



# Smartphone data during the COVID-19 pandemic can quantify behavioral changes in people with ALS

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## Abstract

**Introduction:** Passive data from smartphone sensors may be useful for health-care research. Our aim was to use the coronavirus disease-2019 (COVID-19) pandemic as a positive control to assess the ability to quantify behavioral changes in people with amyotrophic lateral sclerosis (ALS) from smartphone data.

**Methods:** Eight participants used the Beiwe smartphone application, which passively measured their location during the COVID-19 outbreak. We used an interrupted time series to quantify the effect of the US state of emergency declaration on daily home time and daily distance traveled.

**Results:** After the state of emergency declaration, median daily home time increased from 19.4 (interquartile range [IQR], 15.4-22.0) hours to 23.7 (IQR, 22.2-24.0) hours and median distance traveled decreased from 42 (IQR, 13-83) km to 3.7 (IQR, 1.5-10.3) km. The participant with the lowest functional ability changed behavior earlier. This participant stayed at home more and traveled less than the participant with highest functional ability, both before and after the state of emergency.

**Discussion:** We provide evidence that smartphone-based digital phenotyping can quantify the behavior of people with ALS. Although participants spent large amounts of time at home at baseline, the COVID-19 state of emergency declaration reduced their mobility further. Given participants' high level of daily home time, it is possible that their exposure to COVID-19 could be less than that of the general population.

## KEYWORDS

ALS, COVID-19, digital phenotyping, mobile health, smartphones

## 1 | INTRODUCTION

The novel coronavirus (coronavirus-2019, or COVID-19) pandemic has required social distancing and stay-at-home-orders, changing the behavior of the general population.<sup>1</sup> The risk of severe COVID-19

**Abbreviations:** ALSFRS-R, ALS Functional Rating Scale—Revised; COVID-19, coronavirus disease-2019.

Anna L. Beukenhorst and Ella Collins contributed equally to this study.  
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infections is higher for people with serious underlying medical conditions,<sup>2</sup> such as amyotrophic lateral sclerosis (ALS).

Insight into the behavioral change of people with ALS is useful for future studies of the risk of contracting COVID-19, as well as the consequences for social support, social withdrawal, and quality of life of patients. However, behavioral change can be difficult to quantify using traditional research methods such as surveys, which require participant effort and are subject to recall bias.

Smartphone sensors provide an opportunity to measure behavior passively, including mobility, and construct digital phenotypes.<sup>3</sup> The COVID-19 measures, with recommendations to reduce mobility, are a useful positive control to test the feasibility of using smartphones to quantify behavioral change in neurologic populations. We therefore used personal smartphone data to identify behavioral changes in people with ALS due to the COVID-19 outbreak.

## 2 | METHODS

For this analysis, participants in an ongoing study were selected if passive mobility data were available between February 13 and April 13, 2020. These participants had been recruited from the ALS Multi-disciplinary Clinics at Massachusetts General Hospital (Boston, Massachusetts) and Washington University (St. Louis, Missouri). Participation required informed consent. The study was approved by the local institutional review boards.

### 2.1 | Smartphone data collection

Participants installed the Beiwe smartphone app on their personal smartphones. Beiwe is an open-source, end-to-end encrypted digital phenotyping platform that consists of Android and iOS smartphone applications, a web-based platform for study setup, HIPAA-compliant cloud-based data storage, and a data analysis back-end.<sup>4</sup>

The smartphone app was configured to collect location data using the GPS sensor for 60 seconds every 10 minutes, as described elsewhere.<sup>5</sup> All data were collected and stored in compliance with local, state, and national laws, and all regulations and policies.

