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Healey Center

Sean M. Healey & AMG Center
for ALS at Mass General



MASSACHUSETTS
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Innovative Approaches to Sensor Measurements in Patients with ALS

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Digital Health & AI Innovation Summit

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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.

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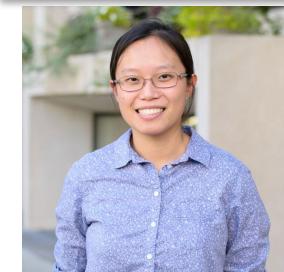
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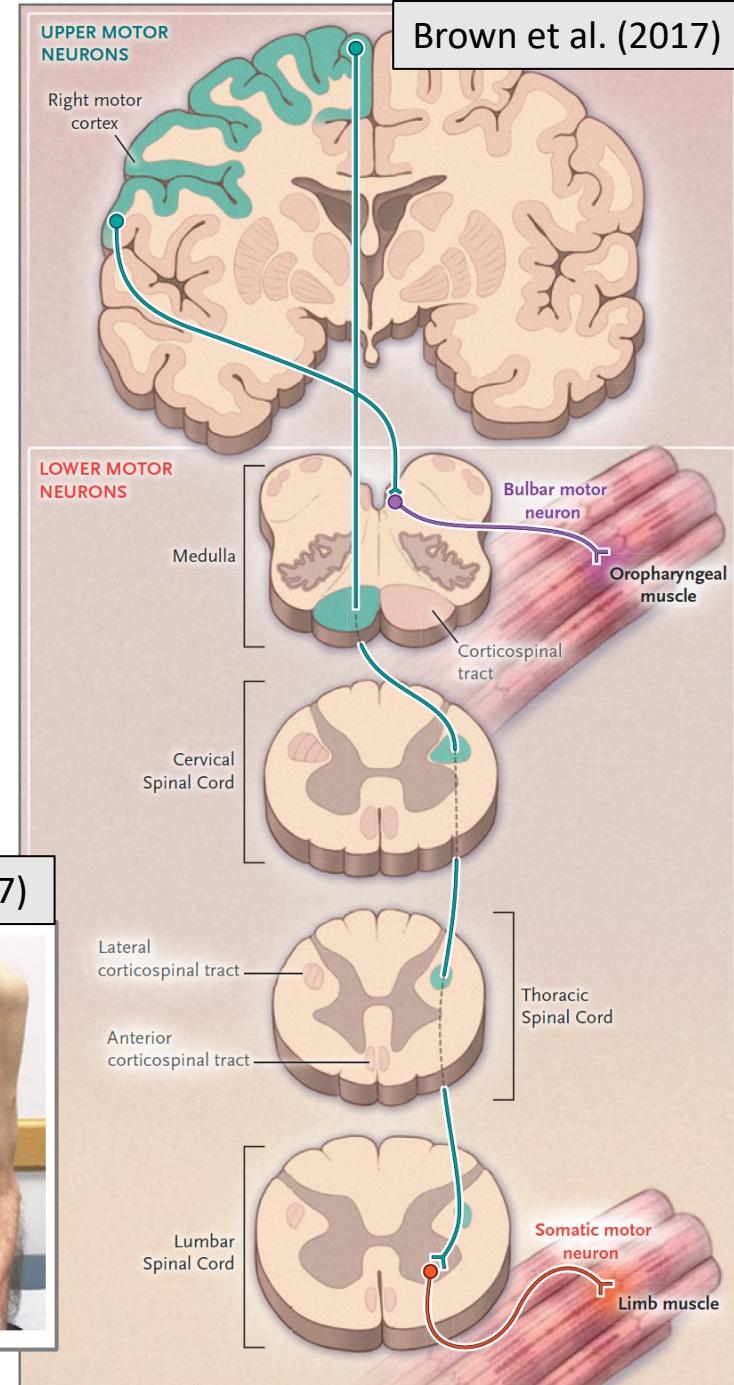
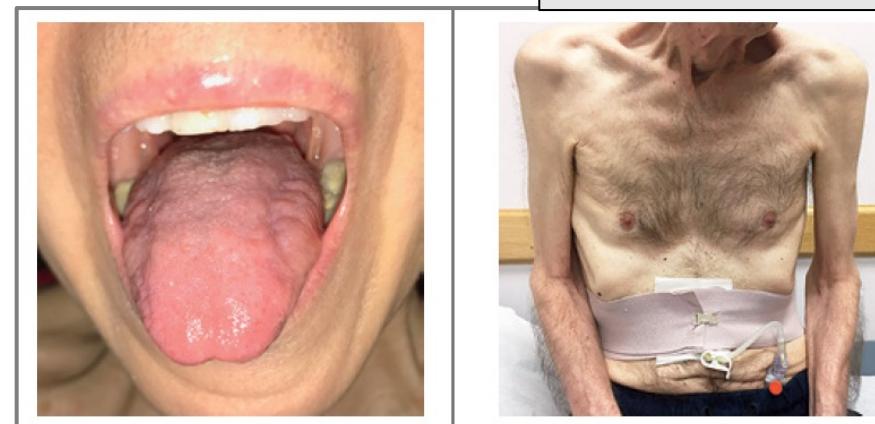
Wake Forest University



