Neurological soft signs in comorbid learning and attention deficit hyperactivity disorders

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SUMMARY: Uslu R, Kapçı EG, Öztop D. Neurological soft signs in comorbid learning and attention deficit hyperactivity disorders. Turk J Pediatr 2007; 49: 263-269.

The present study aimed to examine whether neurological soft signs identified in children with attention deficit hyperactivity disorder (ADHD), learning disorders (LD), comorbid ADHD-LD and children with no known disorders could be grouped and whether these groups of soft signs would differentiate between the clinical groups and the non-clinical group. A total of 148 children (114 boys, 34 girls) participated in the study, with a mean age of 8.84. The exploratory factor analysis for Neurological Examination for Subtle Signs (NESS) items revealed five factors, explaining 81.7% of the variation. Multivariate analysis of variance showed that these factors of NESS were significantly different between the clinical groups and the non-clinical group. The discriminant functional analysis also yielded significant canonical discriminant functions, correctly classifying 85% of the clinical and non-clinical groups of children. Certain factors of NESS such as speed of movement, dysrhythmia and overflow with timed movements, provide important information that may enhance our understanding of the neurobiological bases of ADHD and LD and the clinical implications of neurological soft signs.

Key words: learning disorder, attention deficit hyperactivity disorder, neurological soft signs.

Academic underachievement is a common reason for child psychiatric admissions. Attention deficit hyperactivity disorder (ADHD) and learning disorders (LDs) are two major child psychiatric disorders that cause underachievement[1]. ADHD is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically observed in children at a comparable level of development. On the other hand, LDs are characterized by academic functioning substantially below that expected, given the person's chronological age, measured intelligence and age-appropriate education. These two disorders have shown comorbidity[2-5] and are known for their strong neurodevelopmental bases[6-9]. ADHD-LD comorbidity has also been studied in relation to several neuropsychological measures. Comorbid subjects who fulfill the diagnostic criteria for both disorders have demonstrated poorer performance compared to other groups in all or some of these assessments[10-12].

Neurological soft signs (NSS) have been described as non-normative performance on a neurological examination of motor and sensory functioning in the absence of a focal lesion[13]. The relationships between NSS, behavioral problems and academic underachievement have been demonstrated in a substantial amount of research[14-16]. Earlier studies in this area as reviewed by Rie et al.[17] have yielded controversial results, mostly against the association between soft signs and psychiatric disorders. However, more recent studies have consistently found a relationship between NSS and clinical diagnoses. Children with problems such as hyperactivity[18,19], impulsivity[20], reading difficulties[19,21] or school underachievement[16] were found to differ significantly with respect to soft signs.

Overall, studies have demonstrated a relation between NSS severity and neurodevelopmental disorders such as ADHD and LD. Recent studies have focused on whether it was the

type or severity of NSS that predicted a clinical diagnosis of these disorders. For example, Batstra et al.[22] studied minimal neurological dysfunction (MND) and cognitive achievement in a non-psychiatric population of school-aged children. They found that children with more MND clusters performed worse in school and showed more signs of attention deficit. Specific forms of MND were found to be related to externalizing and internalizing behavior problems. NSS, referred to as minor neurological signs, were found to predict a clinical diagnosis of ADHD in pre-school children as well[23].

Despite the overall agreement on the significance of NSS in relation to neurodevelopmental disorders, we found a limited number of studies that were conducted to assess NSS in children with clinical diagnoses of ADHD or LD[24-26]. In addition to the difficulties in motor performance such as writing skills reported by parents and teachers, our clinical observations during NSS examinations of comorbid children have led us to notice that children who had comorbid ADHD and LD performed worse than children with ADHD or LD alone. Therefore, we designed the present study aiming to examine whether NSS of children with ADHD, LD and ADHD-LD could be grouped and whether these groups of soft signs would differentiate between the clinical groups and a non-clinical group.

