

# Soft Neurological Signs in Patients with Chronic Psychiatric Illness in a Rehabilitation Center: A Cross-sectional Study

Bhanu Dahiya<sup>1</sup>, Shashwath Sathyanath<sup>2</sup>, Anil Kakunje<sup>3</sup>

Received on: 02 June 2023; Accepted on: 28 July 2023; Published on: 26 July 2024

## ABSTRACT

**Background:** Numerous neurological soft signs (NSS), which act as a measure of illness severity, are frequently experienced by the susceptible group of people with chronic mental illnesses. An individual's social functioning may be greatly impacted by NSS, with subsequent long-term effects on their mental health and well-being. However, nothing is known about how common NSS are in the Indian context.

**Materials and methods:** In a rehabilitation facility, 95 randomly chosen participants aged between 18 and 60 participated in a cross-sectional study. Using the neurological evaluation scale (NES), NSS were evaluated.

**Results:** The frequency of neurological soft symptoms did not change by gender ( $p = 0.916$ ), age ( $p = 0.304$ ), or literacy ( $p = 0.067$ ), duration of treatment ( $p = 0.187$ ), marital status ( $p = 0.134$ ), age of onset of illness ( $p = 0.685$ ). However, the NSS scores did differ significantly ( $p = 0.045$ ) according to the length of the illness in one component of the NES scale.

**Conclusion:** The results were different from those of earlier research in other populations, which found lower prevalence rates for NSS. The study stresses the need for more research to completely understand the complex interactions between NSS and chronic mental illnesses, and also the effects of many environmental factors on their comorbidity.

**Keywords:** Chronic mental illness, Neurological soft signs, Rehabilitation.

*Indian Journal of Private Psychiatry* (2024): 10.5005/jp-journals-10067-0168

## INTRODUCTION

Neurological soft signs (NSS) are "objectively measured, non-localizing anomalies which show dysfunctional corticosubcortical and intercortical connections but are not associated with impairment of a particular brain region."<sup>1</sup>

The term "soft" is typically understood to mean that the person exhibiting the sign does not exhibit any additional symptoms indicating a fixed or temporary neurological lesion or condition.<sup>2</sup> Many scales have been devised to study dysfunction of the brain in schizophrenia, including the Heideberger Scale,<sup>3</sup> the Cambridge Neurological Inventory,<sup>4</sup> and the neurological evaluation scale (NES).<sup>5</sup> Numerous studies have been done over the past few decades to determine the prevalence of such signs in schizophrenia, and the estimated range is 50–65%.

It has been previously discussed how soft signals affect cognitive and mental disorder in both children and adults.<sup>6,7</sup> Male pediatric psychiatric patients exhibit soft symptoms more frequently than healthy controls.<sup>8,9</sup> Soft indicators are more prevalent in impulsive, distractible, dependent, and sloppy children than in other types of disturbed children in a group.<sup>10</sup> NSS are more prevalent in those with a history of social difficulties as children and patients with labile mood. In nonclinical pediatric populations, NSS are more prevalent in boys and are linked to social immaturity, lack of motivation and cooperation, and a low achievement in reading.<sup>11,12</sup>

Individual differences in age, gender, and intellect may have an impact on the occurrence of NSSs, according to previous meta-analytic investigations.<sup>13</sup> Additionally, psychiatric disorders like obsessive-compulsive disorders (OCD)<sup>14,15</sup> and mood disorders<sup>16,17</sup> also show NSSs. However, this link weakens when individual variables like age, gender, and education are matched between patients and controls.<sup>15</sup>

<sup>1-3</sup>Department of Psychiatry, Yenepoya Medical College, Mangaluru, Karnataka, India

**Corresponding Author:** Bhanu Dahiya, Department of Psychiatry, Yenepoya Medical College, Mangaluru, Karnataka, India, Phone: +91 8971552402, e-mail: bhanudahiya95@gmail.com

**How to cite this article:** Dahiya B, Sathyanath S, Kakunje A. Soft Neurological Signs in Patients with Chronic Psychiatric Illness in a Rehabilitation Center: A Cross-sectional Study. *Ind J Priv Psychiatry* 2024;18(2):80–84.

