Assessment of neurological soft signs in pediatric patients with HIV infection

Najla Eiman, Rajesh Raman, S. N. Mothi, T. S. Sathyanaryana Rao, Nawab Akhtar Khan, Vaishnawi Kunusegaran, R. Tharun Krishnan

Departments of Psychiatry and Clinical Psychology, JSS Medical College and Hospital, JSS University, Department of Pediatrics, Asha Kiran Charitable Trust, Mysore, Karnataka, India

ABSTRACT

Background: Children and adolescents comprise a significant proportion of people living with HIV. The effects of HIV on the growing brain have generated interest among researchers in this field. Deficits arising during this crucial phase of neuromaturation due to HIV infection need to be assessed and addressed. Neurological soft signs (NSSs) can act as a proxy marker for underlying neuropsychological deficits. The present study aims to study the NSSs in pediatric patients with HIV and compare with healthy controls (HCs).

Materials and Methods: Forty-eight children aged between 6 and 16 years diagnosed with HIV were selected by purposive sampling, and the Physical and Neurological Examination of Soft Signs (PANESS) scale was applied. Fifty children matched by age and sex were recruited from a nearby school, and the PANESS scale was applied. Children were divided into age- and gender-specific groups. The outcome scores of cases and controls groups were compared.

Results: Males and females aged 13–16 years with HIV showed more soft signs as compared to HCs, with respect to gait errors, dysrhythmia, impersistence, speed of repetitive and sequenced movements, overflow with gaits, overflow with sequenced movements, total overflow, and overflow in excess of age. The differences in scores were less marked in younger age groups among both the genders.

Conclusions: The persistence of NSSs in older age group in HIV-infected children may point toward the presence of HIV-associated neurological disorder.

Key words: Neurological soft signs, pediatric HIV infection, Physical and Neurological Examination of Soft Signs

INTRODUCTION

Globally, over 3.2 million children are affected by HIV who comprise 9.1% of all people living with HIV.[1] The relation between HIV and neurological damage is well known with HIV causing direct neurological damage as well as due to HIV-related states. HIV-associated neurocognitive disorder is a well-researched entity in adults, but when it comes to children, there is a scarcity of literature. Childhood and adolescence are the crucial periods for neurodevelopment, and hence, any insult to the immature brain during this phase can lead to the development of permanent neurological sequelae.

The predominant mode of transmission of HIV in children is from mother to child transmission. In children affected by HIV, the virus enters the brain within days to weeks of the primary infection and leads to neuronal damage and cell
HIV infection does not cause neurological damage by directly affecting the neurons, but there exists a complex interplay between the uninfected cells and neurons that ultimately lead to neuronal damage. Neurocognitive deficits in HIV patients can occur as a primary HIV-related disorder or as sequelae of HIV encephalopathy or other secondary infections. Children who have suffered HIV encephalopathy are 9.4 times more likely to develop neurocognitive disorders.

Previous research has shown a poorer functioning of children with HIV on various measures of neurodevelopmental assessment. Even in those children who are neurologically asymptomatic, there may be ongoing neuronal damage. The neuropathogenesis is often disproportionate to the findings on clinical neurological examination, and only a focused neurological examination can pick up the deficits in apparently asymptomatic children. Cognitive profiling of HIV-infected children reveals deficits in attention, language, verbal learning and memory, visuomotor functions, fine motor performance, and executive functions. Neuropsychological deficits in asymptomatic patients, especially deficits in executive functions, language, and memory, may interfere with activities of daily living as well as scholastic difficulties.

There may be subtle neurological abnormalities in HIV-infected children who are asymptomatic, which may go unnoticed on routine neurological examination. These deficits can manifest as neurological soft signs (NSSs) which, although developmental, can point toward underlying neurological damage.

Schilder coined the term soft signs. These were defined by Shafer et al. as nonnormative performance on neurological examination by people who are not mentally retarded and are without focal neurological deficits. Softness refers to the validity and reliability of these signs. NSS being developmental may be observed in younger children and reflects a failure of cortical motor inhibition. These subtle signs can serve as markers for inefficiency in neighboring parallel brain systems important for control of cognition and behavior. Persistence of subtle signs into later childhood and adolescence, however, may indicate an abnormal neurological development. NSSs in children have been associated with a number of neuropsychiatric disorders such as psychosis, autism, specific learning disabilities (SLD), attention-deficit and hyperactivity disorder (ADHD), and obsessive–compulsive disorder.