Material and Methods

Subjects

A total of 148 children participated in the study. The clinical and control groups consisted of 60 boys/14 girls and 54 boys/20 girls, respectively. Children under the age of six or those who had a physical handicap were excluded from the study in order to eliminate factors that could impede the child's cooperation during assessment. Children with an IQ<70 were excluded as well during diagnosis of the clinical groups. The non-clinical group of children was randomly selected from a pool of students of a public school who were reported by their teachers to have no significant physical, academic or behavioral problems. Since there were no differences between girls and boys in both clinical and control groups with respect to age and NSS findings, girls' and boys' findings were evaluated together (Table I).

Instruments

***Neurological Examination for Subtle Signs*[27]:** The Neurological Examination for Subtle Signs (NESS) is a widely used instrument to assess NSS in children. The items are mainly derived from the revised form of the Physical and Neurological Examination for Soft Signs (PANESS) developed by Guy in 1976[27]. Revision was reported to be necessary to eliminate items that were difficult to administer or score and that were unreliable or seldom scored, and also to add reliable and significant items to be used in child psychiatric populations. It is a practical tool requiring minimum time (15-20 minutes) and equipment. NESS assesses the lateral preference pattern, gait and balance, quality of rapid movement (dysrhythmia), impersistence, involuntary movements, speed of repetitive and sequenced/patterned movements, overflow and symmetry of errors.

Although a majority of the categorically scored items were found not stable at two-week intervals and researchers were cautioned regarding taking repeated measures, reliability studies concluded that it had acceptable levels of interrater reliability (Kappa >.50), intraclass correlation (>.70) and internal consistency of.74[28].

Table I. Descriptive Data of Children by Clinical Diagnosis, Age and Sex and T-Test Comparisons by Age and Sex

Clinical diagnosis	N	Boys	Girls	Age (M)	t-tests of sexes for age	t-tests of sexes for NESS total scores
LD	21	14	7	8.71	t(19)=1.92, p>.07	t(19)=.61, p>.54
ADHD-LD	23	20	3	8.52	t(21)=.52, p>.60	t(21)=1.31, p>.20
ADHD	30	26	4	9.20	t(28)=.66, p>.51	t(28)=1.58, p>.12
Controls	74	54	20	8.78	t(72)=1.32, p>.65	t(72)=.33, p>.74
Total	143	112	31	8.82	t(146)=1.67, p>.10	t(146)=1.77, p>.08

LD: Learning disorder. ADHD-LD: Comorbid attention deficit hyperactivity disorder and learning disorder. ADHD: Attention deficit hyperactivity disorder.

Turgay DSM-IV-Based Child and Adolescent Behavior Disorders Screening and Rating Scale (T-DSM-IV-S): This instrument was developed by Turgay[29] in 1994 and adapted by Ercan et al.[30] in 2001. It is based on the Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition (DSM-IV) diagnostic criteria and assesses hyperactivity-impulsivity (9 items), opposition-defiance (8 items) and conduct disorder (15 items). The items are rated on a 4-point Likert-type scale from 0 to 3. In the study, the instrument was used to assess children's ADHD symptoms based on parent and teacher reports with the purpose of supporting the clinical diagnosis of ADHD.

Wechsler Intelligence Scale for Children-Revised (WISC-R; Turkish standardization by Savaşır and Şahin[31]) and ***Reading and Writing Battery for Turkish Children*** (RWB[32]) were used for the diagnosis of learning disorders according to the DSM-IV[33]. RWB is a standardized instrument that assesses the reading and writing abilities of Turkish children.

Procedure

All consecutive subjects admitted to the outpatient clinic of the Child Psychiatry Department of the University of Ankara and diagnosed as ADHD, LD or comorbid ADHD-LD according to DSM-IV criteria were included in the study. NESS was administered to clinical and non-clinical groups. All children in the clinical groups underwent a thorough standard neurological examination to ensure that the findings of the NESS reflected soft signs. Informed consent was obtained from a parent of all participants and the research protocol was approved by the Medical School Board of Ethics at Ankara University.