**Source of support:** Nil

**Conflict of interest:** None

The neurodevelopmental and the continuum theory of schizophrenia<sup>18,19</sup> suggest that it is not simply a binary phenotype, but the result of interplay between multiple etiological factors.<sup>20</sup> Since neurodegeneration may also alter NSSs, outlining the trajectories of NSSs in people with psychosis and healthy individuals would be necessary for the concurrent evaluation of NSSs.<sup>21</sup>

Due to their ambiguous presentation, these symptoms are frequently disregarded by professionals yet actually indicate an existing or impending mental disease. In order to find this association and also the frequency, pattern, and intensity of NSS among patients with chronic psychiatric disease in a rehabilitation clinic, we undertook this study in the southern region of India. Our study will differ from earlier research in this area since it is conducted in a rehabilitation context and makes use of the NES, which is a very comprehensive instrument and shall hopefully provide better insights into the presentation and clinical implication of the condition.

## MATERIALS AND METHODS

The study was carried out in a rehabilitation center in South India after obtaining clearance from the institution's Ethics Committee for a period of 6 months, from December 2022 to May 2023. The sample size was calculated with the formula  $N = Z^2 P (1-P)/E^2$  with the anticipated prevalence of 62% along a level of confidence of 95% and a margin of error of 10%, the sample size required for the study was 90. Adding 5% non-response rate, the sample size was rounded to 95. The study, with ethics approval number YEC-1/2022/237.

### Inclusion/Exclusion Criteria

- Participants diagnosed with schizophrenia/non-organic psychosis/bipolar affective disorder according to ICD 10 criteria.
- Minimum illness duration of 2 years.
- Participants of any gender aged 18–60 years were included in the study.

Participants diagnosed with dementia, intellectual disability, with comorbid medical or neurological illnesses were excluded. Convenient sampling technique was employed for the study.

### Assessment Tools

The principal investigator assessed the incidence of NSS using the NES, for evaluating the neurological abnormalities frequently observed in schizophrenia. It comprises 26 items and is divided into three domains: (a) motor coordination, (b) sequencing of complicated motor acts, and (c) sensory integration.

Relevant sociodemographic and clinical data were recorded using a semistructured proforma. After receiving sufficient informed consent, all pertinent information was gathered from the participants' carers. Information on the state of people's mental health was gathered using standardized evaluation methods.

### Statistical Methods

The IBM SPSS Statistics 26.0 statistical program was used to further analyze the data once it was entered into an MS-Excel Worksheet. Frequency and percentage were used to represent the qualitative factors. The quantitative variables were shown as mean standard deviation. An independent sample *t*-test was used to do additional statistical analysis. Approximately, 5% was chosen as the degree of significance. The *p*-values under 0.05 were all considered significant.

## RESULTS

Out of 95 participants in the study, 25 (26.3%) were female and 70 (73.7%) were male. A total of 38.9% of the patients were between the ages of 20 and 40, while 61.1% were in the 40–60 age range.

A total of 17 participants (17.9%) were illiterate, whereas 78 (82.1%) were literate. A total of 24 (25.3%) were single, compared to 71 (74.7%) who were married.

Out of the total study population, 32 (33.7%) had illnesses that lasted less than 5 years, and 63 (66.3%) had illnesses that lasted longer than 5 years.

In our study population, the age of disease onset was less than 30 years in 64 (67.4%) and was greater than 30 years in 31 (32.6%) study participants.

The average score for all the four domains has been depicted in Table 1.

There were no gender-related differences in all domains of NES found in our study (Table 2).

