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for ALS at Mass General



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# Innovative Approaches to Sensor Measurements in Patients with ALS

Marta Karas

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# Statement

The content of the slides and my talk do not represent the official views of Takeda Pharmaceuticals or its affiliated organizations.

# Co-authors

## Harvard University



Marta Karas



Jukka-Pekka Onnela

## Massachusetts General Hospital



James Berry



Katherine Burke



Alison Clark

## Mitsubishi Tanabe Pharma Holdings America, Inc.



Amir Lahav

## Mayo Clinic



Stephen A.  
Johnson



Marcin  
Straczekiewicz



Julia Olsen



Zoe Scheier



Amrita Iyer



Tim Royse



Satoshi Iwasaki

## Wake Forest University



Emily Huang



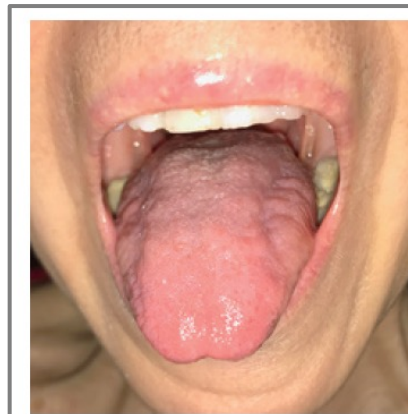
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# ALS

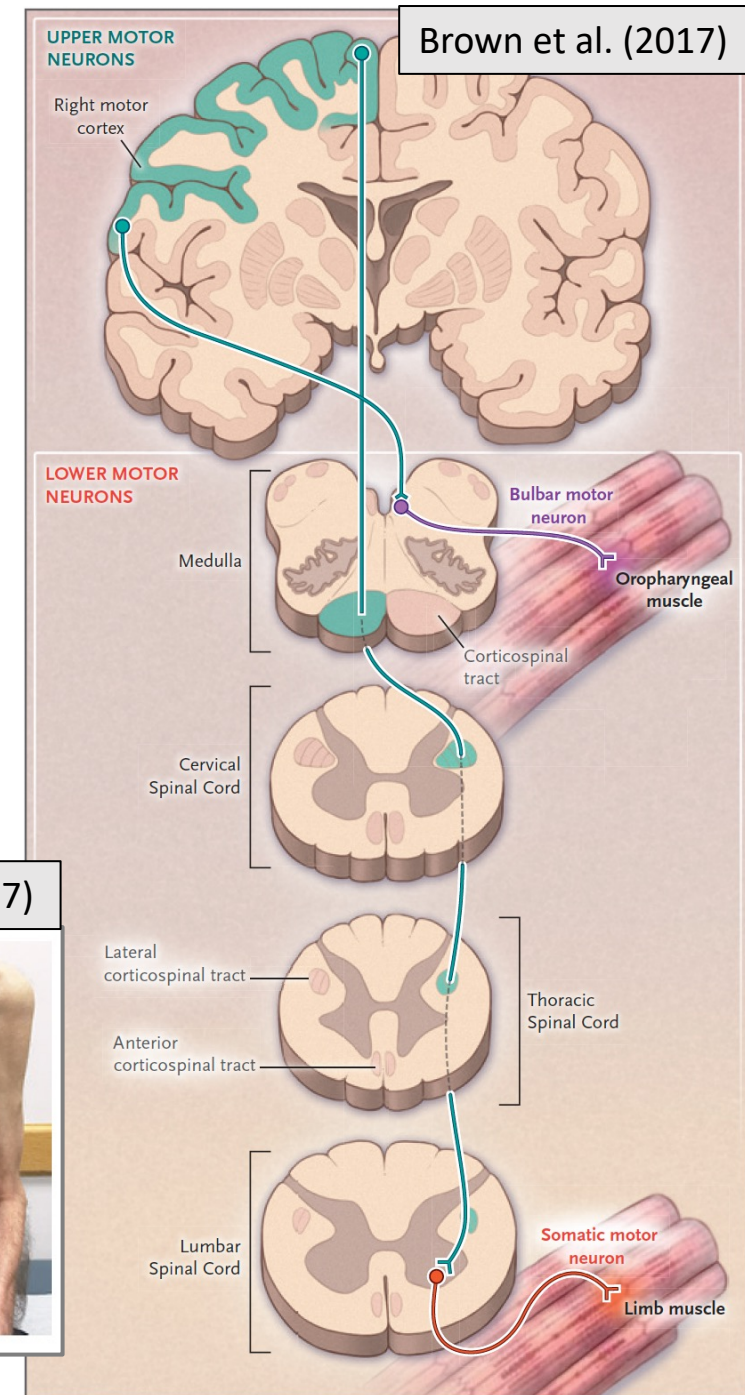
- Amyotrophic lateral sclerosis (ALS) -- fatal disorder characterized by progressive **loss of motor neurons in brain and spinal cord**
- In the US and Europe, cumulative lifetime risk is about **1 in 400**
- Symptom onset: 50-65y
- **Average life expectancy after diagnosis is 2-5y**
- 3 kinds of symptom onset: limb (70%), bulbar (25%), trunk/respiratory (5%)

