**Soft Signs in Movement Disorders: Friends or Foes?**

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**INTRODUCTION**

In movement disorders, emphasis on pure phenomenology to make diagnoses can lead to significant variability and diagnostic disagreement [1,2]. This is illustrated by difficulty among experts in deciding whether possibly equivocal signs (“soft” signs) are present or absent,. A tight pen grip, slightly asymmetric arm swing, or hyperextended fingers may be judged by some to be within the broad spectrum of normal. Others may consider such signs to be pathological. Hence, the relevance of such signs can be uncertain. Furthermore, we are often asked to judge on the presence and clinical relevance of soft signs in "neurologically healthy" individuals and this can be challenging (e.g. in clinical genetic studies). Although classification systems tend to include clinical signs to define boundaries of disease, the relevance of soft signs may be questionable if inter-rater reliability is variable.

Initially introduced in the psychiatric literature[3], the term “soft signs” has also recently been applied to movement disorders. In the recent Consensus Statement on the Classification of Tremor, the detection of soft signs has, for the first time, become an integral part of tremor classification[4]. Because of the uncertainty surrounding the interpretation of soft signs, we asked movement disorders experts (MDE) and experts in fields other than movement disorders (non-MDE) to rate videos of patients and healthy control subjects to assess inter-rater reliability on the presence or absence of soft signs.

**METHODS**

We asked seven MDE (AJE, AEL, TL, DM, FM, NPQ, MV) and six non-MDE (listed in the acknowledgements section) to rate 30 videos for the presence or absence of soft signs. Raters were advised that videos may feature control subjects or patients, but no other clinical information was provided. Twenty-five control subjects were recorded (9 men; age 49.6±18.9 years), recruited from patients without neurological illnesses, and healthcare professionals; and five videos showed subjects with diagnosed neurological disorders (cervical dystonia, Parkinson’s disease, dystonic tremor, obstructive hydrocephalus). The content of the videos was standardized to show head position, assessment of tremor (rest, posture, finger-nose testing), bradykinesia and gait. Raters were asked to report on the presence parkinsonism, dystonia, ataxia or tremor (or any combination thereof) or whether there was no neurological abnormality. The MDE group rated a subset of the videos a second time. Inter-rater reliability and intra-rater reliability were calculated using Cohen’s kappa. The number of videos rated as normal/abnormal by each group was compared with unpaired t-tests. Data are expressed as mean±standard deviation.

**RESULTS**

Absolute agreement regarding the movement phenomenology was fair for MDE (κ=0.31) and poor for non-MDE (κ=0.14). In deciding whether examinations were normal or abnormal, agreement was moderate for MDE (κ=0.42) and fair for non-MDE (κ=0.32). There was no significant difference between groups when rating the videos as normal or abnormal (p=0.19) and the number of videos rated as normal was similar for both groups (MDE 14.0±4.7 vs. non-MDE 14.8±7.6, range: 6-29, see Supplementary Table 1). Only one video was considered normal by all raters.

Agreement among non-MDE for dystonia (κ=0.01), ataxia (κ=0.05) and tremor (κ=0.10) was slightly better than chance. Inter-rater agreement for each movement disorder with statistical comparisons are shown in Figure 1. Intra-rater reliability was strong among MDE with mean κ=0.83 (range 0.17-1.00).

The videos and ratings by MDE and non-MDE of two illustrative control subjects are available as supplemental material.

**DISCUSSION**

Poor inter-rater reliability is a significant problem in all movement disorders and, unsurprisingly, the inter-rater reliability of the detection of soft neurological signs was poor (non-MDE) to fair (MDE). Specifically, agreement among raters on whether the examinations were normal/abnormal was only fair (κ=0.38). Agreement among the MDE group was better than among non-MDE when rating tremor and dystonia. However, even among MDE, agreement was fair to moderate.

A primary difficulty with diagnostic characterization of any movement disorder (for example, ET) is identification of soft signs. Determining the relevance of such signs can be problematic, leading to misdiagnoses and treatment dilemmas. This uncertainty will lead to difficulties in classification of specific disorders within epidemiological, genetic and pathological studies.

Advances in ET have been difficult because “heterogeneity” of phenotype has been widely accepted to be part of this entity[5]. The recent classification recommends a diagnosis of “ET plus” when isolated action tremor is combined with “additional neurological signs of uncertain significance such as impaired tandem gait, questionable dystonic posturing, memory impairment or other mild neurologic signs of unknown significance”[4].

The integral role that soft signs play in this classification questions whether we agree on what constitutes a soft sign. Which signs are relevant and which are to be ignored? Overall, the utility of an “ET plus” designation is highly questionable in view of the poor agreement in detection of soft signs shown here.

Our findings have implications for management of individual patients and for research on a population basis. In order to better understand genetic, biological/molecular and pathologic features of any neurological disorder, we must be able to separate patients into homogenous diagnostic groups.

Some limitations of our study should be mentioned. The videos were strongly weighted towards healthy control subjects and raters were asked specifically to look for the presence/absence of subtle signs, which may have led them to overcall signs. Interestingly, the analysis limited to the 25 control subjects yielded similar results (Supplementary Figure 2). Furthermore, the line between normality and abnormality in movement disorders can be thin and we often use other information to achieve a diagnosis (history, medications, family history). No clinical information about the subjects was given to the raters. However, the concept of dichotomizing examinations by the presence or absence of subtle signs has important implications in any classification system. For this reason, we asked the raters to assess phenomenology in isolation.

In conclusion, this study suggests that inter-rater agreement regarding the presence or absence of soft neurological signs is at best fair, even among experienced movement disorders specialists. This has consequences in the interpretation of subtle abnormalities in individual patients in a clinical setting and in the implementation of clinical criteria relying on ascertainment of soft signs.

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3) Manuscript: A. Writing of the first draft, B. Review and Critique.

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AJE 1C, 3B

AEL 1C, 3B

TL 1C, 3B

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**Figure Legend**

**Figure 1.** Light's kappa values for inter-rater agreement of absolute phenomenology, the presence or absence of any neurological signs and individual movement disorders. MDE: Movement disorders specialists; Non-MDE: Specialists in areas other than movement disorders \*=p<0.05; \*\*=p<0.01; \*\*\*=p<0.00.