Using Active Digital Phenotyping to Quantify Function and Cognition in Amyotrophic Lateral Sclerosis (ALS)

Zoe Scheier[1], Alison P. Clark[1], Mackenzie Keegan[1], Kelley Erb[2], Evan Remington[2], Sheena Chew[2], Roland Brown[2], Jessey Ouillon[1], Vineet Pandey[3], Krzysztof Z. Gajos[3], Anoopum S. Gupta[1], Katherine M. Burke[1], James D. Berry[1]

1.) Healey Center for ALS, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
2.) Biogen Inc, Cambridge, MA, USA
3.) Harvard School of Engineering and Applied Sciences, Cambridge, MA, USA

Background:
Amyotrophic lateral sclerosis (ALS) clinical trials rely on a standard set of outcome measures, including the revised ALS Functional Rating Scale (ALSFRS-R), vital capacity (VC), and handheld dynamometry (HHD). Digital Quantitative Monitoring (DQM), uses tasks performed on digital devices to obtain more frequent, quantitative and granular measurements of function alongside patient reported outcome measures in order to improve on standard ALS outcome measures.

Methods:
The study originated with two intensive clinic visits separated by a week during which daily self-administered test and continuous passive data (DQM) was collected remotely. With COVID-19, the study was re-designed to a fully-remote and longitudinal format, comprising telemedicine visits at baseline, 12, and 24 weeks, weekly self-administered testing, and continuous passive data collection. During telemedicine visits, study staff administered traditional ALS outcome measures including the ALSFRS-R, neurological fatigue index – Motor Neuron Disease (NFI-MND), and a quality of life scale. DQM assessments were delivered via mobile application (Digital Artefacts) on a provided iPhone and Apple Watch, as well as via web browser on their computer. The mobile app included a symptom questionnaire, self-administered ALSFRS-R, fine motor, gait, stance, speech, and cognitive tests, and collected continuous passive data. Participants used their home computer and mouse to complete a point and click task assessing fine motor movements. Twenty-five healthy controls (HC) and 25 people with ALS (PALS) will be enrolled.

Results:
All PALS participants have been enrolled and HC enrollment is projected to complete in August 2021. Thirteen PALS and 3 HC have completed participation.

Of 456 scheduled sessions mobile application sessions, participants have completed 385, with 50 further partially completed sessions. Test-retest reliability at baseline varies across tests, but ICC values above 0.9 have been observed (alternating finger-tapping rate, passage reading speaking rate). Correlation with relevant baseline ALSFRS-R subscores (i.e. bulbar, fine motor, gross motor, respiratory) are moderate (0.4 – 0.6) or weak (0.2 – 0.4) for most test features analyzed.

Considering participants with at least 2 sessions, the median value of several computer mouse task features demonstrated strong correlations (0.6 – 0.9) with baseline ALSFRS-R handwriting and/or total scores. These features included normalized jerk, execution time, maximum speed, and temporal location of the main submovement.

Available data will be presented.

Conclusion:
This pilot study in PALS and HC is helping to clarify the utility of a variety of mobile technology-based DQM tools in ALS, to compare these tools to traditional ALS outcome measures, and to extend our ability to assess cognition in people with ALS. Early results suggest compliance is acceptable and at least a subset of the digital tests included in this study may have promise as reliable measurements of function and cognition in people with ALS.