The current study aims to study the NSSs in HIV-infected children as the previous research showed that NSSs and neuropsychological assessment may be two different ways of capturing the same construct—the brain functioning. Testing for NSS may be easier when compared to a detailed neuropsychological assessment and is time-saving, and NSS could act as a proxy indicator for underlying neuropsychological deficits.

**MATERIALS AND METHODS**

The present study is a prospective, observational-matched, cross-sectional cohort study comparing NSSs in pediatric HIV patients and matched controls. Forty-eight children diagnosed with HIV were recruited by purposive sampling from Asha Kiran Hospital at Mysore after obtaining an ethical clearance. Fifty matched controls were recruited from a private school at the same town after holding parent–teacher meetings where informed consent was obtained from the guardians as well as the controls above 12 years of age. The cases and controls were recruited after ruling out for criteria as per the ICD-10 Diagnostic Research Criteria for Mental retardation and Conduct disorder; ADHD was assessed through the Swanson, Nolan, and Pelham-IV (SNAP-IV) 26-item screening tool; Screening measures which were used to rule out the confounding factors included detailed clinical history to exclude cases of Mental retardation, Conduct disorder, Seizure disorder, neuroinfections, cerebrovascular accidents, physical disability and visual and/or hearing impairment. Screening tool to rule out ADHD was Swanson, Nolan, and Pelham-IV (SNAP-IV) 26-item screening tool. Specific Learning disability was ruled out using Short Screening tool for SLD.

**Tools**

**Sociodemographic and clinical datasheet**

A semi-structured form especially designed for the study was used. It consisted of questions covering all areas of sociodemographic details and questions related to evidence of intellectual disability, ADHD, SLD, any past neuroinfections, seizures, and physical impairments.

**Screening tools**

**Gesell’s drawing test**

It is an intelligence test to screen out intellectual disability. It can be used in children with mental handicap, hearing impairments, and other developmental disabilities. The test items have been divided into three levels and comprise 45 items. The reliability for the scale for the three levels varies between 0.66 and 0.78 and the validity is 0.982.

**SNAP-IV 26-item attention-deficit and hyperactivity disorder Rating Scale**

This is the original scale which was devised consisted of 90 items which assessed for ADHD, oppositional defiant disorder, and some other symptoms as per the DSM-IV. A 26-item SNAP-IV version (short form), also referred to as the MTA version, was devised to assess for the ADHD core symptoms which include hyperactivity, impulsivity, and inattention.

**Short Rating Scale for learning disability**

It has been developed and validated at our institute and is not yet published. The scale consists of 31 items divided...
into seven subcategories of vision and hearing, coordination and organization, memory, reading, writing, calculation, and miscellaneous category, with a global score ranging between 0 and 93.

NCHS normalized reference weight-for-length and weight-for-height by sex\cite{21} It is used to assess for malnutrition.

**Modified Kuppuswamy Scale\cite{22}**
It is used to assess the socioeconomic class. This classification was originally proposed in 1976. In our study, we have used the revised version of it. The Kuppuswamy scale continues to be one of the most important tools for research in India. The socioeconomic class global score is derived from subcategory scores of monthly income of family, education score, and occupation score. The total score varies from 3 to 29, and there are five outcome groups of socioeconomic class.

**Assessment tool**
**Revised Physical and Neurological Examination for Soft Signs scale – Denckla, 1955**
The revised version of Physical and Neurological Examination of Soft Signs (PANESS) consists of 21 items. It is an observational scale with questions covering gait, stance, laterality and quality of rapid movements, im-persistence score, involuntary movement score, repetitive speed of movement score, sequenced speed of movement score, and asymmetrical movement score. It assesses in terms of laterality and timed and untimed motor movements. It has been found to have adequate test–retest reliability, inter-rater reliability, and internal consistency.\cite{23}

**Scoring of Physical and Neurological Examination for Soft Signs**
The outcome scores of PANESS have been divided into 13 components, which include lateralization pattern assignment, gait and balance error score, impersistence score, dysrhythmia errors, involuntary movement score, speed of repetitive movements, speed of patterned movements, overflow with gait, overflow with repetitive movements, overflow with patterned movements, grand total overflow, overflow in excess for age, and asymmetric error score.