**Table 1:** Descriptive statistics for the NES scores among study subjects

Score	N	Mean	Median	SD	Range
Sensory integration	95	6.316	6.000	3.541	(0.0–17.0)
Motor coordination	95	1.968	2.000	1.395	(0.0–5.0)
Sequencing of complex motor acts	95	3.547	3.000	2.015	(0.0–9.0)
Primitive reflexes	95	1.158	1.000	1.055	(0.0–5.0)
Total score	95	15.937	17.000	7.465	(0.0–31.0)

**Table 2:** Gender-wise comparison of NES score

Gender	N	Mean	SD	SEM	t-stat	p-value
Sensory integration						
Male	70	6.386	3.552	0.425	0.321	0.749, NS
Female	25	6.120	3.574	0.715		
Motor coordination						
Male	70	1.929	1.344	0.161	−0.464	0.644, NS
Female	25	2.080	1.552	0.310		
Sequencing of complex motor acts						
Male	70	3.771	2.141	0.256	1.837	0.069, NS
Female	25	2.920	1.470	0.294		
Primitive reflexes						
Male	70	1.186	1.040	0.124	0.428	0.670, NS
Female	25	1.080	1.115	0.223		
Total score						
Male	70	15.986	7.461	0.892	0.106	0.916, NS
Female	25	15.800	7.627	1.525		

NS, not significant of *p*-value

The scores did not significantly change by age ( $p = 0.304$ ).

There was no significant difference in the four domains according to literacy level ( $p = 0.067$ ).

In our study, there was no significant difference in the NES scores based on marital status ( $p = 0.134$ ).

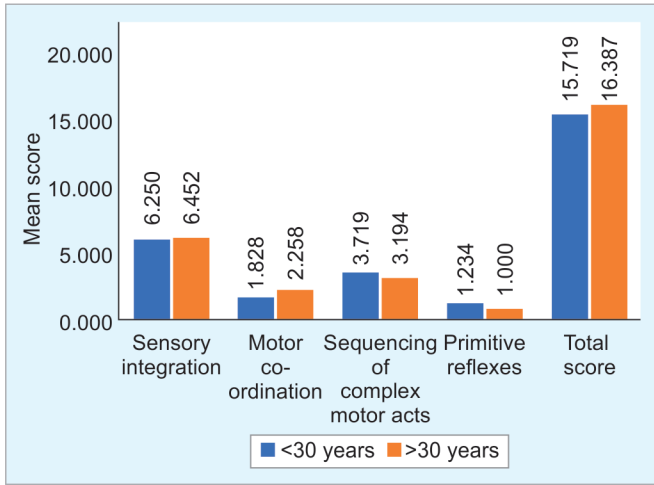
The four domain scores did not significantly differ by age of onset (Fig. 1).

According to the length of the illness, sequencing of complex motor acts showed a significant change depending on the length of the sickness ( $p = 0.045$ ) (Table 3; Fig. 2). However, there was no discernible change between other three domains ( $p = 0.225$ ).

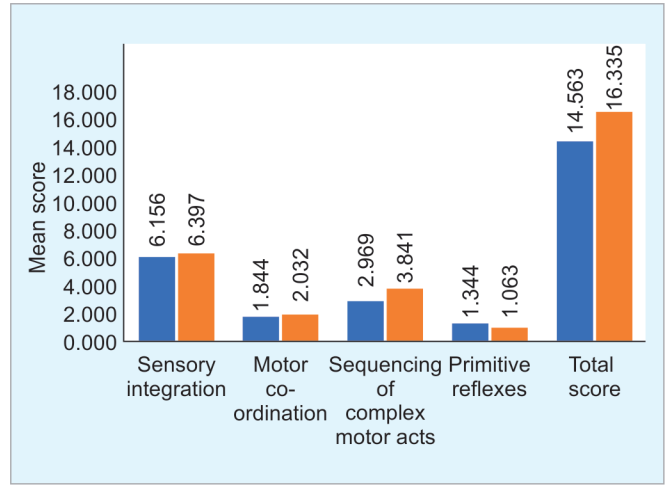
There was no difference in the scores based on the length of treatment ( $p = 0.187$ ) (Fig. 3; Tables 1 to 3).