## Symptom:

- Progressive weakness and wasting of the limb and axial muscles
- Bulbar (speech, swallowing)
- Respiratory



Brown et al. (2017)



# ALS FDA approved therapies

	Medicine	Mechanism of action	Brand name	Formulation	FDA approved
1	Riluzole	Decreasing the release of glutamate	Rilutek	Oral tablet	<b>1995</b>
			Tiglutik	Oral suspension	2018
			Exservan	Oral film	2019
2	Edaravone	Relieving the effects of oxidative stress	Radicava	Intravenous infusion	<b>2017</b>
				Oral suspension	2022
3	Sodium phenylbutyrate and tauroursodiol	Blocking stress signals in cells	Relyvrio	Oral suspension	<b>2022</b> (to be removed in US in 2024)
4	Tofersen	Reduction of SOD1 protein synthesis	Qalsody	Intrathecal injection	<b>2023</b>
5	Nuedexta	Regulating the signaling of glutamate and other neurotransmitters	Nuedexta	Oral tablet	2011

# Primary endpoints in clinical trials for ALS

- **ALS Functional Rating Scale-Revised (ALSFRS-R)** is most commonly used primary endpoint in clinical trials for ALS
- Rating scale for monitoring disability progression in patients with ALS
- **12-item, 0-4 points/item scale** (total score range 0-48)
- Assess the fine motor, gross motor, bulbar, and respiratory function
- Traditionally staff-administered
- Limitations: it is ordinal, may not adequately reflect changes in certain areas

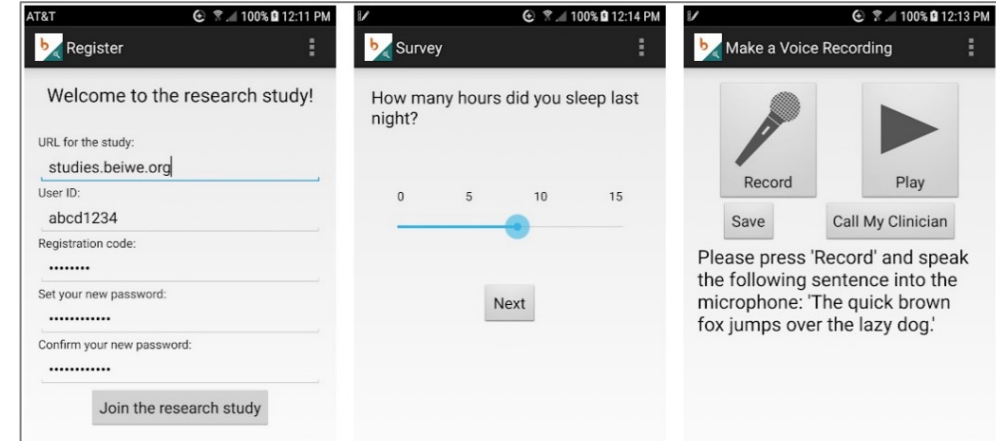


# New avenues for outcome measures: mobile apps and wearable devices

- Remote study, N = 63 people with ALS
- Age median (range) of 62 (34-81) years
- Baseline ALSFRS-R of 33 (11-47)
- Staff-administered ALSFRS-R by televisit