**Statistical analysis**
The Statistical Package for the Social Science-22 (IBM Corp, Armonk, NY) was used to analyze the data. The cases and controls were divided into three age- and gender-specific groups of 6–16 years. Data were dichotomized on measures of gender, antiretroviral therapy (ART) status versus pre-ART status. Descriptive and inferential statistics were used. Taking into account the nonparametric distribution of data, median and interquartile range were considered. Comparisons in NSS were made between cases and controls in each age and gender groups. Comparisons were also made between cases on ART and not on ART, malnourished versus normal cases; NSS between males and females was compared among cases. The significance level was set at \(P < 0.05\). Correlational statistics were used to assess the NSS in relation to CD4 cell count and stage of disease.

**RESULTS**
The mean age of cases was 12.12 years and that of controls was 10.6 years. There was a significant difference in the means between the two groups [Table 1]. However, the cases and controls were compared by considering age-specific groups, which did not reveal a significant difference in the means. Males represented for 56.3% of cases and 48% of controls. The mean CD4 count was 716.8 cells/cumm and the mean duration while on ART was 4.36 years. 79.2% of all the cases were on ART. The cases included in the study belonged to WHO Stage 1 and 2 of HIV and none in the Stage 3 or 4. Malnutrition was assessed using the WHO/NCHS normalized data, and 14.6% of the cases were found to be falling into the category of moderate malnutrition. About 85% of the population belonged to the lower-middle and upper-lower socioeconomic class as per the modified Kuppuswamy scale [Table 2].

There was no statistically significant difference noted in the lateral preferences between the cases and the controls, wherein both showed a predominant righthandedness followed by mixed laterality. In the age group of 13–16 years males [Table 3], significant difference was noted on measures of gait errors, dysrhythmia score, involuntary movement score, speed of repetitive movements bilaterally, speed of sequenced movements on left side, overflow with gait, overflow with sequenced movements, total overflow, and overflow in excess of age. In the age group of 10–12 years, significant differences were noted with respect to speed of repetitive movement score on right side, total overflow, and overflow in excess of age. Among the age group of 6–9 years, higher frequency of NSS was found in relation to dysrhythmia score, speed of sequenced movement score on the right side, overflow with repetitive movements, overflow with sequenced movements on the right side, and total overflow. It is worthwhile to note that the differences in NSS between cases and controls in males in age group 13–16 years were significant as compared to the younger age group, where both cases and controls scored comparatively on most of the components of the PANESS scale.

Similarly, in females of age group 13–16 years, statistically significant differences were noted among eight components of PANESS scale, which included gait errors, dysrhythmia errors, speed of repetitive movement and sequenced movement on right side, overflow with gait, overflow with repetitive movements, total overflow, and overflow in excess of age [Table 4]. As compared to the younger age
groups, the age group of 13–16 years revealed significant differences on higher number of components of NSS between cases and controls.

The lateralization of errors was more toward the left in both the groups, and no statistically significant differences were noted with laterality between cases and healthy controls (HCs). No significant differences were noted in SS with respect to gender, which was not consistent with the findings of previous studies which showed that at developmental NSS in girls resolved earlier than boys.[24,25] NSS showed a negative correlation with age which has been consistent with the previous studies. Significant differences in NSS between the ART-receiving group and those not on ART were noted on involuntary movement score, speed of repetitive movement, total overflow, and overflow in excess of age [Table 5].

No significant correlation was found between NSS and CD4 count, stage of disease, and duration of ART and malnutrition [Tables 6 and 7].