Emily Huang

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



ALS FDA approved therapies

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

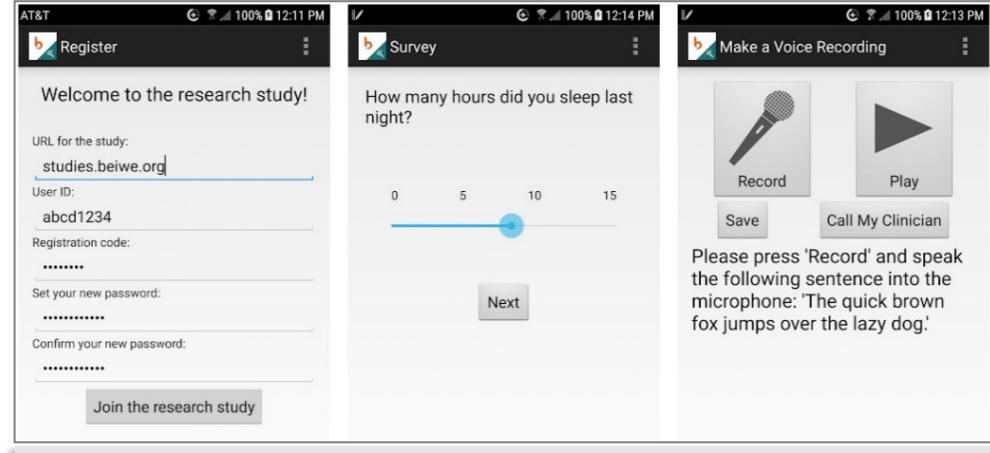


New avenues for outcome measures: mobile apps and wearable devices

- 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** (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)