### 2.2 | Calculating mobility metrics from location data

To calculate mobility metrics from location data, we imputed the missing location data caused by the intermittent location sampling scheme. Latitude-longitude coordinate pairs were projected on a sphere and converted into a temporal sequence of flights (periods of linear movement) and pauses (stationary periods). Missing data were imputed using a method described elsewhere.<sup>6</sup>

From the complete location trajectories, we calculated daily home time (in hours) and distance traveled (in kilometers) each day for each participant. Home location was inferred by selecting the location where the participant

spent most of their time between 7:00 PM and 9:00 AM. Distances over 150 km traveled were recorded as 150 km, as differences in distance traveled would otherwise be driven by few less-relevant long-distance trips.

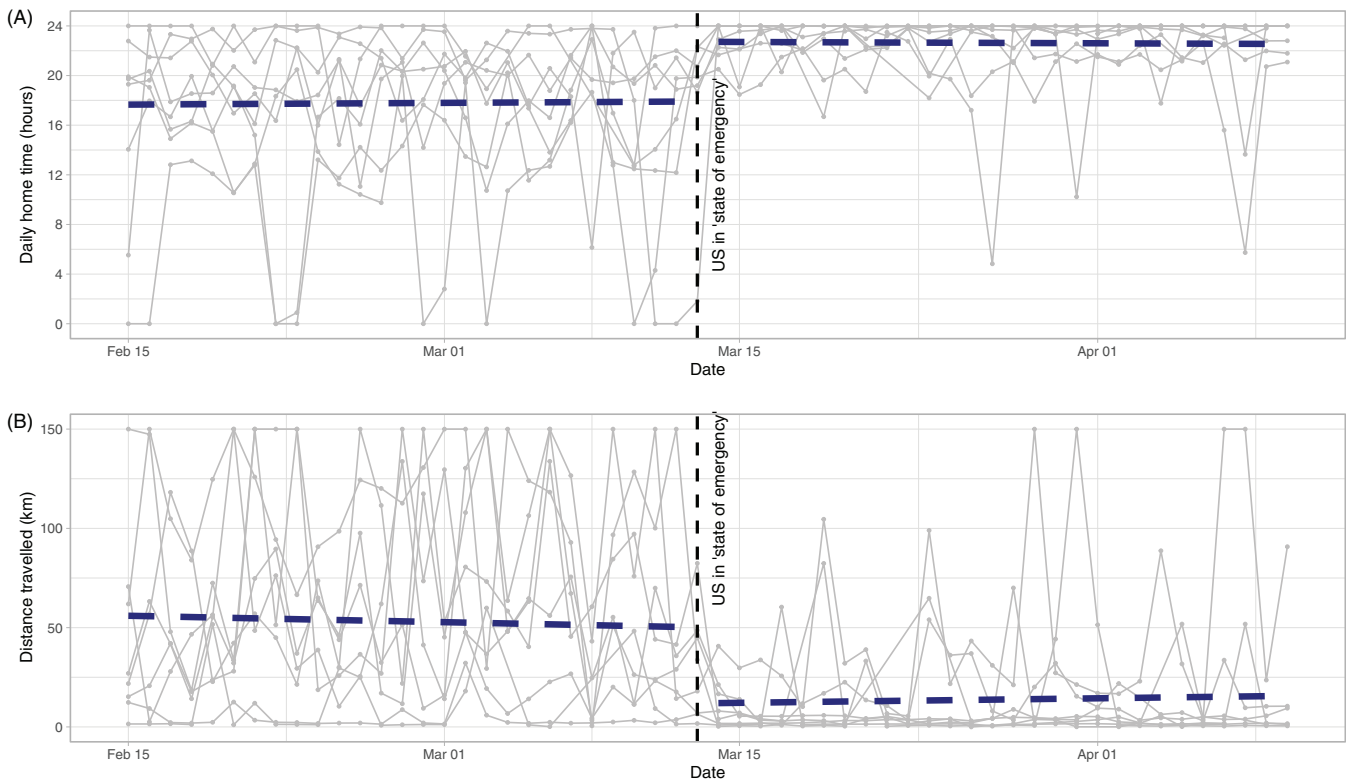