## Digital technology:

- All subjects: **Beiwe mobile app** to collect self-entry ALSFRS-R and smartphone sensor data (12 months)
- N = 20 wrist-worn **ActiGraph Insight Watch** (6 months)
- N = 20 ankle-worn **Modus StepWatch 4** (6 months)



Beiwe smartphone app (Harvard University, the Onnela Lab)



ActiGraph Insight Watch



Modus StepWatch 4

# Wearable device and smartphone data quantify ALS progression and may provide novel outcome measures (*npj Digital Medicine*, 2023)



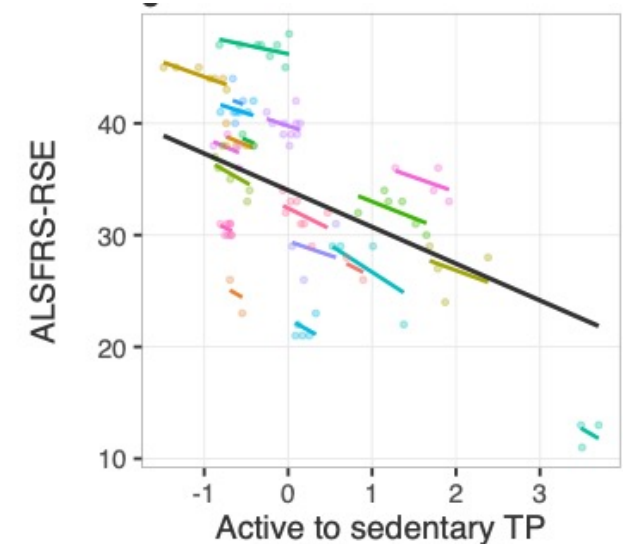
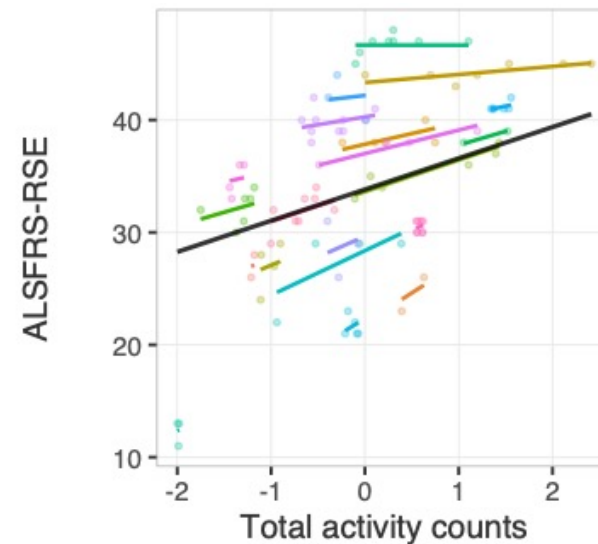
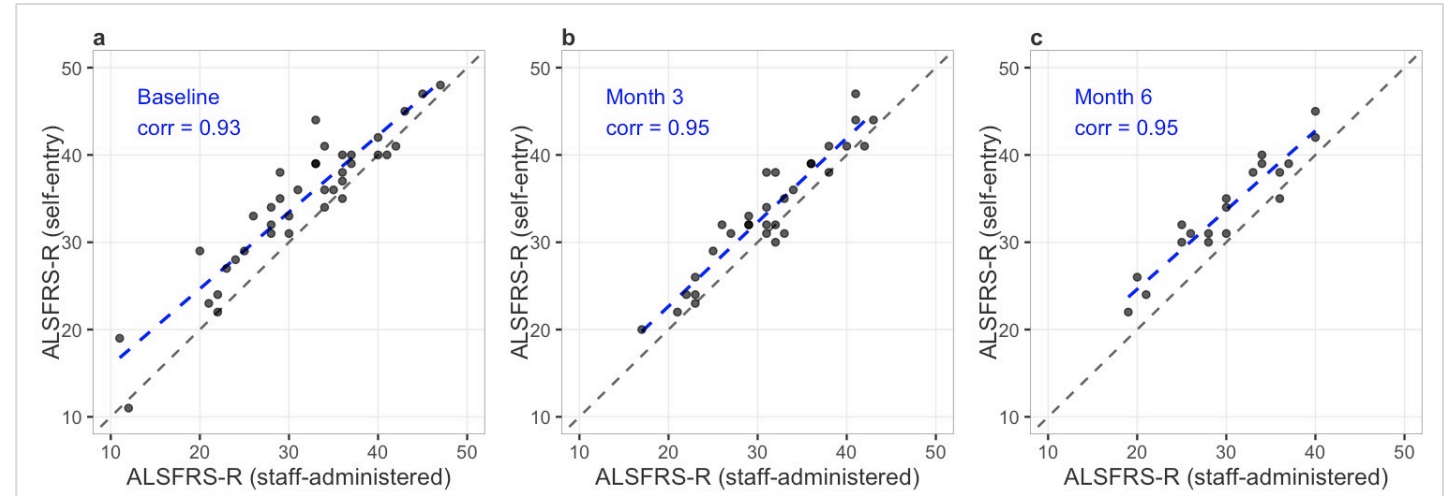
Stephen A. Johnson