Results

Factor Analysis for Neurological Soft Signs

Exploratory factor analysis techniques were used to identify the number of underlying factors as well as the pattern of factor loadings on the 24 NESS items. A total of five factors emerged with eigen values of 1.0 or more. All items except three had loadings on one of the factors and none of the items had loadings below 0.30 (Table II). Items related to gait and balance error, impersistence and involuntary movements scores that were found to have loadings below.30 and/or loadings on more than one factor were excluded from the factor analysis.

Table II. Factor Loadings for the Neurological Soft Signs Items (NESS; N=148)

	Factors and loadings				
Abbreviated NESS Items	Factor I	Factor II	Factor III	Factor IV	Factor V
1. Total repetitive speed of movement	.91				
2. Total sequenced/patterned speed of movement	.91				
3. L-S sequenced/patterned speed of movement	.90				
4. R-S repetitive speed of movement	.88				
5. L-S repetitive speed of movement	.87				
6. R-S sequenced/patterned speed of movement	.85				
7. Overflow grand total		.89			
8. R-S overflow with repetitive timed movement		.86			
9. R-S overflow with sequenced/patterned timed movement		.84			
10. L-S overflow with sequenced/patterned timed movement		.83			
11. L-S overflow with repetitive timed movement		.78			
12. Grand total of asymmetrical overflow			.97		
13. Total asymmetrical error			.87		
14. R-S asymmetrical errors			.85		
15. L-S asymmetrical errors			-.79		
16. Total dysrhythmia errors				.86	
17. R-S dysrhythmia errors				.81	
18. L-S dysrhythmia errors				.78	
19. R-S overflow with gaits					.83
20. L-S overflow with gaits					.65
21. Asymmetrical overflow with gaits					-.62

L-S: Left-sided. R-S: Right-sided. Factor I: Speed of movement. Factor II: Overflow with timed movements. Factor III: Asymmetry of error. Factor IV: Dysrhythmia. Factor V: Overflow with gaits.

These five factors accounted for 81.7% of the total variation. The strongest factor, "speed of movement", loaded with six items accounted for 38.2% of the total variance. Items related to the cerebral coordination of alternate muscle groups were found to have grouped in this factor. This factor also had the highest reliability of .91 The second strongest factor, "overflow with timed movements", accounted for 16.5% of the variance, with an internal reliability of .78 Overflow movements that presented during repetitive and patterned/sequenced timed movements grouped in this factor. The least reliable factor was the third, "asymmetry of error", which accounted for 12.7% of the variance and had an internal reliability of .32 The fourth factor, "dysrhythmia", referring to the group of items assessing the quality of movement, had the second highest reliability of .88 and added an additional 8.9% to the total variance. The final factor, "overflow with gaits", which had items related to overflow movements that were observed during gaits, accounted for 5.5% of the total variance with an internal reliability of .62

Factor analysis results showed that NESS items explained a high proportion of the total variance with an acceptable level of reliability ranging from .32 to .91 suggesting that NESS items could be grouped into five factors.

Types of NSS in Children with ADHD, LD and ADHD-LD

In order to examine differences between children with ADHD, LD, ADHD-LD and children without these disorders, we performed a multivariate analysis of variance (MANOVA), according to Wilks' criterion, followed by the univariate analysis of variance (ANOVA) for each of the NESS factors: a) speed of movement, b) overflow with timed movements, c) asymmetry of error, d) dysrhythmia, and e) overflow with gaits (Table III).

The MANOVA for main effect of diagnosis was significant, $F(4,148) = 7.05$, $p<.0001$, $\eta^2=.20$, showing a relation between diagnosis and NESS types. The Tukey's HSD procedure was employed to find the source of difference for each of the NESS types. The univariate analysis for the first factor -speed of movement- was found significant, $F(4,145)=16.04$, $p<.0001$. Tukey's HSD showed that groups LD and ADHD-LD were significantly different from the control group. This factor also significantly differentiated ADHD-LD and ADHD groups. Additionally, it may be important to note that speed of movement had approached significance to differentiate ADHD and LD groups ($p<.06$). The second factor -overflow with timed movements- ($F(4,145)=15.66$, $p<.0001$) and the fourth factor –dysrhythmia- $F(4,145)=27.36$, $p<.0001$ were found to significantly differentiate only the control group from the three clinical groups. The third and fifth factors were found nonsignificant.