### 2.3 | Statistical methods

We used an interrupted time series to analyze pre-pandemic (February 13 to March 12 2020) and pandemic phase (after the government's state of emergency declaration: March 13 to April 13, 2020) behavior.<sup>7</sup> We used mixed effects models to investigate how the declaration of a national emergency impacted on daily home time and daily distance traveled, each with a fixed effect for time since February 13, an indicator for whether a time was pre- or post-pandemic, and an interaction between these two effects, and a random intercept and slope for each participant. Within-subject covariance was unstructured. As our participants live in different states, it is possible that local declarations of emergency had a more profound effect on behavior. We did a secondary analysis, using the state of emergency declaration in participants' state of residence.

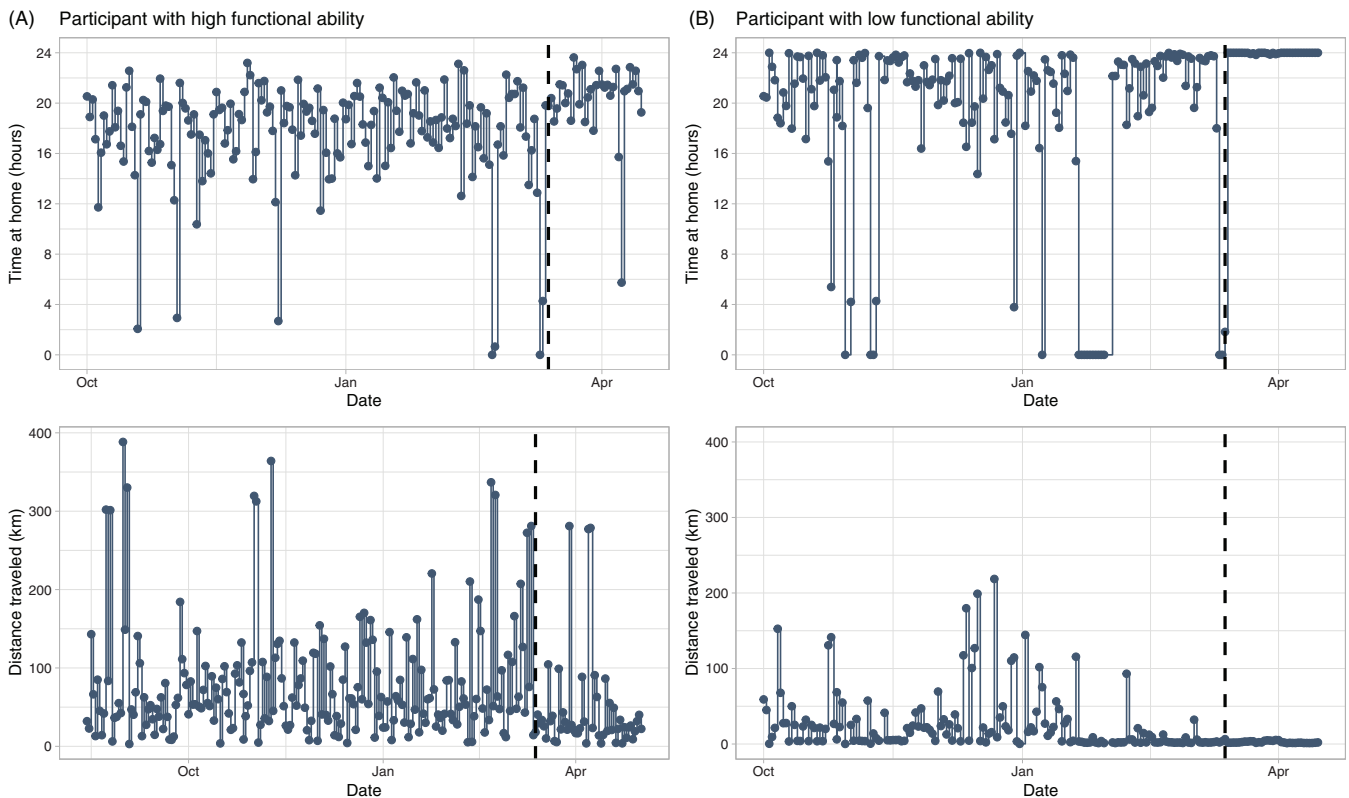
**TABLE 1** Demographics of eight eligible participants