## DISCUSSION

Out of 95 study participants, the majorities were men and were in the 40–60 age range. This was because of the sample population being from a rehabilitation setting where the age demographic was such. The participants were mostly married and literate, however, knowledge about NSS was absent throughout the population. In a contrasting study carried out in 2016, Chan et al.<sup>22</sup> analyzed a sizable sample of 3,105 individuals and found that 63% of the subjects were men and 22% were in the 40–59 age range. Similarly, Thomas and Tharyan.<sup>23</sup> used the NES to evaluate 21 women and 44 men, with a mean of 32.4 years of age, for the existence of neurological soft symptoms. The participants' average age in the



**Fig. 1:** It indicates comparison of neurological sign scores according to age of onset. According to age of onset, no significant difference was observed in the sensory integration ( $p > 0.05$ ), motor co-ordination ( $p > 0.05$ ), sequencing of complex motor acts ( $p > 0.05$ ), primitive reflexes ( $p > 0.05$ ), and total score ( $p > 0.05$ )



**Fig. 2:** It indicates a comparison of neurological sign scores according to the duration of illness. According to the duration of illness, no significant difference was observed in the sensory integration ( $p > 0.05$ ), motor coordination ( $p > 0.05$ ), primitive reflexes ( $p > 0.05$ ), and total score ( $p > 0.05$ ). According to the duration of illness, a significant difference was observed in the sequencing of complex motor acts ( $p = 0.045$ )

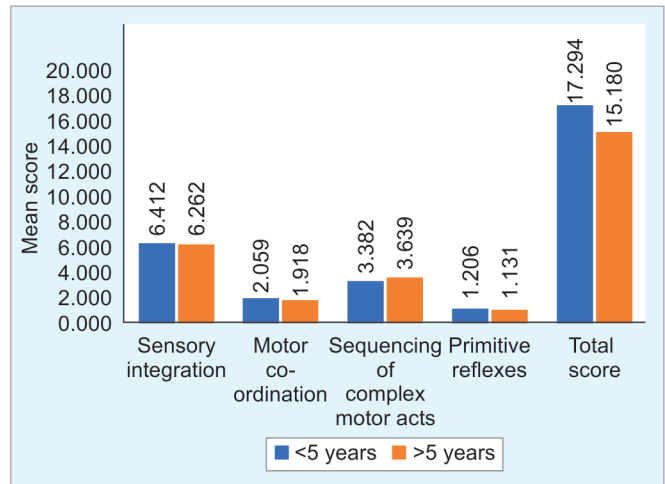
**Table 3:** Comparison of NES score according to duration of illness

Duration of illness	N	Mean	SD	SEM	t-stat	p-value
<b>Sensory integration</b>						
<5 years	32	6.156	3.352	0.592	-0.31	0.756, NS
>5 years	63	6.397	3.657	0.461		
<b>Motor co-ordination</b>						
<5 years	32	1.844	1.247	0.220	-0.619	0.538, NS
>5 years	63	2.032	1.470	0.185		
<b>Sequencing of complex motor acts</b>						
<5 years	32	2.969	2.055	0.363	-2.03	0.045*
>5 years	63	3.841	1.944	0.245		
<b>Primitive reflexes</b>						
<5 years	32	1.344	1.066	0.188	1.227	0.223, NS
>5 years	63	1.063	1.045	0.132		
<b>Total score</b>						
<5 years	32	14.563	8.124	1.436	1.226	0.225, NS
>5 years	63	16.635	7.072	0.891		

\*Significant of  $p$ -value. NS, not significant of  $p$ -value

study by Gunasekaran et al.<sup>24</sup> was 36.2 years. About 60% of the participants were women.

Out of 95 study participants, the majority have illnesses that have lasted more than 5 years. This could be attributed to the study population being from a rehabilitation setting where majority of inmates have already endured long standing illnesses before getting access to mental healthcare. According to Gunasekaran et al.,<sup>24</sup> patients with acute transitory psychosis had an average illness time of 5 months, while those with schizophrenia had an average sickness time of 2 years. Approximately, 1.55 years on average were spent unwell. All of the patients in the study conducted by Biswas and Ghosh.<sup>25</sup> had illness durations of less than 10 years, had stable clinical conditions, and were cooperative during clinical evaluations.