Following MANOVA, a discriminant functional analysis was applied using each of the NESS items that yielded statistically significant canonical discriminant functions, comparing the clinical and non-clinical groups. The NESS items were found to correctly classify 85% of the children (127 of the 148 children). False

Table III. Group Differences Between Children with ADHD, LD, Comorbid ADHD-LD and Non-Clinical Children

Types of NSS	ADHD (n=30) M (SD)	LD (n=21) M (SD)	ADHD-LD (n=23) M (SD)	CONTROLS (n=74) M (SD)	F	η^2
1. Speed of movement	162.59 (34.70)	188.31 (46.67)	195.55 (43.75)	143.85 (31.02)	16.04*	.25
2. Overflow with timed movements	21.13 (14.29)	22.04 (12.63)	24.90 (12.85)	10.98 (6.34)	15.66*	.24
3. Asymmetry of error	2.28 (2.79)	3.23 (2.71)	2.63 (2.98)	2.70 (2.40)	.55	.01
4. Dysrhythmia	13.68 (5.04)	14.52 (4.98)	16.36 (5.98)	7.93 (3.93)	27.36*	.36
5. Overflow with gaits	5.37 (2.14)	5.80 (2.08)	5.81 (1.94)	5.62 (1.77)	.29	.001

ADHD: Attention deficit hyperactivity disorder. LD: Learning disorder. ADHD-LD: Comorbid attention deficit hyperactivity disorder and learning disorder.

Eta-squared (η^2), which is a proportion of the variance explained, is used as a measure of the effect size (.01=small,.06=medium,.14=large).

*$p<.0001$.

positives were higher than false negatives, 18.1% (n=13) versus 10.8% (n=8). A series of discriminant factor analyses were also used to differentiate between clinical and non-clinical groups of children for the five factors. Using the first factor -speed of movement- 73% of children were correctly classified. The second and the third factors correctly classified 77% and 57% of the children, respectively. The fourth factor had the highest classification percentage of 78.9. The fifth factor was found to correctly classify 54.1% of the children.

Discussion

One of the aims of the present study was to examine whether NSS assessed by NESS could be assembled in statistically significant groups. For this aim, an exploratory factor analysis was conducted which yielded a total of five factors explaining 81% of the variation ranging from medium to high reliability. These five factors consisted of items related to speed of movement, overflow with timed movements, asymmetry of error, dysrhythmia (quality of movement) and overflow with gaits. These factors were partly consistent with the findings of a study by Batstra et al.[22] in which six factors had emerged. For example, factors named as "fine manipulative disability" and "rarely occurring miscellaneous dysfunctions" in the above-mentioned study had items common with the fourth and second factors of NESS. The differences between the clusters found in the study by Batstra et al.[22] and the present one could be attributed to the utilization of different measures of NSS and to the difference of the populations (clinical vs. non-clinical) that were addressed.

The second aim of the present study was to compare the relation of these clusters of NSS to clinical groups of children with ADHD, LD, comorbid ADHD-LD and non-clinical groups of children. For this aim, the factors were subjected to MANOVA and it was found that the four groups of children significantly differed with respect to these factors, indicating that certain types of NSS differentiate children with ADHD, LD and comorbid ADHD-LD from their non-disabled peers. When we examined the source of the difference, the factors of speed of movement, overflow with timed movements and dysrhythmia were found to differ between the clinical and control groups. We should note that the first factor, speed of movement, which was assessed with timed-tasks of the extremities, explained a high proportion of the variance (38.2%) in NESS. This factor not only differentiated clinical and control groups, but children with ADHD and comorbid ADHD-LD as well. Furthermore, this factor approached significance in differentiating ADHD and LD groups ($p<.06$). These findings are consistent with previous findings, which showed that timed performance was related to neuromotor development in non-clinical populations[34].

