Clinically 'slight' bradykinesia in Parkinson's disease is accurately detected using evolutionary computation analysis of finger tapping

Jane E Alty[1,2], Jeremy Cosgrove[1,2], Michael A Lones[3], Stephen L Smith[4], Katherine Possin[5], Norbert Schuff[6,7] and Stuart Jamieson[1,2].

[1] Neurosciences, Leeds Teaching Hospitals NHS Trust, UK;
[2] Hull York Medical School, University of York, UK;
[3] Computer Science, Heriot Watt University, Edinburgh, UK;
[4] Electronics, University of York, UK;
[5] Neurology, University California San Francisco, USA;
[6] Radiology and Biomedical Imaging, University California San Francisco, USA;
[7] Radiology, San Francisco Veterans Affairs Medical Center, USA.

Background:

- Bradykinesia is the fundamental motor feature of Parkinson's disease (PD) but may be difficult to detect clinically, especially in the early stages.
- The commonest reason that movement disorders specialists misdiagnosed PD for other tremulous movement disorders was misinterpretation of bradykinesia [1].
- Bradykinesia is a complex clinical sign encompassing movements with slow speed, small amplitude, irregular rhythm, brief pauses and progressive decrements.
- Clinical ascertainment of the presence and severity of bradykinesia relies on subjective interpretation and integration of these components during a dynamic test.
- Not surprisingly, there is inter-rater variability for assessing bradykinesia, particularly when the severity is slight or mild [2].
- The need exists for a simple, non-invasive test that can provide an accurate, objective measurement of slight bradykinesia.

Objective: To assess whether MDS-UPDRS grade one PD bradykinesia can be accurately detected by a novel non-invasive device that analyses a standard finger tapping clinical assessment using evolutionary computation methods.

Electromagnetic tracking sensors

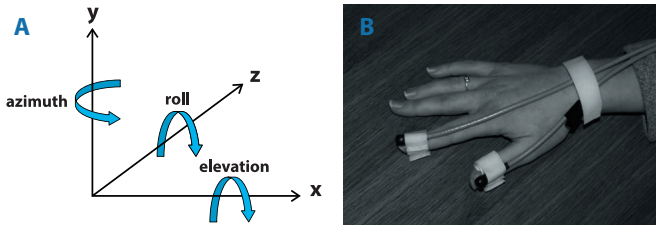

Figure 1: A The movement of each sensor is measured in 3-dimensional space using 3 positional (x, y, z) and 3 orientation (azimuth, roll, elevation) coordinates; B two electromagnetic sensors attached to a subject's right hand.

Methods: Forty-nine PD patients and 41 healthy controls (HC) performed finger tapping for 30 seconds with each hand separately, whilst wearing electromagnetic tracking sensors on the index finger and thumb. Movement data was analysed by purpose written evolutionary computation algorithms. The algorithm prediction of the diagnostic group was compared to clinical assessment using receiver operator characteristic (ROC) curves and was further validated by testing on an independent sample of finger tapping data collected from 13 PD patients and 9 HC in an international centre.

What are evolutionary algorithms?

Evolutionary algorithms provide a generic method for optimising classifier models to fit data. The algorithm refines a population of classifiers through a repeated process of variation and selection based on the theory of Darwinian evolution. Selection is based on maximising a fitness criteria, in this case the area under the ROC curve (AUC) when separating PD patients from controls in the training set. Since evolutionary algorithms are stochastic (i.e. different solutions are found in each run), we carried out 50 independent runs and then used the AUC score on the test set to identify the best performing classifiers across all the runs. The left-out data in the validation set then provides us with an unbiased estimate of classifier performance.

Quantifying bradykinesia during finger tapping

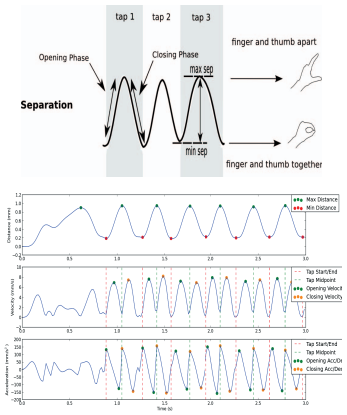

Figure 2: A Positional separation data recorded from a healthy control demonstrating the opening and closing phases of three consecutive finger tap cycles; B The finger tapping separation data is differentiated once to quantify speed and twice to quantify acceleration data. The acceleration data is used to train the computer algorithms.

Diagnostic accuracy of the device to detect grade 1 MDS-UPDRS 'slight' bradykinesia

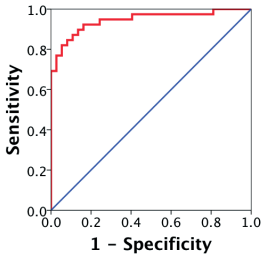

Figure 3: The area under the ROC curve (AUC) is 0.952 (red line) for the device; 95% CI 0.894-0.997, p <0.0001. An AUC of 1 denotes 100% sensitivity and specificity and AUC of 0.5 (blue line) denotes a test that is no better than chance ie 50% sensitivity and specificity.

Results: 45 of the PD finger tapping assessments exhibited MDS-UPDRS grade one 'slight' bradykinesia and all 82 HC finger tapping assessments were MDS-UPDRS grade zero 'normal'. The grade one PD FT kinematic data was accurately distinguished from HC dominant hand data with an area under ROC curve of 0.952 ($p < 0.001$), equivalent to sensitivity/specificity of 0.91/0.93 at the threshold of equal trade-off. In the validation sample, the algorithm correctly classified 93% of the 'slight' bradykinesia finger tapping data.

Conclusions: This technology is able to accurately detect the subtlest clinical grade of bradykinesia. Potential applications include aiding accurate early diagnosis of PD or screening populations for epidemiological studies.

References:

1. Bajaj NP et al. Accuracy of clinical diagnosis in tremulous parkinsonian patients: *a blinded video study.* JNNP (2010) 81;11:1223-1228.

2. Goetz CG et al. Assuring interrater reliability for the UPDRS motor section: *Utility of the UPDRS teaching tape.* Mov Disord (2004) 19;12:1453-1456.

Declaration of potential conflicts of interest : JA, SJ, ML and SS are shareholders in ClearSky, medical diagnostics