



Motor-cognitive dual tasking in the clinical setting: a sensitive measure of functional impairment in early Alzheimer’s disease

Anna-Katharine Brem^{1,2*}, Gaetano Scebba^{3*}, Jelena Curcic³, Marijn Muurling⁴, