test	Digit Vigilance Test	Digit Symbol Substitution Test	*P*
NSS	−0.434	−0.134	−0.394*	−0.0382*	−0.0396*	<0.001
Motor sequencing	−0.638*	0.152	0.198	−0.389*	−0.384*	<0.001
Motor coordination	0.229	0.233	0.117	−0.387*	−0.498*	<0.001
Sensory integration	0.062	−0.560*	−0.115	0.005	0.204	<0.001
Primitive reflex	0.053	0.055	0.033	0.037	0.055	<0.001

Table 4: Correlation of neurological soft signs and neurological performance in Group 2 (control group)

	Tower of London	Token test	Stroop Color-Word Test	Digit Vigilance Test	digit Symbol Substitution Test
NSS	0.069	0.001	0.047	0.028	0.013
Motor sequencing	0.048	0.071	0.037	0.055	0.056
Motor coordination	0.075	0.106	0.056	0.140	0.059
Sensory integration	0.86	0.013	0.031	0.030	0.026
Primitive reflex	0.165	0.091	0.034	0.010	0.089

DISCUSSION

This was a cross-sectional study that we carried out to investigate whether or not NSS and NP are present in people who have schizophrenia and to investigate whether or not there is a link between

the two. In the course of our research, NSS were investigated with the use of NES, and a comparison was carried out between Groups 1 and 2, as presented in Table 1. On the NES, individuals in Group 1 had a mean NSS score of 32.03 with a standard deviation of 5.05, whereas participants in Group 2 had a mean NSS score of 0.7 with a standard deviation of 1.7. When comparing the NSS scores of the two groups, a statistically significant gap was discovered between them (t = 32.17, df = 58, P 0.001). According to the findings shown above, individuals diagnosed with schizophrenia had a statistically significant increase in NSS when compared to the normal healthy control group. The results of our research are consistent with those found in prior investigations. The findings of our study are strongly supported by earlier meta analyses and other studies that used NES for evaluating NSS and compared it as one of patients with schizophrenia and normal healthy controls. These studies were conducted in different time periods. In light of the findings presented above, the results of our research make it abundantly clear that the NSS were discovered to be more prevalent in the schizophrenic group in comparison to the control group.

As can be seen in Table 2, our research revealed that patients diagnosed with schizophrenia had considerably lower scores across the board on neuropsychological tests when compared to the healthy individuals who served as controls. When comparing the performance of Group 1 (the schizophrenia group) to Group 2 (the control group), we found that the performance on the TT, which tests verbal comprehension, was significantly lower in Group 1 (the schizophrenia group) than in Group 2 (the control group) (df = 58, t = 13.01, P 0.001). Because the performance of Group 1 in TOL is considerably worse than that of Group 2 (df = 58, t = 18.33, P 0.001), it may be deduced that individuals who suffer from schizophrenia have subpar abilities in the area of planning. This further suggests that individuals with schizophrenia have deficiencies in their executive functioning.

The performance of participants from Group 1 on the SCWT, which tested the response inhibiting ability, was significantly poor when compared to Group 2 (df = 58, t = 21.75, P 0.001), which indicated that individuals with schizophrenia had a poor ability in impairing two different kinds of responses, which is a function of the frontal lobe, and therefore supported the earlier hypothesis of hypofrontality.

Similarly, the performance of the participants from Group 1 in the DSST was found to be significantly poor when compared to Group 2 (df = 58, t = 9.21, P 0.001), which indicates that there is an impairment in the sustained attention, visuomotor coordination, and response speed in individuals who have schizophrenia.

Similarly, it was discovered that the performance of the participants from Group 1 in DVT was significantly worse than that of the controls (df = 58, t = 9.66, P 0.001) This suggests that people who have schizophrenia have problems both with their ability to retain attention and with their psychomotor speed.

The findings presented here are consistent with those discovered by a number of other researchers, who came to the conclusion that people with schizophrenia had a lower NP than normal people.

The Pearson's correlation was utilized in this study to determine whether or not there was a connection between the NSS and the NP in patients diagnosed with schizophrenia (which is shown in Table 3). The co-relation between NES and NSS in the control group is displayed in Table 4, and none of the findings were statistically significant. We discovered that there was a statistically significant inverse association between NSS and TOL, SCWT, DVT, and DSST. A substantial inverse association was found between NSS – motor sequencing and TOL, DVT, and DSST. A substantial inverse connection was found between DVT and DSST and the motor coordination component of the NSS. It was shown that NSS, which measures sensory integration, had a

significant inverse connection with TT (P 0.05, two-tailed).The findings of the present study were well supported by the earlier studies which have reported that in persons suffering from schizophrenia, NSS were significantly correlated with NP and these individuals did poorly in the neuropsychological tests.

In our study, we used the control group which showed the magnitude of both neurological and cognitive impairments associated with persons with schizophrenia. This is clearly evident from lack of correlation between NSS and NP in the control group.

These above findings suggest that persons with schizophrenia who have NSS have poor NP, supporting the presence of neurological abnormalities and their potential influence on cognitive abilities of persons with schizophrenia.

Even though our study sample size was less compared to the above studies, we found that the presence of NSS had influenced poor performance in the neuropsychological tests in schizophrenia patients. They influenced planning, inhibition, sustained attention, psychomotor speed, and visuomotor coordination in persons with schizophrenia.

CONCLUSION

From the findings of our study, we conclude that NSS were more in persons with schizophrenia compared to healthy normal controls. The NP of the persons with schizophrenia was poor compared to the normal healthy control group, suggesting that schizophrenia patients have cognitive deficits. Furthermore, there is a negative correlation between NSS and NP in persons with schizophrenia, which is differing from the control group. We conclude that the presence of NSS is associated with poor NP, and also contributes to poor cognitive abilities of persons with schizophrenia.

Limitations of the study

Sample being small was a major limitation, also majority of the participants in the study group were male (which might be a confounding factor), and hence the results of the study cannot be generalized. Literature suggested that exposure to neuroleptic drugs can have an adverse effect on the NP of persons with schizophrenia; in this study, we did not have control over the neuroleptic medication, so this could have influenced some of the findings.

References

[1] B. W. Palmer, S. E. Dawes, and R. K. Heaton, “What do we know about neuropsychological aspects of schizophrenia?,” *Neuropsychol. Rev.*, 2009.

[2] W. S. Kremen, L. J. Seidman, J. R. Pepple, M. J. Lyons, M. T. Tsuang, and S. V. Faraone, “Neuropsychological risk indicators for schizophrenia: a review of family studies,” *Schizophr. Bull.*, vol. 20, no. 1, pp. 103–119, 1994.

[3] R. K. Heaton, J. A. Gladsjo, B. W. Palmer, J. Kuck, T. D. Marcotte, and D. V. Jeste, “Stability and course of neuropsychological deficits in schizophrenia,” *Arch. Gen. Psychiatry*, vol. 58, no. 1, pp. 24–32, Jan. 2001.

[4] W. S. Kremen, L. J. Seidman, S. V. Faraone, R. Toomey, and M. T. Tsuang, “The paradox of normal neuropsychological function in schizophrenia,” *J. Abnorm. Psychol.*, vol. 109, no. 4, pp. 743–752, Nov. 2000.

[5] D. M. Censits, J. D. Ragland, R. C. Gur, and R. E. Gur, “Neuropsychological evidence supporting a neurodevelopmental model of schizophrenia: a longitudinal study,” *Schizophr. Res.*, vol. 24, no. 3, pp. 289–298, Apr. 1997.

[6] L. J. G. Rothi and K. M. Heilman, *Apraxia: the neuropsychology of action*. Psychology Press, 2014.

