Real-time capture of gait and actigraphy using industry-grade wearable devices in older adults with and without subjective cognitive decline: Preliminary findings regarding feasibility, sensitivity and correlations with cognition

Alexandra Atkins[1], William Horan[1], Michael Kraus[1], Jared Linthicum[1], Angela Boctor[1], Heather Dickerson[1], Lisa Zweede[1], & Richard Keefe[1,2]

(1) VeraSci (Durham, NC); (2) Duke University Medical Center (Durham, NC)

INTRODUCTION

Integration of wearable devices into regulated clinical trials for the assessment of cognition and function continues to be a topic of growing interest. If appropriately implemented, measurements from validated wearable technologies have the potential to revolutionize the conduct of clinical trials by facilitating development of site-less clinical trial designs. In order to be truly informative, however, endpoints collected by these devices must undergo the same clinical and technological validation process required by other currently accepted tools.

OBJECTIVES

We report preliminary findings from an ongoing NIH-funded study examining the relationship between real-time measurements of gait and actigraphy collected by industry grade wearable devices and established cognitive and functional endpoints with sensitivity to decline early in the AD continuum.

METHODS

Participants

- Participants were recruited by VeraSci's Innovation Lab located in Durham, NC.
- Our sample currently includes 38 older adults (age 55 or greater), including 26 healthy controls (HC) and 12 individuals with subjective cognitive decline (SCD).
- Individuals with SCD were categorized as such based on total scores of ≥ 4 on the Cognitive Functional Instrument (CFI).
- Participant characteristics are displayed in Table 1.

Table 1. Participant Characteristics

	Mean	SD
Age	68.71	7.67
Education (Years)	15.00	3.34
Height (cm)	167.74	10.70
Weight (kg)	82.13	19.54
Gender		
Male	17 (44.7%)	
Female	21 (55.3%)	
Race		
White	25 (60.7%)	
African American	12 (35.7%)	
Other	1 (3.6%)	
Subgroup		
Healthy Controls	26 (68.4%)	
Individuals with subjective cognitive decline	12 (31.6%)	

Procedure

- Participants attended two in-person site visits separated by a one-week period of passive data collection using wearable technologies provided at Visit 1.
  - At Visit 1, participants were fitted with wearable technologies and completed rater administered assessments of motor function and tablet-based assessments of cognition and iADL function
  - At Visit 2, participants repeated a portion of in-office walking assessments to allow for evaluation of test-retest reliability of wearable endpoints.

Assessments of Motor Function

- The Computerized Finger Tapping Test (CTAP)
- Timed 25-Foot Walk test (T25-FW)
- Timed 25-Foot Walk test Serial 3's (T25-FW S3's
- Timed "Up and Go" (TUG)
- Self-paced 500-Foot Walk (500FW)

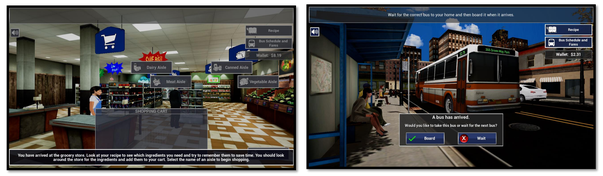
Cognitive Assessments

Cognition was assessed at Visit 1 with the expanded Brief Assessment of Cognition (BAC), which includes the following measures:

- **BAC-Expanded Verbal Memory:** List learning of 15-item list of word from three distinct semantic categories, 5 learning trials followed 20 minutes later by delayed free and cued recall and delayed recognition
- **Visuo-Spatial Working Memory**: Participants encode object-location pairs by tapping items as they appear in sequence on a grid, then tap the location on a blank grid where the object first appeared. Sequence length and grid size increase throughout the task.
- **Digit sequencing task**: Subtest that presents clusters of numbers of increasing length. Participants are asked to respond with the numbers in order, from lowest to highest.
- **Token motor task**: This subtest presents a screen with a virtual container and automatically replenishing set of tokens. Participants are asked to touch tokens simultaneously and slide them two at a time into the container as quickly as possible. A 60-s time limit is imposed.
- **Verbal fluency:** Category Instances: Animals; Controlled Oral Word Association: F, S.
- **Symbol coding**: As quickly as possible, participants enter numerals 1 –9 as matches to symbols into a virtual response sheet for 90 s.
- **Tower of London**: Participants are shown two pictures simultaneously on the tablet screen, where each picture shows three balls of different colors arranged on three pegs (unique arrangement in each picture). Participants are asked to give the total number of times the balls in one picture need to be moved in order to make the arrangement of balls identical to that of the other, opposing picture. There are 20 trials.

Functional Assessment

Performance-based assessment of iADL function was assessed using the The Virtual Reality Functional Capacity Assessment Tool (VRFCAT©). The VRFCAT uses a realistic simulated environment to recreate routine activities of daily living (i.e., Meal planning and preparation, using transportation for getting places, shopping for groceries, and handling money). The VRFACT has demonstrated sensitivity to differences between healthy older adults with and without SCD (Atkins et al., 2018).



Wearable Technologies

Empatica E2 Wristband – Actigraphy

- Wrist-worn device providing continuous measurement of motor activity (i.e., actigraphy), galvanic skin response, skin temperature, and sleep
- Empatica logfiles summarize sensor activity over 1 minute epochs. For each minute epoch, the logfile reports electrodermal activity (EDA) and temperature sensor averages, as well as values from proprietary algorithms that reflect movement intensity, total steps taken, sleep state, and whether the E2 wrist band was on the wrist or not. From the 1 minute epoch logfile, the following daily summaries were calculated:
  - Compliance – the total time the device was flagged as being on the wrist
    - Compliance criteria: To be considered a valid day of data collection, the E2 had to be worn a minimum of 10 hours; Subjects with at least 3 days of valid data were included in further analyses
  - Steps – total steps taken throughout the day
  - Sleep – Total sleep time recorded for that day
  - EDA and temperature averages – the sensor values averaged over the minutes during which the device was being worn, calculated separately for awake and asleep times
  - Movement intensity – average value of proprietary algorithm while the device was worn, calculated separately for awake and asleep times
- Daily E2 measures were averaged over days 2-6 for each day meeting compliance criteria

Figure 1. Phases of the Gait Cycle

Moticon Science Insoles - Gait

- Fitted shoe insoles designed to passively collect gait and movement data through 3-axis accelerometer and angular rate sensors as well as 16 unique pressure sensors.
- Provides measures that characterize a subject's gait across a gait cycle, as well as within specific phases of the gait cycle (Figure 1)
- Gait Line: At the beginning of the gait cycle, marked by the initial heel strike, the center of pressure (COP) of the subject's weight on the insoles starts near the heel. The COP sweeps forward throughout the gait cycle until the toe off for that foot. Each of these sweeps creates a gait line (Figure 2). The mean gait line length and width are reported.
- Ground Reaction Force: The force exerted by the ground on the subject's foot. The mean GRF and maximum GRF during the stance phase are reported.
- Temporal parameters:
  - Cycle Time: The mean time to complete a single gait cycle (a stride)
  - Cadence: The mean number of strides per minutes
  - Double support time: Time during which both feet are in contact with the ground. We report here side-specific mean double support time, with the left mean double support time considering the time starting from the right foot's initial contact, until the left foot's toe off.
  - Stance duration: Time that a given foot (left or right) is in contact with the ground. We report here both the mean and standard deviation of stance duration.
  - Swing duration: Time that a given foot is not in contact with the ground (toe off until next heel contact for that foot)
- Spatial parameters:
  - Mean stride length: The displacement of the same foot in walking direction.
  - Mean walking speed: The mean stride length divided by the mean gait cycle time.