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- Very high correlation between staff-administered and self-entry ALSFRS-R scores
- Significant monthly decline and longitudinal association with ALSFRS-R for several daily measures:

total activity counts, sedentary time, non-sedentary time, active-to-sedentary transition probability (TP), sedentary-to-active TP, steps, calories

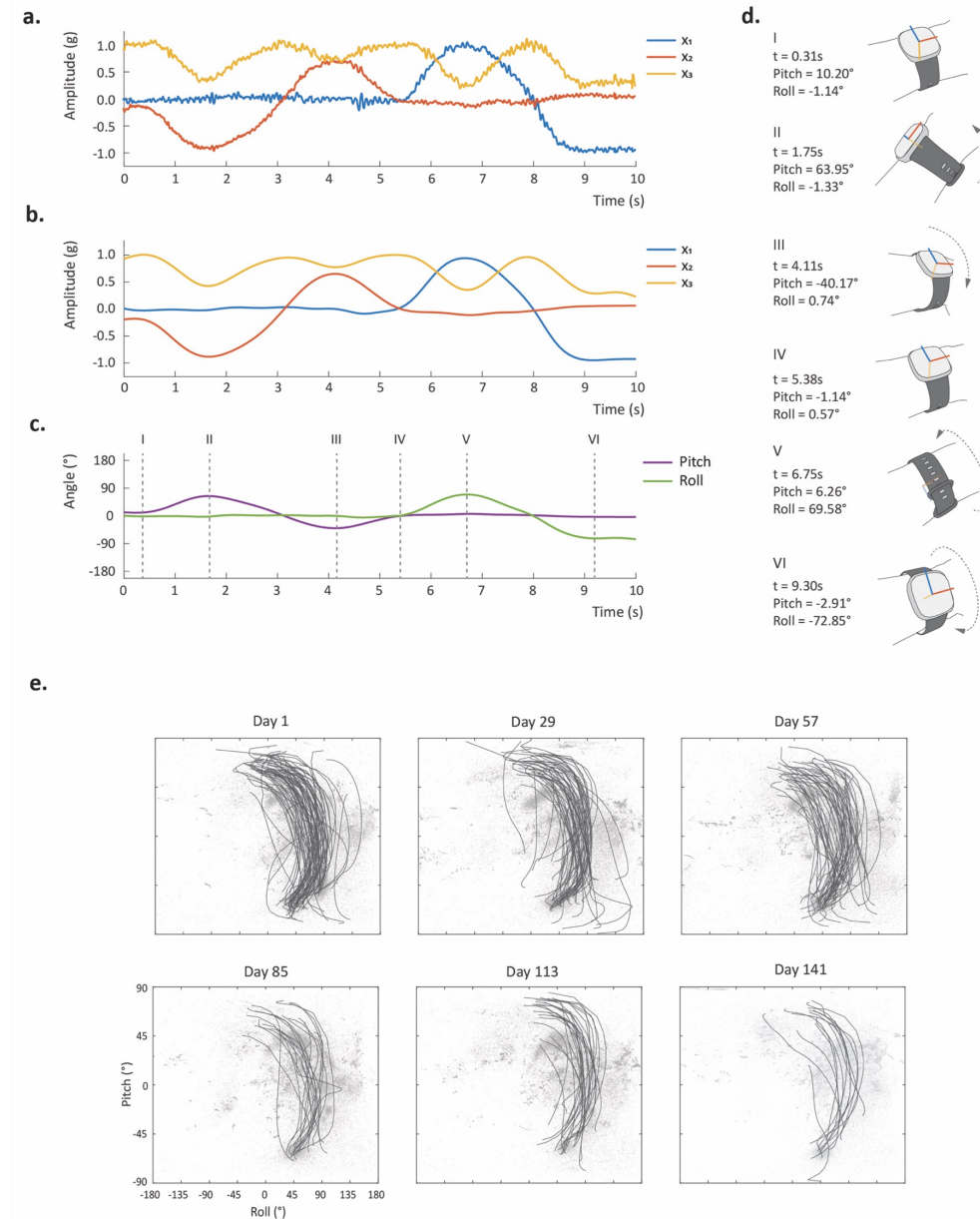




# Upper limb movements as digital biomarkers in people with ALS

(*eBioMedicine*, 2024)

- Developed method to quantify upper limb movements – flexion, extension, supination, and pronation – from raw accelerometer data
  - Daily count and duration measures for all four movements were significantly associated longitudinally with the ALSFRS-R total score
- All duration measures remained significant after adjusting for total activity counts