DISCUSSION AND CONCLUSIONS

HIV has shown to cause neurocognitive and motor deficits in children. Insult to the growing central nervous system (CNS) of a child has implications on the trajectory of neurodevelopment.[26] NSSs are considered to be developmental, and their association has been found with neurodevelopmental disorders such as ADHD, SLD, and certain neuropsychiatric conditions. We hypothesized that with HIV-bearing implications on neurocognitive and motor development, NSS may be used as a useful marker to identify these deficits in HIV-infected children. An effort was made in our study to capture these subtle neurodeficits in HIV-infected children, which may actually act as a proxy marker for underlying neuropsychological deficits. Our results showed that the differences in NSS were more marked in the age groups of 13–16 years in both the sexes while the previous studies showed that NSSs decrease with onset of puberty and adolescence reflecting maturation of CNS.[24] The presence of >2 NSS is clinically significant after puberty.[27] Their persistence in the present study could point to a maturational lag in the nervous system of HIV-infected individuals. The presence of NSS could also indicate an abnormal neurological development in these children predisposing them to other neuropsychiatric disorders. The failure to pick up the differences in NSS in younger age groups could be due to the fact that NSS is inherently present at a higher frequency even in controls within this age group.

Previous research has shown that NSS and assessment of neuropsychological deficits may be two different ways of measuring similar constructs.[16] Further studies are needed to assess the correlation between NSS and different constructs of neuropsychological battery. This may have implications in the use of NSS in clinical setting to screen neuropsychological deficits, which may be less time-consuming.

The present study did not find any gender differences with respect to NSS in HCs in contrast to earlier studies, which show that gender differences existed in soft signs with girls.
Table 3: Neurological soft signs in males

|                      | Cases Median | Controls Median | P   | Cases Median | Controls Median | P   | Cases Median | Controls Median | P   |
|----------------------|--------------|-----------------|-----|--------------|-----------------|-----|--------------|-----------------|-----|
| Gait errors          | 10.00        | 7.00            | 0.29| 2.00         | 0.00            | 0.16| 5.00         | 2.00            | <0.001|
| Dysrhythmia errors   | 8.00         | 5.00            | 0.01| 5.00         | 3.00            | 0.16| 5.00         | 2.00            | 0.03 |
| Impersitence         | 1.00         | 1.00            | 0.34| 0.00         | 0.00            | 0.65| 2.00         | 0.00            | 0.05 |
| Involuntary movement score | 1.00     | 0.00            | 0.12| 0.00         | 0.00            | 0.32| 1.00         | 0.00            | 0.03 |
| Repetitive movement speed (left) | 7.98     | 7.84            | 0.14| 7.48         | 7.15            | 0.41| 6.51         | 5.16            | 0.01 |
| Repetitive movement speed (right) | 7.30     | 6.90            | 0.44| 7.52         | 5.66            | 0.04| 6.11         | 4.46            | <0.001|
| Sequenced movement speed (left) | 10.74    | 10.14           | 0.34| 9.81         | 8.08            | 0.32| 8.17         | 6.81            | 0.01 |
| Sequenced movement speed (right) | 9.99      | 8.61            | 0.02| 8.79         | 6.90            | 0.23| 6.91         | 6.40            | 0.12 |
| Overflow with gaits  | 4.00         | 4.00            | 0.34| 2.00         | 0.50            | 0.11| 3.00         | 1.00            | <0.001|
| Overflow with repetitive (movements) | 5.00     | 3.00            | 0.02| 4.00         | 1.00            | 0.16| 3.00         | 1.00            | <0.001|
| Overflow with sequenced movements | 7.00      | 4.00            | 0.14| 3.00         | 1.00            | 0.07| 3.00         | 1.00            | <0.001|
| Total overflow       | 16.00        | 12.00           | 0.03| 10.00        | 3.50            | 0.01| 8.00         | 4.00            | <0.001|
| Overflow in excess of age | 7.00      | 2.00            | 0.08| 9.00         | 2.50            | 0.01| 8.00         | 4.00            | <0.001|
| Asymmetric error score | −3.00      | −1.00           | 0.12| −3.00        | −1.50           | 0.53| −1.00        | −1.00           | 0.53 |