RESULTS

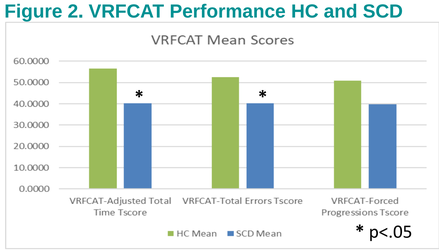
Cognition and iADL Functioning

- Consistent with prior work, participants with SCD performed significantly worse than HCs on the BAC ($p<.05$ for tests of episodic verbal memory, working memory, processing speed, executive functions and verbal fluency) and MMSE (Table 2). Similarly, subjects with SCD performed significantly worse on the VRFCAT ($p<.05$ for both completion time and errors) (Figure 4). These results indicate objective impairments in the SCD sample.

Table 2. Cognitive Test Performance in HC and SCD

	SCD		HC				
	Mean	SD	Mean	SD	t	Sig	Cohen's d
MMSE	26.5	3.3	28.7	1.3	-2.23	0.04	-0.95
Digit Sequencing	16.5	4.5	20.8	4.1	-2.75	0.01	-1.01
Token Motor	43.6	13.3	65.0	23.4	-2.71	0.01	-1.17
Symbol Coding	22	11.3	36.4	12.7	-3.13	0.00	-1.20
Tower of London	11.5	4.8	16.3	4.8	-2.67	0.01	-1.00
Semantic Fluency	15.6	6.2	20.6	5.1	-2.45	0.02	-0.88
Letter Fluency	25.8	9.5	33.4	11.1	-1.88	0.07	-0.73
Combined Fluency	41.4	14.9	53.9	14.0	-2.35	0.03	-0.87
Expanded Verbal Memory	29	9.5	36.1	7.9	-2.25	0.03	-0.81
Delayed Free Recall Total Score	5.4	4.7	9.2	4.0	-2.43	0.02	-0.88
Visuospatial Working Memory	10.4	8.4	14.8	5.7	-1.79	0.08	-0.62

Figure 2. VRFCAT Performance HC and SCD



Motor Functioning

- Participants with SCD performed worse than HC on a portion of motor functioning assessments administered at Visit 1.
  - Individuals with SCD were significantly slower than HC completing the TUG (11.11 sec vs. 9.54 sec, t=2.07, p=.047).
  - On the CTAP, individuals with SCD produced significantly fewer button presses with their non-dominant hand (46.18 vs. 51.38, t=-2.21, p=.034) and combined hands (87.09 vs. 97.62, t=-2.07, p=.046); the difference between the groups for the dominant hand did not reach significance (46.18 vs. 51.38, t=-1.80, p=.081).

E2 Actigraphy: Compliance and Correlations with Cognition and Function

- For the wrist-worn Empatica device, compliance rates during the at home portion of the study were significantly lower for individuals with SCD (average of 13.65 hours of usable data/day) than HCs (20.16 hours/day, t(37)=-2.87, p=.01 (Figure 3).
- Eight of 12 individuals with SCD and 25 of 26 HCs met our predefined compliance requirement by wearing the devices a minimum of 10 hours on 3 or more days. Although there were no group differences in Empatica-assessed actigraphy during lab-based assessments, there were strong positive correlations between performance-based cognition and function and measures of daily activity/movement collected between study visits (Table 3): Average waking activity level was positively correlated with BAC verbal fluency (r=.61, p<.001), verbal list learning (r=.44,p<.05), symbol coding (r=.45, p<.05), MMSE (r=.38, p<.05), and VRFCAT completion time (r=.42, p<.05) (Table 4).