Two other factors, overflow with timed movements and dysrhythmia, also significantly differentiated clinical groups from the non-clinical group. This may suggest that in clinical groups of children with neurodevelopmental problems, the quality of movement is compromised as much as its speed. The increase in overflow movements in the clinical groups in our study is consistent with the findings of Szatmari and Taylor[19], who reported that hyperactive children had significantly higher scores of overflow movements compared to children with other types of behavioral problems.

In a similar study by Batstra et al.[22], groups of NSS derived from factor analysis were found to relate to scholastic performance and signs of attention deficit. This finding shows that grouping of NSS is possible and that these groups are related to externalizing and internalizing behavioral problems in a non-clinical population of children. The present study not only verified that NSS could be grouped into meaningful clusters but that these clusters were significantly related to clinical groups of ADHD, LD, comorbid ADHD-LD and non-clinical controls. Additionally, our results support the study of Sato et al.[23] who reported that NSS were found to predict criteria of ADHD in pre-school children, by showing the significance of NSS in school-aged children with ADHD and LD.

The present study was limited with firstly, a relatively small sample size, which precluded comparisons according to sex and age of children. Secondly, the control group was recruited from schoolchildren who were reported by their teachers to show no academic underachievement. Therefore, clinical interviews or diagnostic tools were not utilized to exclude ADHD or LD in these children. However, based

on the presumption that a moderate to severe ADHD or LD would lead to underachievement, we believe that even if there were children with ADHD or LD in the control group they would have had mild forms of the disorders which would still enable a comparison with the clinical groups.

Another limitation was that other possible comorbid disorders, such as developmental coordination disorders or conduct disorders, were not evaluated. Future studies could address these issues. Also, since the relationship of NESS factors, such as speed of movement, to development is well established[27,34], the change in these factors by age could be verified by future longitudinal studies.

In conclusion, our study findings indicate that NSS could be grouped into factors, some of which significantly differentiate children with ADHD, LD, comorbid ADHD-LD and non-clinical children. The most prominent factors that differentiated the diagnostic groups were speed of movement, followed by overflow with timed movements and dysrhythmia. These prominent findings in children with ADHD-LD may etiologically indicate functional deficits in corresponding cerebral regions. For example, overflow movements that are considered developmentally normal in young children persist over time when cortical inhibitory functions fail to develop in order to stop the radiation of motoric impulses to body parts other than the target body part[35]. The deficit in cortical inhibitory functions is a cardinal neurophysiological feature of ADHD and the relationship between overflow movements and hyperactivity has already been shown[19]. Similarly, dysrhythmia and slowed speed of movement are findings connected with functional deficits in the cerebellum and basal ganglia[36]. It has been suggested that brain structures such as the frontal cortex, basal ganglia, and cerebellum and dopamine transmission systems are related with both motor and cognitive functioning[36-38].

The clinical importance of these findings, should they be replicated, may be two-fold: 1) They may have predictive value in the development of a comorbid LD in children who present with early signs and symptoms of ADHD. This view is consistent with the findings of the study by Kroes et al.[39] that showed the predictive value of qualitative aspects of movement (i.e. dynamic balance, diadochokinesis and manual dexterity) and to some extent the quantitative aspects of movement (i.e. speed of movement) for the development of ADHD at a later stage. 2) They may indicate the necessity of including in the treatment of children with ADHD and LD therapeutic measures which address their developmental motor difficulties.

Thus, it seems to be worth examining in future studies how these three factors, namely, speed of movement, followed by overflow with timed movements and dysrhythmia, contribute to the maintenance of these disorders and how the changes in these factors predict the changes in the academic and social difficulties that these children experience. Further studies on these factors will not only enhance our understanding of the neurobiological bases of neurodevelopmental disorders but will also provide a basis for designing clinical interventions for these disorders.

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