Table 4: Neurological soft signs in females

|                      | Cases Median | Controls Median | P   | Cases Median | Controls Median | P   | Cases Median | Controls Median | P   |
|----------------------|--------------|-----------------|-----|--------------|-----------------|-----|--------------|-----------------|-----|
| Gait errors          | 16.00        | 8.00            | 0.298| 8.00         | 5.00            | 0.095| 5.00         | 1.50            | 0.002|
| Dysrhythmia errors   | 7.00         | 3.00            | 0.001| 2.00         | 4.00            | 1.000| 5.00         | 3.00            | 0.011|
| Impersitence         | 2.00         | 2.00            | 0.797| 1.00         | 1.00            | 0.548| 1.00         | 0.00            | 0.211|
| Involuntary movement score | 0.00    | 0.00            | 1.000| 0.00         | 0.00            | 1.000| 0.00         | 0.00            | 0.235|
| Repetitive movement speed (left) | 8.42     | 8.54            | 0.699| 7.23         | 6.61            | 0.548| 7.00         | 6.14            | 0.079|
| Repetitive movement speed (right) | 7.77     | 7.86            | 0.699| 6.78         | 5.29            | 0.421| 6.04         | 5.00            | 0.011|
| Sequenced movement speed (left) | 9.90     | 9.23            | 0.606| 8.39         | 8.24            | 0.421| 8.10         | 5.88            | 0.051|
| Sequenced movement speed (right) | 8.62      | 9.84            | 0.147| 8.14         | 6.83            | 0.095| 7.62         | 5.40            | 0.032|
| Overflow with gaits  | 6.00         | 2.00            | 0.112| 2.00         | 2.00            | 0.310| 3.00         | 1.00            | 0.013|
| Overflow with repetitive (movements) | 3.00     | 3.00            | 0.518| 1.00         | 3.00            | 0.841| 1.00         | 0.00            | 0.044|
| Overflow with sequenced movements | 3.00      | 4.00            | 1.000| 2.00         | 2.00            | 0.690| 2.00         | 1.00            | 0.051|
| Total overflow       | 14.00        | 9.00            | 0.190| 5.00         | 7.00            | 0.421| 9.00         | 2.50            | 0.006|
| Overflow in excess of age | 9.00      | 3.00            | 0.004| 3.00         | 7.00            | 0.421| 9.00         | 1.00            | 0.003|
| Asymmetric error score | −1.00      | −1.00           | 0.606| −1.00        | −1.00           | 0.548| 0.00         | −1.00           | 0.169|

Performing faster and having better coordination. This finding could be due to the smaller sample size taken in our study which failed to reflect differences with regard to gender and also the smaller number of subjects in age-specific groups.

Significant differences were noted in four of the components of NSS in the ART and non-ART groups with ART group performing better than those not on ART. There are studies which have assessed for the neuroprotective effects of the ART medication and studies which support the early initiation of ART in the prevention of permanent neurological damage. However, the other facet of early initiation of ART is neuropsychiatric and other side effects due to ART itself which has to be carefully balanced with the plausible benefits.

No significant differences were noted with respect to the stage of the disease. This could imply that HIV could cause direct viral damage to the CNS independent of stage of disease or degree of immune compromise. None of the children in the study belonged to Stage 3 or higher clinical stage, which naturally ruled out the possibility of the confounding effects of possible opportunistic infections affecting the CNS in the subjects chosen. The presence of NSS in this clinical sample which included clinical Stages 1 and 2 may point toward the onset of neurological damage even in children with early clinical stages of HIV. This is consistent with the findings of previous research that has found neurocognitive and motor deficits in children with high lymphocyte counts.

We did not find a correlation between NSS and nutritional status of children. Malnutrition which is highly prevalent in developing countries itself could independently affect neurocognitive development in HIV children. Studies have shown that malnutrition could act as a comorbid factor in HIV-related cognitive impairment. The failure to identify cognitive deficits with respect to malnutrition can be explained in that children included in the study fell into mild and moderate degrees of malnutrition and none of them qualified for severe category.
functioning of HIV-infected children, especially scholastic difficulties, participation and sports, and other day-to-day activities. NSSs are non-specific, but their presence during adolescence and at older ages could signify neurological abnormality. There are several attempts to map NSS to neuroanatomical regions. Higher scores on gait errors and dysrhythmia could be related to cerebellar dysfunction. Time taken for repetitive and sequenced movements could represent deficits in motor speed and executive functions, which can be mapped to the anterior cerebellar lobe and basal ganglia. The higher scores on overflow movements seen among cases may point toward a disorder in corpus callosal connectivity, resulting in poorer cortical inhibition. Performance of fine motor movements is dependent on corticospinal tracts and corpus callosal connectivity. Similarly, motor impersistence is characterized by choreiform movements and lapses in postural control, which indicate deficits in executive functions mapped to the frontal cortex. As motor system matures, behavioral inhibition increases leading to a decrease in overflow movements. An asymmetry in lateralization errors which was shown toward the left side points out at the hemispheric differences during maturation. The persistence of NSS can have implications for the development of behavioral disturbances and the vulnerability to develop psychiatric disorders in these children.

