ARCHEMEDES' SPIRAL CLINICAL RATING PREDICTION BY DIGITAL SPIRAL ANALYSIS IN A GENERAL POPULATION SAMPLE.

Melotti Roberto[1], Hopfner Franziska[2], D'Elia Yuri[1,3], Barin Laura[1], Barbieri Giulia[1,4], Gögele Martin[1], Del Greco-M. Fabiola,[1] Pramstaller Peter P.[1], Pattaro Cristian[1], Kuhlenbäumer Gregor[5]

1. *Institute for Biomedicine (affiliated to the University of Lübeck), Eurac Research, Bolzano/Bozen, Italy.*
2. *Department of Neurology, Ludwig-Maximilians University, Munich, Germany*
3. *Prusa Research a.s., Prague, Czech Republic*
4. *Unit of Epidemiology and Medical Statistics, Department of Diagnostics and Public Health, University of Verona*
5. *Department of Neurology, Kiel University, Kiel, Germany*

Introduction

Tremor represents a precursory symptom of several neurological syndromes, including Parkinson's disease and essential tremor. Physiologic tremor is common in the population and may exacerbate at specific tasks, postures or by psychosomatic conditions. Spiral drawing on paper represents an ordinary clinical assessment tool of task-directed forms of kinetic tremor in the upper limbs during intentional movement of the hand. Digital spiral drawing is a replicable and multi-featured tool for hand tremor assessment. Among participants of the Cooperative Health Research in South Tyrol (CHRIS) study,[1] we derived a set of novel metrics for tremor assessment through digital spiral analysis (DSA), based on the extant literature. On subsamples, Archimedes' spiral ratings (ASR) were assessed clinically for prediction by DSA.

Objectives

To explore the variance components of the ASR both within and between participants, and to develop ASR predictive models based on relevant variance components and DSA metrics.

Methods

Digital spiral drawing was performed by 10 983 consenting participants of the CHRIS study. We selected 2 valid sequential digital traces from each participant, who drew with alternate hands. The trace proceeded clockwise from the centre and outwards within margins of an Archimedes' spiral template. Participants reported their hand dominance at the start of the session as either right, left, or ambidextrous, and started the recording session with their hand of preference. They were instructed to draw at their own pace with the digital pen, with no sight of their trace. Eight trained study assistants (operators) alternatively managed each session and monitored the task on screen. DSA was performed on the horizontal, vertical and depth (pressure) raw digital coordinates through ad hoc algorithms or time series analysis to derive several tremor-related metrics, which comprised measures of tremor amplitude, acceleration, speed, pressure, tremor direction and power, and trace length.

We collated spirals, previously selected over three separate non-mutually exclusive sampling strategies for separate research questions, which covered the whole range of CHRIS participants and DSA metrics. One expert neurologist rated all sampled spirals, which were displayed at random on screen, on a scale between 0 (no evidence of tremor) and 9 (maximum evidence of tremor), according to the Bain-Findley's adapted criteria (ASR).[2] Overall, there were 5 810 paired spirals (1 for each hand) from 2 905 participants with clinical ratings available. Due to sampling overlap, 1 004 spirals had 2 or 3 ratings. Intra-rater reliability by the same neurologist was assessed on 416 paired spirals by the Lin's concordance correlation coefficient (LCC).

We investigated the variance components of ASR with hierarchical linear models, including the participants nested within operators as random intercepts, as well as age and sex (between participants) and drawing-hand dominance and sequence (within participants) as fixed effects. We conducted random forest (RF) analysis to investigate the importance of multiple DSA metrics and other variables for best ASR prediction in a random training set of 50% of participants. We next assessed model performance in the remaining 50% testing set. Each variable importance was determined as the proportion of maximum improvement in root mean square error (RMSE) by the most important variable (normalized to importance, I=1) across all 5 000 iterations of the random forest. Prediction performance, evaluated through RMSE, was compared between the RF and the hierarchical linear model, which included a subset of the most important variables.

Results

Participants with both ASR and DSA had a median age of 50 years (range: 18-93) and 52.7% were females. Intra-rater LCC was 0.85 (95% confidence interval, CI: 0.82 to 0.88). The 93rd percentile of maximum ASR differences among multiple ratings of the same spirals corresponded to one score. Taking the maximum score over 3 possible ratings for enhanced sensitivity, ASR ranged between 0 and 9, with only a minority of ratings of 5+ (n=120, 2.1%), as a threshold of possible pathologic tremor.[3]

In the training set, the participants' random effect was evident (intraclass correlation coefficient, ICC=0.516, 95%CI: 0.478 to 0.553; likelihood ratio test vs fixed effect linear model: p-value<0.0001), while the higher order operators' effect was negligible (ICC=0.002, 95%CI: *nil* to 0.039). After including sex, age, age^2, drawing sequence and dominance of the drawing-hand, along with their interaction, both within and between participants' residual errors were reduced, but the ICC remained stable (ICC=0.519).

Among all possible variables included in the RF model, the most important was the drawing-hand dominance (I=1), followed by the drawing sequence (I=0.70) and the 90th individual percentile of tremor amplitude (I=0.64). All other lower ranking variables were alternative versions of these same metrics, while importance values of age and sex were 0.44 and 0.32, respectively.

A two-level hierarchical linear model built on the RF results in the training set showed better performance at predicting ASR scores than the RF in the testing set (RMSE=0.418 vs 0.620).

Conclusions

Large scale DSA is a feasible alternative to spiral drawing on paper for kinetic tremor assessment. Our population-based study uniquely showed that a mixture of DSA ad-hoc derived metrics in addition to task related meta-data and personal characteristics such as age, sex and hand dominance can build a reliable predictive model for Archimedes' spiral clinical ratings in a general population setting.

Bibliography

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