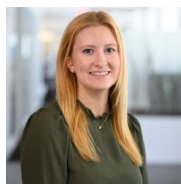
Marcin Straczekiewicz

# Tracking ALS disease progression using passively collected smartphone sensor data

*(Annals of Clinical and Translational Neurology, 2024)*

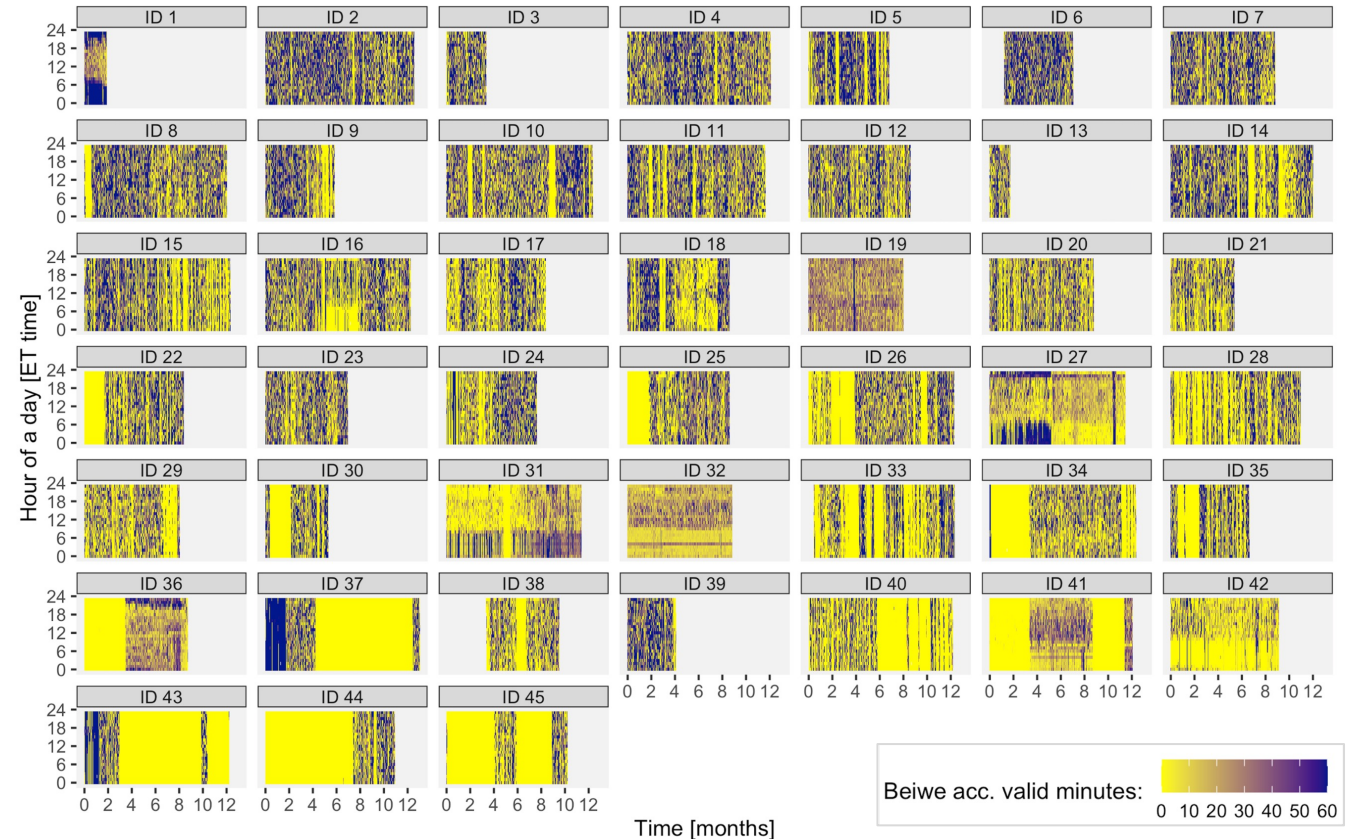


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- Data collection via Beiwe mobile app
  - (1) active data: self-entry ALSFRS-R
  - (2) passive data: accelerometer and GPS smartphone sensor data
- Derived daily measures
  - From smartphone GPS: time spent at home, distance travelled
  - From smartphone accelerometer data: walking cadence and step count; Activity Index
- Significant monthly decline and/or longitudinal association with ALSFRS-R for a subset of measures



# Discussion and ongoing work

- Affirms the feasibility and utility of remote monitoring with apps and wearable devices in people with ALS
- Other considerations
  - Challenges with remote digital data collection
  - Interpreting measures in the absence of context
  - Differences in smartphone use habits, operating systems and data quantity and quality
- Further research areas
  - Incorporation of digital outcome measures into interventional clinical trials

- Wearable device and smartphone data quantify ALS progression and may provide novel outcome measures (2023) *npj Digital Medicine* <https://doi.org/10.1038/s41746-023-00778-y>
- Upper limb movements as digital biomarkers in people with ALS (2024) *eBioMedicine* <https://doi.org/10.1038/s41746-023-00778-y>
- Tracking ALS disease progression using passively collected smartphone sensor data (2024) *Annals of Clinical and Translational Neurology* <https://doi.org/10.1002/acn3.52050>

- Free-living monitoring of ALS progression in upper limbs using wearable accelerometers (2024+) <https://ssrn.com/abstract=4926621>

**Marta Karas**

<https://martakarass.github.io/>