Characteristic	Percent (N) or mean (SD)
Age (years)	56.6 (9.9)
Sex	
Female	62% (5)
Male	38% (3)
Ethnicity	
Non-Hispanic or Latino	100% (8)
Race	
White	100% (8)
Disease characteristics	
Disease duration pre-COVID (in months)	34.5 (17.0)
ALSFRS-R total score pre-COVID (N = 7)	35.9 (9.4)
Location of onset	
Legs	38% (3)
Arms	50% (4)
Bulbar (speech/swallow)	12% (1)
Operating system	
iOS (iPhone)	88% (7)
Android	12% (1)
State of residence	
Massachusetts	25% (2)
Rhode Island	12% (1)
Wisconsin	12% (1)
Connecticut	25% (2)
North Carolina	12% (1)
Missouri	12% (1)

Note: ALSFRS-R, ALS Functional Rating Scale—Revised; COVID: novel coronavirus (coronavirus-2019).



**FIGURE 1** A, Daily home time in hours of 8 people with ALS. B, Daily distance traveled in kilometers. Each gray line shows the data of one participant. The thick blue dotted line shows the interrupted time series model. The vertical black dotted line indicates the declaration of state of emergency on March 13, 2020 [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



**FIGURE 2** Daily home time, in hours (top plots), and daily distance traveled, in kilometers (bottom plots), of two case studies. A, Participant with low disability (ALSFRS-R of 46 of 48). B, Participant with high disability (ALSFRS-R of 23 of 48). Data from October 1, 2019 until April 13, 2020, with a vertical black dotted line indicating the declaration of state of emergency (March 13, 2020) [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

In addition, we compared home time and distance traveled over time for the participant with the lowest functionality and the participant with the highest functionality. Functionality was defined by participants' score on the 48-point ALS Functional Rating Scale—Revised (ALSFRS-R, where 48 points = “normal function” and lower scores denote lower function<sup>8</sup>) measured at a clinical visit prior to the start of the pandemic (February 2020).<sup>5</sup>

### 3 | RESULTS

Eight participants contributed data (Table 1). In the pandemic phase, median home time increased from 19.4 (interquartile range [IQR], 15.4–22.0) hours to 23.7 (IQR, 22.2–24.0) hours and median distance traveled decreased from 42 (IQR, 13–83) km to 3.7 (IQR, 1.5–10.3) km.

The interrupted time series showed that the state of emergency declaration had a significant effect on both outcomes (home time: +5.2 hours, 95% confidence interval [CI], +0.75 to +9.7 hours; distance traveled: –48 km; 95% CI, –77 to –19 km; Figure 1). The secondary analysis, individualizing each participant's estimate of behavior change to the date of the local state of emergency declaration, rather than the national state of emergency declaration, showed a more gradual change that remained significant (data not shown).

We compared the mobility of an ambulatory participant with near-normal function (ALSFRS-R: 46 of 48; Figure 2A) and a nonambulatory participant with low function (ALSFRS-R: 23 of 48; Figure 2B). The ambulatory participant had a wide day-to-day variability in daily home time (median, 17.7 hours; IQR, 14.9–19.8 hours) and distance traveled (median, 68 km; IQR, 46–152 km) before the pandemic. This individual showed a sizeable change in these parameters (median home time, +3.4 to +21.1 hours; median distance traveled, +38 to +30 km) during the pandemic. For the nonambulatory participant, median pre-pandemic daily home time was 23.4 (IQR, 21.3–23.7) hours and daily distance traveled was 2.2 (IQR, 2–3.4) km. Both of these parameters showed a small change during the pandemic (median home time, +0.6 hour to +24 hours; median distance traveled, –0.1 to a median of +2.1 km; Figure 2B). In addition, this participant changed behavior earlier in the COVID pandemic, beginning to spend more time at home and traveling less distance in February, a trend that continued into the pandemic phase.

