Remote assessment of functional impairment in Alzheimer's disease: results of the RADAR-AD study

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BACKGROUND

Remote monitoring technologies (RMTs), such as smartphone apps and smartwatches, are changing the way functional and cognitive performance are measured in Alzheimer's disease (AD). Due to their sensitivity, objectivity, and the option of long-term and continuous measurement, RMTs have the potential to detect a subtle decline in the earliest stages of AD.

AIM OF THE STUDY

Here, we present the results of the European RADAR-AD project (Remote Assessment of Disease and Relapse – Alzheimer's disease), which aims to test feasibility, acceptability and validity of RMT measures across all stages of AD, from cognitively normal to mild dementia.

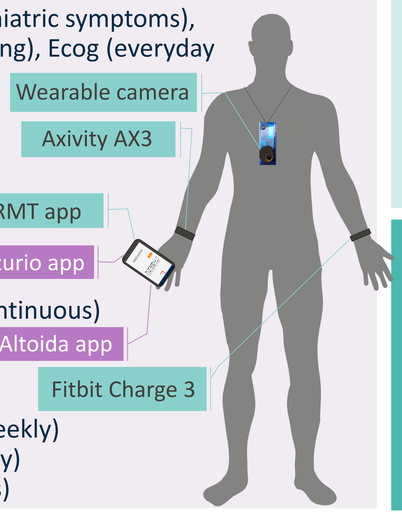
STUDY DESIGN

Active monitoring

Passive monitoring

In-clinic baseline assessment:

- CERAD: cognition
- Questionnaires PSQI (sleep), ESS (sleepiness), GLTE (physical activity), GDS (depressive feelings)
- Caregiver questionnaires: NPI-Q (neuropsychiatric symptoms), Amsterdam IADL (IADL), SFS (social functioning), Ecog (everyday cognition)
- Digital tests:
  - Banking app: managing finances
  - Altoida augmented reality app: cognition
  - Physilog sensors: gait
- Smartphone proficiency test



At-home remote assessments (8 weeks):

- Fitbit Charge 3: activity, heart rate, sleep (continuous)
- Axivity AX3: activity, sleep (continuous)
- Mezurio app: cognition (daily)
- pRMT app: smartphone use (continuous)
- Altoida augmented reality app: cognition (weekly)
- Amsterdam IADL Questionnaire: IADL (weekly)
- Wearable camera: activities (optional, 6 days)

METHODS

- We included 229 participants from 12 different European countries, in 4 study groups (Table 1).
- Features were extracted for all RMTs and compared across groups using ANCOVA, with adjustment for relevant confounders.

DATA & RESULTS

- **Feasibility**: Compliance was high, but decreased with disease severity. Real-time monitoring and involvement of study partner increased compliance.
- **Acceptability**: Problem rates were highest for the active apps, and increased with disease severity.
- **Validity**: Various individual sensors discriminated symptomatic AD participants from asymptomatic participants ($p<0.05$), and even discriminated preclinical AD from healthy controls, for example the Altoida app and Axivity activity tracker.
- Table 1 shows example features, full table available on request of the author

CONCLUSION

The RADAR-AD study provides unique insights in the feasibility, acceptability, and validity of remote monitoring of functional abilities in AD and their potential to differentiate between syndromic stages.

