Laterality Index - A means of identifying sites of concern in Parkinson’s disease clinical trials

A. Kott, MUDr¹; J. Swartz, MD, PhD²
¹Bracket, Prague, Czech Republic; ²Bracket, Goring-on-Thames, UK

INTRODUCTION
Clinical trials in Parkinson’s disease (PD) rely on subjective outcome measures such as the UPDRS, prone to procedural and data recording errors
Early identification of these errors, followed by corrective action, is known to improve the quality of data collected from the sites, thereby enhancing the validity of study outcomes
The asymmetrical nature of Parkinson’s disease results in unilateral predominance of clinical motor symptoms
» Expectations are that, during the course of a clinical trial, changes of lateral predominance (CLP) should be rare
» We have previously reported that up to 10% of clinical trial data demonstrate possible CLP – a concerning finding implying questionable/flawed data
» Because on-site monitoring may fail to detect CLP, a targeted monitoring system is necessary

RESULTS
A change of lateral predominance occurred at 5.3% of visits
A change of lateral predominance occurred at 50% of sites (Figure 1) with a median of three CLPs per site
Sites with more than three CLPs accounted for 77% of all CLPs in the dataset
Utilizing the Laterality Index we were able to identify highly concerning sites both as far as magnitude of change of lateral predominance as well as number of changes of lateral predominance from visit to visit (Table 1)
Figure 2 shows an example of a highly concerning site from the dataset with a total of 28 changes in lateral predominance and changes as large as 14 UPDRS points in the lateral predominance from visit to visit

CONCLUSION
Identifying and addressing study misconduct represents a powerful tool for increasing the validity of collected study data. We present a simple and easily applicable method of identifying possible misconduct by analysing laterality predominance changes within subjects. Utilizing available data we identified 16% of all subjects in the dataset to be affected with at least one predominance change. While at the majority of affected research sites laterality predominance changes were observed to have occurred in one subject only and to a small degree, we were able to identify sites where these changes occurred with large amplitude and, in some cases, at high frequency as well. One site accounted for 10% of all laterality predominance changes in the dataset with one of the largest amplitudes of these changes observed, leading to a questioning of the validity of data provided by this site. While the current analysis represents a retrospective analysis of collected data, a real time review of changes in lateral predominance changes offers the opportunity to identify potentially concerning sites early.

Such identification facilitates the provision of such sites with support in the form of additional training or, if deemed necessary, the limitation of ongoing recruitment at that particular site. In the long term, such early intervention may help to ensure that only good quality sites are included in a study, thereby significantly reducing errors and noise and thus increasing the overall outcome validity of the clinical trial.

REFERENCES