### 4 | DISCUSSION

People with ALS spent more time at home than the general population both before and during the COVID-19 pandemic. US mobility research based on smartphone data show that the average daily home time for the general population in March and April increased from 10 hours pre-pandemic to 14 hours during the pandemic (varying by state; range, <5 to 17 hours).<sup>9</sup> In people with ALS, the absolute change in daily home time was similar, yet they were less mobile both before and during the pandemic.

We demonstrated differences in mobility and behavior between participants with low and high function according to the ALSFRS-R.

This finding, although based on limited sample size, supports the clinical meaningfulness of the ALSFRS-R and opens a pathway for using smartphone-based digital phenotyping to quantify the impact of ALS on people's lives. The association between digital phenotypes and disease progression should be further investigated in larger cohorts.

Our finding of high home isolation of people with ALS is relevant for researchers investigating the impact of COVID-19 on people with neurologic disorders. These researchers should investigate the generalizability of our findings in larger samples.

Compliance with stay-at-home-orders results in a lower exposure to community spread of the virus. Whether this results in a lower total exposure to the virus for a given individual ultimately depends on the number of cohabitants, caregivers, and visitors who come into close contact with the person, and their behavior. Further investigating the extent of social isolation, which has its own negative health implications, is therefore necessary.<sup>10</sup>

During start of the COVID-19 pandemic, when many clinic-based observational studies were halted, data collection through smartphones continued. Our study demonstrates that digital phenotypes from smartphone data can quantify behavioral changes in people with ALS. The success of digital phenotyping in providing outcome measures will depend on close collaboration of data scientists and clinical researchers for digital data collection, analysis, and disease phenotyping. Further studies should evaluate the best analytical methods and metrics to quantify behavioral changes associated with ALS progression, which could then be used as outcome measures in trials. In future trials, regulatory and operations expertise and patients' perspectives will provide additional information critical for success.

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### CONFLICT OF INTEREST

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## 5 | ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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## Autoantibodies in Japanese patients with ocular myasthenia gravis

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## Abstract

**Introduction:** The majority of patients with myasthenia gravis (MG) initially present with ocular symptoms, but it is difficult to predict which cases will remain as ocular MG (OMG) or will progress to generalized MG. Herein we evaluated the serologic profile of Japanese OMG and its relationship with clinical features.

**Methods:** Seventy-three patients with OMG from five Japanese myasthenia gravis (MG) centers were enrolled. Live cell-based assays (CBAs) were used to determine the presence of autoantibodies (Abs) to clustered adult ( $2\alpha$ ,  $\beta$ ,  $\delta$ ,  $\epsilon$ ) and fetal ( $2\alpha$ ,  $\beta$ ,  $\delta$ ,  $\gamma$ ) acetylcholine receptor (AChR) isoforms, muscle-specific receptor tyrosine kinase (MuSK), and lipoprotein receptor-related protein-4 (LRP4).

**Abbreviations:** Ab, antibody; AChR, acetylcholine receptor; CBA, cell-based assay; cDNA, complementary DNA; DMEM, Dulbecco's modified Eagle's medium; EGFP, enhanced green fluorescent protein; GMG, generalized myasthenia gravis; IgG, immunoglobulin G; IT, immunotherapy; LRP4, lipoprotein receptor-related protein-4; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific receptor tyrosine kinase; OMG, ocular myasthenia gravis; RIA, radioimmunoassay; RT, room temperature.

These findings were presented in part at the 14th annual meeting of the International Society of Neuroimmunology, Brisbane, Australia, August 2018.