Figure 3. E2 Device Compliance in HC and SCD

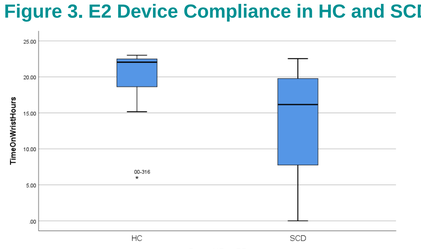


Table 3. Correlations of Empatica Endpoints with Cognitive Measures

	MMSE1-Total Score	BAC-Digit Sequencing	BAC-Token Motor	BAC-Symbol Coding	BAC-Tower of London	BAC-Semantic Fluency	BAC-Letter Fluency	BAC-Combined Fluency	BAC-Expanded Verbal Memory	BAC-Delayed Free Recall Total Score	BAC-Visuospatial Working Memory
EDA AVG Awake	0.17	-0.30	-0.05	0.29	0.08	0.09	-0.05	0.00	0.10	0.20	0.08
EDA AVG Asleep	0.16	-0.34	-0.06	0.21	0.07	0.04	-0.06	-0.03	0.09	0.20	0.06
Temp AVG Awake	-0.07	-0.32	-0.25	-0.26	-0.34	-0.33	-.445*	-.455*	-0.13	-.431*	-.447*
Temp AVG Asleep	0.11	-0.30	-0.18	-0.18	-0.10	-0.08	-0.16	-0.15	0.00	-0.16	-0.27
Movement AVG Awake	.376*	0.35	0.04	.454*	0.30	.520**	.554**	.612**	.438*	0.24	.398*
Movement AVG Asleep	0.10	0.11	0.06	0.00	-0.14	-0.07	0.14	0.07	-0.06	-.381*	0.08
Steps	0.35	.382*	0.09	0.29	0.12	0.33	.382*	.410*	0.17	-0.11	0.34
Rest Total (Minutes)	.372*	-0.14	-0.07	0.12	.362*	0.29	0.11	0.19	0.16	0.24	0.35

Moticon Gait Measures: Compliance and Correlations with Cognition and Function

- 2 participants were deemed ineligible to Moticon insoles based on a foot exam by a study clinician, 1 participant had feet too large for the largest size insoles, and device malfunction resulted in incomplete data for 5 participants.
- Within the remaining participants, those with SCD exhibited differentiated gait parameters, including significantly prolonged mean stance duration and double support time, longer cycle time, and slower cadence on most laboratory-based assessments of mobility (Table 5). It is important to note that we tested 22 Gait parameters gathered during each of 5 walking tests. Only the significant differences are reported due to space issues; no correction for multiple comparisons was applied.

Table 5. Gait Parameters in HC and SCD

		SCD		HC				
Assessment	Gait Variables Exhibitting Group Differences	Mean	SD	Mean	SD	t	Sig	Cohen's d
500 Ft Walk	Cycle Time	0.5033	0.07735	0.4488	0.06613	2.068	0.047	0.759508
	Cadence	126.4379	14.18224	138.7335	14.30715	-2.275	0.030	-0.86317
T25 Ft Walk	Double Support Time(R)	0.0654	0.01225	0.0453	0.01726	3.318	0.002	1.360203
	Stance Duration (L)	0.2966	0.03889	0.2345	0.06198	2.912	0.007	1.230514
	Stance Duration (R)	0.2786	0.04686	0.2333	0.05361	2.439	0.024	0.90124
T25 Serial 3s	Double Support Time (L)	0.0705	0.02891	0.0457	0.01983	2.807	0.009	1.019421
	Double Support Time (R)	0.0787	0.01597	0.0537	0.01899	3.617	0.001	1.431265
	Stance Duration (L)	0.3389	0.08009	0.2451	0.07157	3.337	0.002	1.23597
	Stance Duration (R)	0.3277	0.06411	0.2592	0.06183	2.894	0.007	1.087907
TUG	Mean Force Stance (R)	0.8906	0.18251	0.7653	0.14914	2.056	0.049	0.756137
	Cycle Time	0.4921	0.04968	0.4472	0.05663	2.154	0.039	0.844233
	Cadence	127.8361	9.97827	139.7562	14.62009	-2.333	0.027	-0.96917
At Home	Width of Gait Line (R)	0.1612	0.01066	0.1126	0.03953	4.615	0.000	1.936139