***Table 1** | Demographics and example features per study group.*

Features	Healthy control (N=69)	Preclinical AD (N=39)	Prodromal AD (N=65)	Mild-to-moderate AD (N=56)	ANCOVA
Demographics					
Amyloid status	Negative	Positive	Positive	Positive	
CDR (0/0.5/1/2)	69/0/0/0	38/1/0/0	0/65/0/0	0/6/42/8	p<0.001*
MMSE	29 (1)	29 (1)	27 (2)	22 (3)	p<0.001*
Male [n(%)]	31 (45%)	16 (41%)	38 (59%)	31 (55%)	p=0.218
Age	67 (8)	71 (6)	70 (8)	70 (9)	p=0.087
Years of education	14 (4)	16 (3)	15 (5)	14 (4)	p=0.149
Banking app					
Validity: Total test duration [s]	54.1 (32.2)	51.2 (33.3)	73.0 (54.8)	96.8 (61.0)	P<0.001*
Gait tests (Physilog sensors)					
Validity TUG: Turn duration [s]	2.3 (0.41)	2.4 (0.63)	2.48 (0.75)	2.9 (1.48)	p=0.002*
Validity DTE: Gait speed [%]	-6.15 (10.68)	-6.28 (8.87)	-13.5 (15.51)	-19.55 (20.37)	p<0.001*
Activity tracker 1: Fitbit Charge 3					
Feasibility: wear time [%]	92 (84-97)	94 (85-96)	84 (67-96)	83 (43-93)	p=0.006*
Acceptability: problem rates [%]	4.4 (7.0)	4.0 (4.4)	6.8 (13.6)	10.4 (12.7)	p=0.07*
Validity: Mean number of steps	7486.18 (3848.86)	7196.85 (3514.25)	6235.09 (3809.03)	5682.01 (4051.39)	P<0.001*
Activity tracker 2: Axivity AX3					
Feasibility: wear time [%]	57 (49-98)	95 (50-99)	85 (50-99)	52 (45-95)	p=0.13
Acceptability: problem rates [%]	5.7 (8.1)	6.2 (5.0)	8.0 (15.0)	8.5 (10.4)	p=0.31
Validity: Time sedentary [hours]	7.72 (1.79)	8.74 (1.51)	8.58 (1.91)	8.65 (2.19)	p=0.006*
Active app 1: Altoida research algorithm (DNS-MCI)					
Feasibility: tasks completed [%]	75 (50-112)	75 (50-100)	63 (38-88)	N/A	p=0.09
Acceptability: problem rates [%]	15.2 (20.6)	24.7 (21.0)	24.4 (25.9)	N/A	p=0.09
Validity in clinic: DNS-MCI	62.23 (21.27)	50.39 (21.24)	32.87 (19.77)	NaN (NA)	p<0.001*
Validity at home: DNS-MCI	63.27 (22.08)	53.67 (21.98)	43.1 (22.76)	7.37 (1.19)	p<0.001*
Active app 2: Mezurio (speech task)					
Feasibility: tasks completed [%]	92 (81-96)	94 (81-97)	87 (78-94)	83 (58-92)	N/A
Acceptability: problem rates [%]	6.7 (8.6)	10.3 (10.8)	13.2 (17.6)	12.5 (12.2)	p=0.04*
Validity: Average pause duration	193.33 (90.38)	232.79 (143.8)	198.02 (90.46)	164.44 (97.94)	p=0.009*
Wearable camera					
Feasibility: wear time [h]	14 (10-15)	15 (13-18)	16 (14-22)	14 (6-18)	p=0.55
Acceptibility: problem rates [%]	8.1 (11.1)	10.6 (6.4)	9.9 (24.3)	9.6 (12.0)	p=0.94

All numbers show mean (SD), except for the feasibility numbers, which show median (Q1-Q3). * indicates $p<0.05$. Acceptability was calculated as the percentage of reported problems during bi-weekly semi-structured interviews. Amyloid status was based on either CSF or PET results. Abbreviations: Amsterdam iADL = Amsterdam instrumented activities of daily living questionnaire, BPM = beats per minute, CDR = Clinical Dementia Rating, DNS-MCI = Digital Neuro Signature (the outcome of a machine learning model trained to identify cognitively normal individuals from those presenting with cognitive impairment, DTE = dual task effect (the percentage change when comparing a single walk test with the dual walk test), MMSE = Mini-Mental State Examination, MVPA = mild-to-vigorous activity, s = seconds, TUG = timed up-and-go.

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