**Fig. 3:** It indicates a comparison of neurological sign scores according to the duration of treatment. According to the duration of treatment, no significant difference was observed in the sensory integration ( $p > 0.05$ ), motor co-ordination ( $p > 0.05$ ), sequencing of complex motor acts ( $p > 0.05$ ), primitive reflexes ( $p > 0.05$ ), and total score ( $p > 0.05$ )

The bulk of the 95 study participants (67.4%) had a disease onset age of less than 30 years which is explained by the usual age of onset of schizophrenia and bipolar affective disorder; however, outliers are always present and we aimed to study the same. According to Biswas and Ghosh.<sup>25</sup> patients with childhood-onset schizophrenia exhibited the most fronto-temporal lobe impairment and a smaller degree of parietal lobe dysfunction. However, in the current study, children could not be included due to characteristics of the study population and inclusion criteria and also issues regarding consent of a minor, however we would like to explore the clinical correlates of neurological soft signs in children in the future.

Since we also aimed to evaluate the frequency and variations of NSS in debilitating mental illnesses commonly encountered in clinical and rehabilitation setting, it was noted that out of 95 participants in the study, 53 (55.8%) had schizophrenia and 42 (44.2%) had bipolar affective disorder. In the study by Gunasekaran et al.,<sup>24</sup> patients with had diagnosis of bipolar affective disorder, depression, schizophrenia, delusional disorder, and psychosis not otherwise specified. Schizophrenia was the primary diagnosis for more than 50% of the cases. However, Zhao et al.<sup>26</sup> found that patients with bipolar disorder and schizophrenia both have significantly higher overall NSS scores than patients with severe depressive disorder and healthy controls. It is noteworthy that neither the total NSS score nor any of the subscale scores discriminated between individuals with bipolar disorder and those who had schizophrenia. Gunasekaran et al.<sup>24</sup> reported that people with schizophrenia had a much higher incidence of NSS.

Multiple studies have also compared the four different domains of the neurological examination scale to assess which area the deficits usually lie and if there is any association of a particular illness with a particular domain. Significant differences were discovered across the four groups by Zhao et al.<sup>26</sup> in terms of total NSS ( $F = 7.80, p = 0.01$ ), motor coordination ( $F = 6.89, p = 0.01$ ), sensory integration ( $F = 3.96, p = 0.01$ ), and disinhibition ( $F = 4.29, p = 0.01$ ). When adjusted for age, gender, total brain grey matter volume, negative symptom score, and chlorpromazine equivalent dose, Janssen et al.<sup>27</sup> reported that there was a strong negative correlation between the sensory integration subscale score and the cluster formed by the left and right sides of the anterior thalamus.

According to Biswas and Ghosh<sup>25</sup> the presence of higher scores and a higher frequency of frontal lobe NSS in childhood onset schizophrenia (COS) patients, even after adjusting for IQ and educational level, suggests that primitive reflexes did not become suppressed with cortical maturation. This suggests that damage to the prefrontal/frontal cortex plays a significant role in the pathogenesis of COS. The findings also suggest that COS individuals who have more severe frontal involvement have a different anatomical distribution.

Similar to this, Zhao et al.<sup>26</sup> showed that there was no significant difference between patients with schizophrenia, bipolar disorder, and major depression and healthy controls in terms of age, gender, education level, handedness, and IQ estimates. Our study also shares similar findings in this regard.

According to Mittal et al.,<sup>28</sup> a relationship between the pathophysiology of schizophrenia and NSS has been suggested by various lines of research. NSS was present in almost 60% of schizophrenia patients at baseline.<sup>5</sup> Higher levels of NSS have been seen in first-episode patients compared to controls,<sup>29</sup> as well as both medicated and treatment-naive individuals with schizophrenia.<sup>30</sup>

The reason for such findings in our study could well be attributed to the setup for the study being in a rehabilitation center. Moreover, the sociodemographic variables of the study population (for example, patients belonging to mainly one geographical location) could also have been instrumental in the results which were obtained and thus differed from earlier studies.

There are several advantages to our study. One of the rare researches on NSS conducted in both a rehabilitation setting and an Indian culture was this one. Our findings are more reliable and valid since we measured the outcome using a standardized and validated instrument. Overall, our research offers insightful information that can guide the creation of programs and laws that will enhance the study population's health outcomes.

Our research had certain flaws. First of all, the smaller size of our sample may have restricted the applicability of our findings. Additionally, only one location was used for the study, which limits how broadly applicable the results can be. Despite these drawbacks, our research offers crucial insights and emphasizes the need for more investigation in this field.