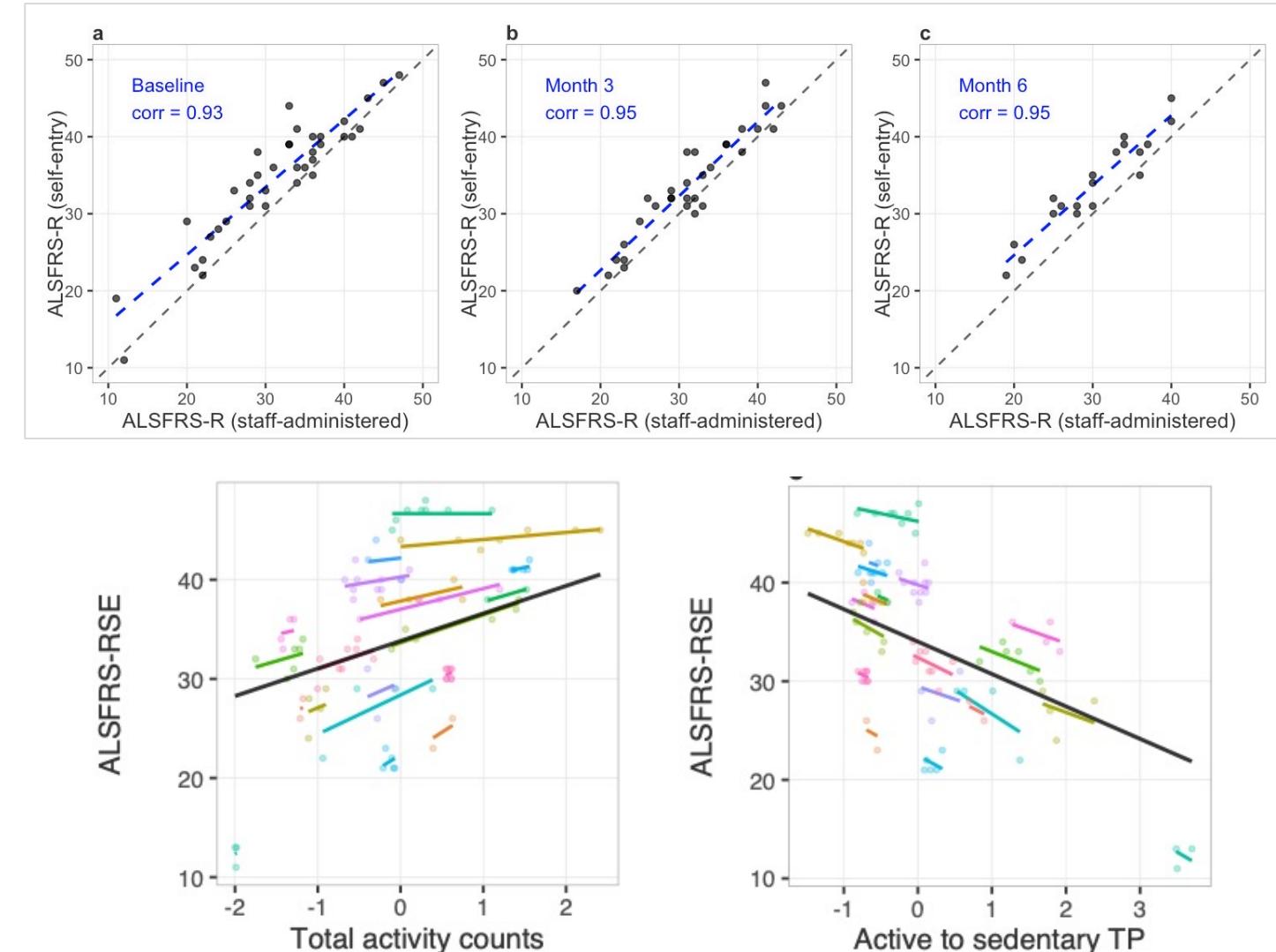


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- Very high correlation between staff-administered and self-entry ALSFRS-R scores
- Significant monthly decline and longitudinal association with ALSFRS-R for several daily measures:

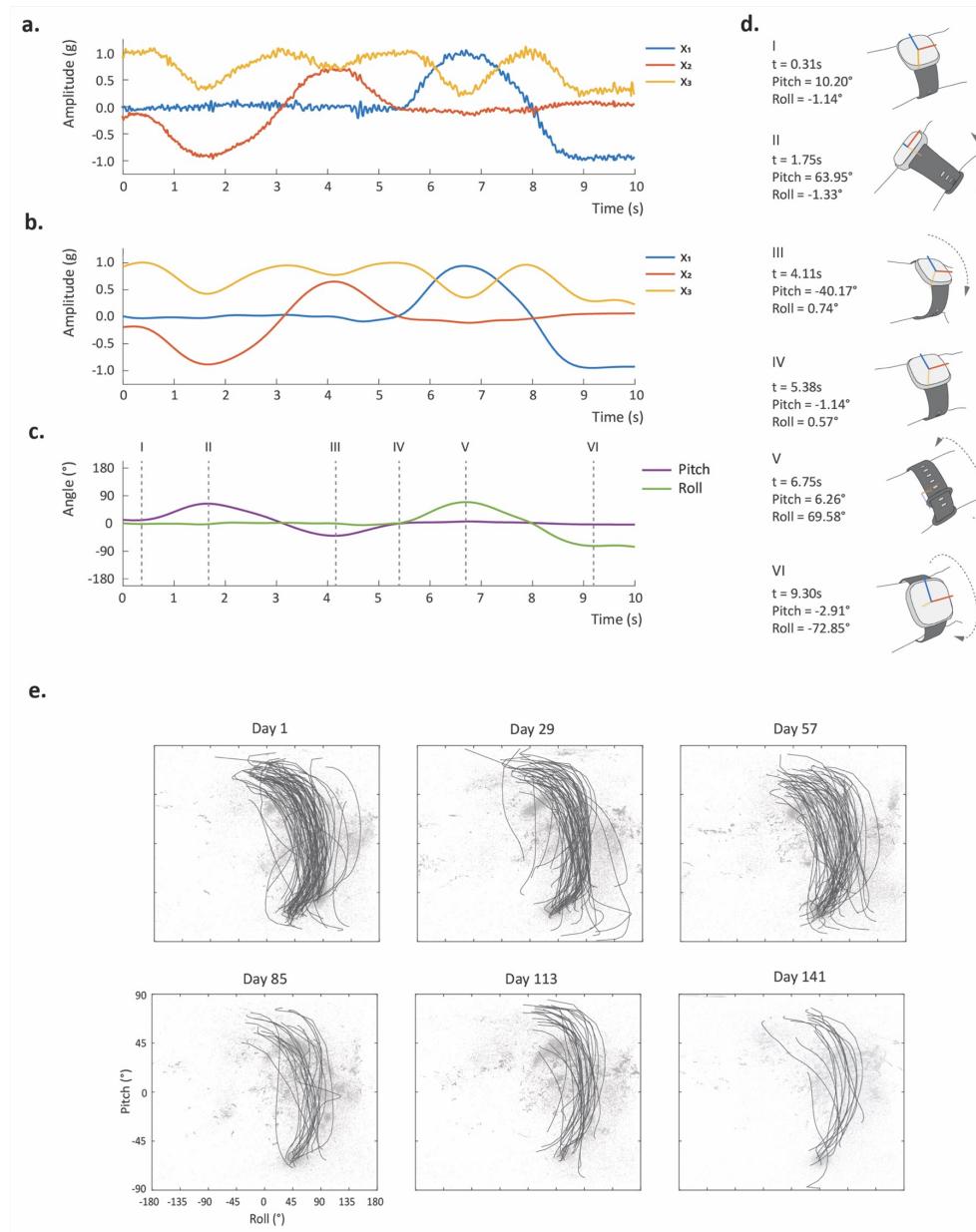
total activity counts,
sedentary time, non-sedentary
time, active-to-sedentary
transition probability (TP),
sedentary-to-active TP, steps,
calories