Association of Gait Measures with Cognition and Functional Capacity

- In the combined sample, several gait measures significantly correlated with functional capacity, such that reduced gait efficiency was associated with lower performance on the VRFCAT: Double support time (i.e. time spent with weight on both legs during walking) was correlated positively with VRFCAT completion time (r=.45, p<.05), as was length and variability in single leg stance duration during walking (correlations ranging from .47 - .54, p<.05 for all). Similar correlations were present for BAC, with correlations in the range of .44 to .53, p<.05 for all (Table 6). It should be noted that correlations were computed for all 22 gait measures, but only those producing significant correlations are reported here.

Table 6. Partial Correlations (Controlling for Height) of Gait Measures with Functional Capacity and Cognition

Gait measures that did not produce significant correlations are omitted for brevity

	VRFCAT-Adjusted Total Time	BAC-Digit Sequencing	BAC-Token Motor	BAC-Semantic Fluency	BAC-Letter Fluency	BAC-Symbol Coding	BAC-Tower of London	BAC-Verbal Memory-Total Learning	BAC-Verbal Memory-Delayed Free Recall	BAC-Verbal Memory-Delayed Cued Recall	BAC-Visuospatial Working Memory
Mean length of gait line (right) (mm)	0.21	-0.10	-0.25	-0.13	-0.36	-0.02	-0.24	-0.16	-0.49	-0.31	-0.16
Max Force Stance (left) (N/kg)	-0.23	0.21	0.07	0.15	-0.03	0.01	0.22	0.45	0.05	0.10	0.25
Max Force Stance (right) (N/kg)	-0.26	0.27	0.24	0.04	0.19	0.18	0.44	0.32	0.09	0.29	0.24
Mean double support time (left) (s)	0.45	-0.40	0.00	-0.39	-0.48	-0.31	-0.50	-0.33	-0.12	-0.43	-0.16
Mean double support time (right) (s)	0.29	-0.20	-0.13	-0.33	-0.50	-0.34	-0.28	-0.18	-0.08	-0.25	-0.10
Mean stance duration (left) (s)	0.47	-0.36	-0.24	-0.33	-0.52	-0.39	-0.37	-0.34	-0.32	-0.48	-0.14
Mean stance duration (right) (s)	0.47	-0.47	-0.29	-0.45	-0.53	-0.31	-0.40	-0.46	-0.28	-0.52	-0.24
SD of stance duration (left) (s)	0.54	-0.26	-0.18	-0.32	-0.24	-0.06	-0.31	-0.53	-0.38	-0.30	-0.36
SD of stance duration (right) (s)	0.03	0.12	-0.21	-0.19	-0.29	-0.22	-0.19	-0.03	0.00	-0.05	-0.15
Highlighted cells: p<.05											

CONCLUSIONS

- Preliminary findings highlight the challenges of integrating wearable technologies into clinical trials for participants with even mild cognitive deficits.
  - Individuals with SCD struggled to comply with the requirements for wearing the E2 device. The device requirements, which include daily charging, and proximity to an external paired mobile device, contributed to these difficulties.
  - Moticon insoles were associated with a higher than expected rate of data loss. In addition, use of insoles is reserved for participants with adequate balance and foot-health, a limitation that may limit use in more diverse samples. As with the E2, the need for regular device changing and maintenance may limit in large-scale longitudinal trials.
- Despite compliance issues, preliminary data indicate moderate correlations between remotely captured actigraphy and gait measures and established assessments of cognition and function, suggesting wearable technologies can provide meaningful information regarding cognitive health and may ultimately contribute to continuous assessment of cognition and function in clinical trials.
- Although enrollment is currently on hold due to COVID-19, we hope to resume enrollment in early 2021 using an alternative wristwork wearable device and incorporating at-home assessments of cognition.

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