## CONCLUSION

Neurological soft indicators play a key role in identifying participants who may experience poorer psychological health outcomes and a lower quality of life. These symptoms don't result in a person having a severe handicap, but they may suggest a continuing neurological imbalance that may require further testing. Due to their ambiguous presentation, these symptoms are frequently disregarded by professionals yet indicate an existing or impending mental disease. In our study, it was noted that the rehabilitation population has minimal awareness about NSS and yet there was high prevalence among them. We also used a standardized instrument in the form of the neurological examination scale which with its four domains help to ascertain which area the deficit lies in. Our study concluded that there were no differences based on age, gender, or literacy in the NES score. Depending on the length of the sickness, considerable variation was noted in the sequencing of complex motor acts. However, further research needs to be carried out on the same subject on a large scale focusing on multiple centers to broaden the understanding of the clinicians on NSS such that they can be identified early and managed effectively.

## REFERENCES

1. Kalużyńska O, Rabe-Jabłońska J. Neurological soft signs as a candidate for an endophenotype of schizophrenia. *Psychiatr Pol* 2014;48(1): 5–18. PMID: 24946431.
2. Shaffer D, Schonfeld I, O'Connor PA, et al. Neurological soft signs: Their relationship to psychiatric disorder and intelligence in childhood and adolescence. *Arch Gen Psychiatry* 1985;42(4):342–351. DOI: 10.1001/archpsyc.1985.01790270028003.
3. Schröder J, Niethammer R, Geider FJ, et al. Neurological soft signs in schizophrenia. *Schizophrenia Res* 1991;6(1):25–30. DOI: 10.1016/0920-9964(91)90017-l.
4. Chen EY, Shapleske J, Luque R, et al. The Cambridge Neurological Inventory: A clinical instrument for the assessment of soft neurological signs in psychiatric patients. *Psychiatry Res* 1995;56(2):183–204. DOI: 10.1016/0165-1781(95)02535-2.
5. Buchanan RW, Heinrichs DW. The Neurological Evaluation Scale (NES): A structured instrument for the assessment of neurological signs in schizophrenia. *Psychiatry Res* 1989;27(3):335–350. DOI: 10.1016/0165-1781(89)90148-0.
6. Shaffer D, Stokman CS, O'Connor PA, et al. Early soft neurological signs and later psychopathology. In: *Life-span research on the prediction of psychopathology*. Routledge; 2021. pp. 31–48.
7. Shaffer D. Soft neurological signs and later psychiatric disorders: A review. *J Child Psychol Psychiatry Allied Discip* 1978;19(1):63–65. DOI: <https://doi.org/10.1111/j.1469-7610.1978.tb01753.x>.
8. Peters JE, Romine JS, Dykman RA. Special neurological examination of children with learning disabilities. *Dev Med Child Neurol* 1975;17(1):63–78. DOI: 10.1111/j.1469-8749.1975.tb04959.x
9. Wikler A, Dixon JF, Parker Jr JB. Brain function in problem children and controls: psychometric, neurological, and electroencephalographic comparisons. *Am J Psychiatry* 1970;127(5):634–645. DOI: 10.1176/ajp.127.5.634.
10. Paulsen K. Reflection-impulsivity and level of maturity. *J Psychol* 1978;99(1):109–112. DOI: 10.1080/00223980.1978.9921448.
11. Rutter M, Graham P, Birch HG. Interrelations between the choreiform syndrome, reading disability and psychiatric disorder in children of