Our study had certain limitations. The sample taken was smaller. The age range was wide and this limited the number of subjects in each age-specific group which may have prevented better comparison. We did not take into account the home environment of the subjects which itself could have bearing on the level of cognitive stimulation a child receives. The HIV status and psychiatric morbidity of the caregiver were not considered which may affect the compliance, the level of engagement of the child, and the opportunities for cognitive growth. Similarly, we did not rule out depression in these children which may affect the performance on tasks. The comment that NSS decrease with adolescence and pubertal onset was not substantiated by actual sexual maturity rating of the subjects.

Overall, the findings of our study indicate that there is neuromaturational delay or an abnormal neurological development in an HIV-infected individual, which manifests as subtle signs on examination. This may put an adolescent at risk for behavioral and psychiatric problems. NSS can also act as a proxy marker for underlying neurocognitive deficits, and there is a need to screen children at risk for the same. Identifying such deficits in initial stages can help us in early intervention in the form of neuropsychological rehabilitation to prevent the progress to more severe degrees of impairment. Examining for soft signs is less time-consuming and needs little training. However, we still need studies to find how well the soft signs correlate with neuropsychological functions in children and what construct of it do they contribute toward.

### Table 5: Neurological soft signs and antiretroviral therapy status

|                      | ART          | PreART       | P  |
|----------------------|--------------|--------------|----|
|                      | Median | Q1 | Q3 | Median | Q1 | Q3 |     |
| Gait errors          | 5.00    | 3.00| 8.00| 7.00    | 5.00|11.00| 0.3 |
| Dysrhythmia          | 6.50    | 4.00| 7.00| 5.50    | 5.00|8.00 | 0.7 |
| ImpERSISTENCE        | 1.00    | 0.00| 3.00| 1.00    | 0.00|5.00 | 0.9 |
| ImpERSISTENCE        | 0.00    | 0.00| 1.00| 1.00    | 1.00|2.00 | 0.04|
| Repetitive movement  | 7.07    | 6.41| 7.92| 7.37    | 6.17|8.08 | 0.8 |
| speed (right)        | 6.55    | 5.76| 7.40| 6.75    | 5.96|8.28 | 0.3 |
| Sequenced movement   | 8.41    | 7.71|10.03| 8.76    | 7.71|10.74| 0.9 |
| speed (left)         | 7.89    | 6.85| 8.89| 8.32    | 6.85|9.51 | 0.5 |
| Sequenced movement   | 3.00    | 2.00| 4.00| 4.00    | 3.00|5.00 | 0.051|
| speed (right)        | 2.00    | 1.00| 5.00| 2.50    | 2.00|4.00 | 0.3 |
| OverFlow with gait   | 3.00    | 2.00| 4.00| 4.00    | 3.00|7.00 | 0.02|
| Impersistence        | 1.00    | 0.00| 3.00| 2.00    | 1.00|4.00 | 0.5 |
| Impersistence        | 0.00    | 0.00| 1.00| 0.00    | 0.00|4.00 | 0.007|
| Repetitive movement  | 7.00    | 6.08| 7.93| 7.79    | 7.23|8.09 | 0.2 |
| speed (left)         | 6.40    | 5.76| 7.40| 7.30    | 6.78|7.70 | 0.4 |
| Sequenced movement   | 8.39    | 7.57| 9.98| 9.46    | 8.39|12.14| 0.1 |
| speed (left)         | 7.89    | 6.85| 8.89| 8.91    | 8.38|11.56| 0.1 |
| OverFlow with gait   | 3.00    | 2.00| 4.00| 2.50    | 2.00|3.00 | 0.7 |
| Impersistence        | 2.00    | 1.00| 5.00| 3.00    | 2.00|5.00 | 0.6 |
| Impersistence        | 3.00    | 2.00| 4.00| 2.50    | 2.00|5.00 | 0.7 |
| Total overflow       | 8.50    | 6.00|14.00|10.50    | 8.00|12.00| 0.8 |
| OverFlow in excess of age | 8.00 | 5.00|11.00| 9.00    | 5.00|11.00| 0.8 |
| Asymmetric error score| −1.00  |−3.00| 1.00| 1.00    |−1.00|2.00 | 0.1 |