[7] C. D. Frith, “The Cognitive Neuropsychology of Schizophrenia: Classic Edition,” 2015.
[8] G. Floris *et al.*, “Constructional apraxia in frontotemporal dementia associated with the C9orf72 mutation: broadening the clinical and neuropsychological phenotype,” *Amyotroph. Lateral Scler. Frontotemporal Degener.*, vol. 16, no. 1–2, pp. 8–15, Mar. 2015.
[9] P. Stefanatou, G. Konstantakopoulos, E. Giannouli, N. Ioannidi, and V. Mavreas, “Patients’ needs as an outcome measure in schizophrenia,” *Eur. Psychiatry*, vol. 33, no. S1, pp. S453–S453, Mar. 2016.
[10] S. P. Stefanatou Pentagiotissa, G. K. George Konstantakopoulos, E. G. Eleni Giannouli, S. V. Silia Vitoratou, and V. M. Venetsanos Mavreas, “The relationship between patients’ needs and psychopathology in schizophrenia: Do patients and therapists agree?,” *Eur. Psychiatry*, vol. 30, p. 1376, Mar. 2015.
[11] P. Flor-Henry, “Neuropsychology and psychopathology: A progress report,” *Neuropsychol. Rev.*, 1990.
[12] M. Catani *et al.*, “Beyond cortical localization in clinico-anatomical correlation,” *Cortex*, vol. 48, no. 10, pp. 1262–1287, Aug. 2012.
[13] P. Whitty, M. Clarke, S. Browne, and O. McTigue, “Prospective evaluation of neurological soft signs in first-episode schizophrenia in relation to psychopathology: state versus trait phenomena,” *Psychological*, 2003.
[14] K. Kollias *et al.*, “The development of the Early Intervention in Psychosis (EIP) outpatient unit of Eginition University Hospital into an EIP Network,” *Psychiatrike*, vol. 31, no. 2, pp. 177–182, Apr. 2020.
[15] C. Pantelis, T. R. E. Barnes, and H. E. Nelson, “Is the concept of frontal–subcortical dementia relevant to schizophrenia?,” *The British Journal of*, 1992.
[16] H. Roxborough, W. J. Muir, D. H. Blackwood, M. T. Walker, and I. M. Blackburn, “Neuropsychological and P300 abnormalities in schizophrenics and their relatives,” *Psychol. Med.*, vol. 23, no. 2, pp. 305–314, May 1993.
[17] A. S. David and J. C. Cutting, “The neuropsychology of schizophrenia—introduction and overview,” *The neuropsychology of schizophrenia*, 2019.
[18] M. O. Krebs, A. Gut-Fayand, M. Bourdel, J. Dischamp, and J. Olié, “Validation and factorial structure of a standardized neurological examination assessing neurological soft signs in schizophrenia,” *Schizophr. Res.*, vol. 45, no. 3, pp. 245–260, Oct. 2000.
[19] S. Abel, “The neurological examination in adults with autism spectrum conditions: a pilot study,” 2018.
[20] P. Stefanatou *et al.*, “Fear of COVID-19 impact on professional quality of life among mental health workers,” *Int. J. Environ. Res. Public Health*, vol. 19, no. 16, p. 9949, Aug. 2022.
[21] A. Reichenberg, P. D. Harvey, and C. R. Bowie, “Neuropsychological function and dysfunction in schizophrenia and psychotic affective disorders,” *Schizophrenia*, 2009.
[22] C. Arango, J. J. Bartko, and J. M. Gold, “Prediction of neuropsychological performance by neurological signs in schizophrenia,” *American Journal of*, 1999.
[23] M. A. Taylor, J. Redfield, and R. Abrams, “Neuropsychological Dysfunction in Schizophrenia,” *Biol. Psychiatry*, 1981.
[24] K. E. Lewandowski, B. M. Cohen, and D. Öngur, “Evolution of neuropsychological dysfunction during the course of schizophrenia and bipolar disorder,” *Psychol. Med.*, 2011.
[25] P. Stefanatou *et al.*, “Patient-reported needs predict perceived psychosocial disability and quality of life beyond symptom severity in schizophrenia,” *Disabil. Rehabil.*, pp. 1–9, Feb. 2022.
[26] S. Dimitrakopoulos, A. Hatzimanolis, P. Stefanatou, L.-A. Xenaki, and N. Stefanis, “S125. The role of dup, DUI and polygenic score for schizophrenia on cognition in Athens fep study sample,” *Schizophr. Bull.*, vol. 46, no. Supplement_1, pp. S82–S83, May 2020.
[27] P. Stefanatou, C. S. Karatosidi, E. Kattoulas, N. Stefanis, and N. Smyrnis, “The relationship between premorbid adjustment and cognitive dysfunction in schizophrenia,” *Eur. Psychiatry*, vol. 33, no. S1, pp. S78–S79, Mar. 2016.

[28] M. W. C. Chan, J. T. H. Yip, and T. M. C. Lee, “Differential impairment on measures of attention in patients with paranoid and nonparanoid schizophrenia,” *J. Psychiatr. Res.*, vol. 38, no. 2, pp. 145–152, Mar-Apr 2004.
[29] C. C. H. Chan, R. Wong, K. Wang, and T. M. C. Lee, “Emotion recognition in Chinese people with schizophrenia,” *Psychiatry Res.*, vol. 157, no. 1–3, pp. 67–76, Jan. 2008.
[30] M. Yu *et al.*, “Neurocognitive Impairments in Deficit and Non-Deficit Schizophrenia and Their Relationships with Symptom Dimensions and Other Clinical Variables,” *PLoS One*, vol. 10, no. 9, p. e0138357, Sep. 2015.
[31] T. Xie, X. Zhang, X. Tang, H. Zhang, and M. Yu, “Mapping convergent and divergent cortical thinning patterns in patients with deficit and nondeficit schizophrenia,” *Schizophrenia*, 2019.
[32] X. Tang, C. Zhou, J. Gao, and W. Duan, “Serum BDNF and GDNF in Chinese male patients with deficit schizophrenia and their relationships with neurocognitive dysfunction,” *Biomed. Chromatogr.*, 2019.
[33] M. Yu, Z. Dai, X. Tang, X. Wang, and X. Zhang, “Convergence and divergence of brain network dysfunction in deficit and non-deficit schizophrenia,” *Schizophrenia*, 2017.
[34] L. Van Assche, M. Morrens, and P. Luyten, “The neuropsychology and neurobiology of late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: a critical review,” *Neuroscience*, 2017.