- 8–11 years. *Dev Med Child Neurol* 1966;8(2):149–159. DOI: 10.1111/j.1469-8749.1966.tb01720.x.
12. Wolff PH, Hurwitz I. Functional implications of the minimal brain damage syndrome. *Semin Psychiatry* 1973;5(1):105–115. PMID: 4803376.
  13. Chan RCK, Xu T, Heinrichs RW, et al. Neurological soft signs in schizophrenia: A meta-analysis. *Schizophr Bull* 2010;36(6):1089–1104. DOI: 10.1093/schbul/sbp011.
  14. Bolton D, Gibb W, Lees A, et al. Neurological soft signs in obsessive compulsive disorder: Standardised assessment and comparison with schizophrenia. *Behav Neurol* 1998;11(4):197–204. DOI: 10.1155/1999/639045.
  15. Jaafari N, Baup N, Bourdel MC, et al. Neurological soft signs in OCD patients with early age at onset, versus patients with schizophrenia and healthy subjects. *J Neuropsychiatry Clin Neurosci* 2011;23(4):409–416. DOI: 10.1176/jnp.23.4.jnp409.
  16. Boks MPM, Liddle PF, Burgerhof JGM, et al. Neurological soft signs discriminating mood disorders from first episode schizophrenia. *Acta Psychiatr Scand* 2004;110(1):29–35. DOI: 10.1111/j.1600-0447.2004.00298.x.
  17. Boks MP, Russo S, Knegtering R, et al. The specificity of neurological signs in schizophrenia: A review. *Schizophr Res* 2000;43(2–3):109–116. DOI: 10.1016/S0920-9964(99)00145-0.
  18. Weinberger DR. Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry* 1987;44(7):660–669. DOI: 10.1001/archpsyc.1987.01800190080012.
  19. Insel TR. Rethinking schizophrenia. *Nature* 2010;468(7321):187–193. DOI: 10.1038/nature09552.
  20. Bigdeli TB, Neale BM, Neale MC. Statistical properties of single-marker tests for rare variants. *Twin Res Hum Genet* 2014;17(3):143–150. DOI: 10.1017/thg.2014.17.
  21. Urbanowitsch N, Degen C, Toro P, et al. Neurological soft signs in aging, mild cognitive impairment, and Alzheimer's disease – The impact of cognitive decline and cognitive reserve. *Front Psychiatry* 2015;6:12. DOI: 10.3389/fpsy.2015.00012.
  22. Chan RCK, Xie W, Geng FL, et al. Clinical utility and lifespan profiling of neurological soft signs in Schizophrenia spectrum disorders. *Schizophr Bull* 2016;42(3):560–570. DOI: 10.1093/schbul/sbv196.
  23. Thomas N, Tharyan P. Soft neurological signs in drug-free people with Schizophrenia with and without obsessive-compulsive symptoms. *J Neuropsychiatry Clin Neurosci* 2011;23(1):68–73. DOI: 10.1176/jnp.23.1.jnp68.
  24. Gunasekaran V, Venkatesh VMK, Asokan TV. A study of soft neurological signs and its correlates in drug-naïve patients with first episode psychosis. *Indian J Psychol Med* 2016;38(5):408–413. DOI: 10.4103/0253-7176.191393.
  25. Biswas S, Ghosh SK. Gross morphological changes of placentas associated with intrauterine growth restriction of fetuses: A case control study. *Early Hum Dev* 2008;84(6):357–362. DOI: 10.1016/j.earlhumdev.2007.09.017.
  26. Zhao Q, Ma YT, Lui SSY, et al. Neurological soft signs discriminate schizophrenia from major depression but not bipolar disorder. *Prog Neuro-Psychopharmacol Biol Psychiatry* 2013;43:72–78. DOI: 10.1016/j.pnpbp.2012.12.006.
  27. Janssen J, Diaz-Caneja A, Reig S, et al. Brain morphology and neurological soft signs in adolescents with first-episode psychosis. *Br J Psychiatry* 2009;195(3):227–233. DOI: 10.1192/bjp.bp.108.052738.
  28. Mittal VA, Hasenkamp W, Sanfilippo M, et al. Relation of neurological soft signs to psychiatric symptoms in schizophrenia. *Schizophr Res* 2007;94(1–3):37–44. DOI: <https://doi.org/10.1016/j.schres.2007.04.017>.
  29. Dazzan P, Murray RM. Neurological soft signs in first-episode psychosis: A systematic review. *Br J Psychiatry Suppl* 2002;181(S43):s50–57. DOI: 10.1192/bjp.181.43.s50.
  30. Venkatasubramanian G, Latha V, Gangadhar BN, et al. Neurological soft signs in never-treated schizophrenia. *Acta Psychiatr Scand* 2003;108(2):144–146. DOI: 10.1034/j.1600-0447.2003.00113.x.