Upper limb movements as digital biomarkers in people with ALS (*eBioMedicine*, 2024)

- Developed method to quantify upper limb movements – flexion, extension, supination, and probation – 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
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Tracking ALS disease progression using passively collected smartphone sensor data

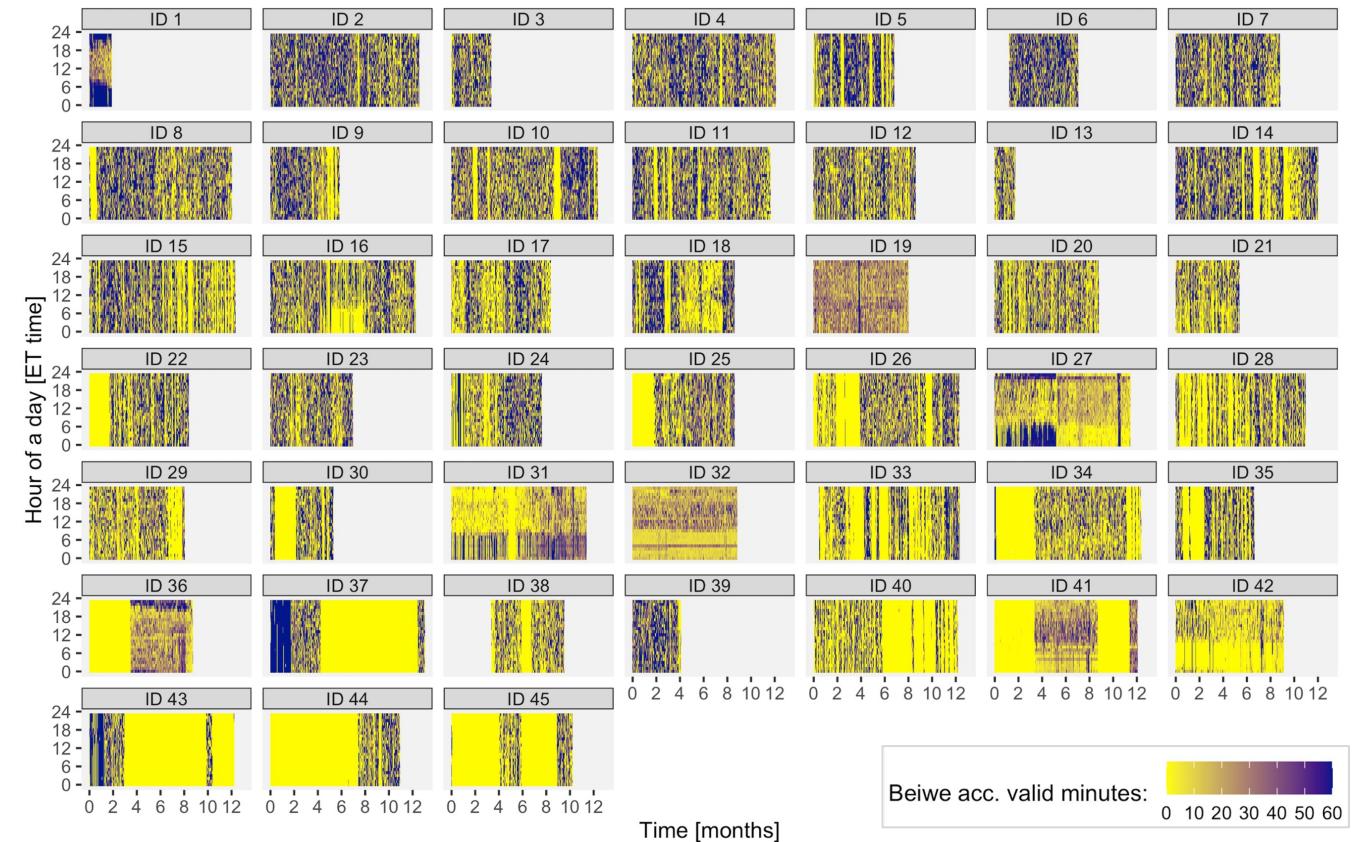
(*Annals of Clinical and Translational Neurology*, 2024)



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Julia Olsen

- 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>

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