ART – Antiretroviral therapy

### Table 6: Neurological soft signs and stage of disease

|                      | Stage | P  |
|----------------------|-------|----|
|                      | 1     | 2  |
|                      | Median | Q1 | Q3 | Median | Q1 | Q3 |     |
| Gait errors          | 5.50  | 4.00| 9.00| 4.00   | 2.00|8.00 | 0.6 |
| Dysrhythmia          | 6.50  | 5.00| 7.00| 4.50   | 4.00|7.00 | 0.3 |
| Impersistence        | 1.00  | 0.00| 3.00| 2.00   | 1.00|4.00 | 0.5 |
| Impersistence        | 1.00  | 0.00| 1.00| 0.00   | 0.00|4.00 | 0.07|
| Repetitive movement  | 7.00  | 6.08| 7.93| 7.79   | 7.23|8.09 | 0.2 |
| speed (right)        | 6.40  | 5.76| 7.40| 7.30   | 6.78|7.70 | 0.4 |
| Sequenced movement   | 8.39  | 7.57| 9.98| 9.46   | 8.39|12.14| 0.1 |
| speed (left)         | 7.89  | 6.85| 8.89| 8.91   | 8.38|11.56| 0.1 |
| OverFlow with gait   | 3.00  | 2.00| 4.00| 2.50   | 2.00|3.00 | 0.7 |
| Impersistence        | 2.00  | 1.00| 5.00| 3.00   | 2.00|5.00 | 0.6 |
| Impersistence        | 3.00  | 2.00| 4.00| 2.50   | 2.00|5.00 | 0.7 |
| Total overflow       | 8.50  | 6.00|14.00|10.50   | 8.00|12.00| 0.8 |
| OverFlow in excess of age | 8.00 | 5.00|11.00| 9.00   | 5.00|11.00| 0.8 |
| Asymmetric error score| −1.00 |−3.00| 1.00| 1.00   |−1.00|2.00 | 0.1 |

Assessment for NSS becomes more useful if there are studies to translate these findings into degree of impairment in daily
Table 7: Neurological soft signs and malnutrition

| Malnutrition |                  |                  | P     |
|--------------|------------------|------------------|-------|
|              | Median | Q1 | Q3 | Median | Q1 | Q3 |
| Gait errors  | 7.00   | 6.7 | 7.9 | 8.75   | 8.6 | 7.8 |
| Dysrhythmia  | 6.48   | 5.7 | 7.6 | 7.11   | 6.1 | 7.7 |
| Impersistence| 8.43   | 7.5 | 9.8 | 8.98   | 8.2 | 11.0 |
| Involuntary  | 8.11   | 6.8 | 9.0 | 8.38   | 7.4 | 9.9 |
| movement score|       |     |     |        |     |    |
| Repetitive movement score (left) | 4.00  | 3.5 | 5.0 | 4.00   | 3.5 | 5.5 |
| Repetitive movement score (right) | 2.00  | 1.5 | 2.5 | 2.00   | 1.5 | 2.5 |
| Sequenced movement score (left) | 5.00  | 4.5 | 5.5 | 5.00   | 4.5 | 5.5 |
| Sequenced movement score (right) | 3.00  | 2.5 | 3.5 | 3.00   | 2.5 | 3.5 |
| Overlap with gait | 10.00 | 9.0 | 11.0 | 10.00  | 9.0 | 11.0 |
| Overlap with repetitive movements | 9.00  | 8.0 | 10.0 | 9.00   | 8.0 | 10.0 |
| Total overlap | 0.00   | 0.0 | 1.0 | 0.00   | 0.0 | 1.0 |
| Overlap in excess of age | 1.00  | 0.0 | 2.0 | 1.00   | 0.0 | 2.0 |
| Asymmetric error score | 0.00  | 0.0 | 0.0 | 0.00   | 0.0 | 0.0 |

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Conflicts of interest
There are no conflicts of interest.

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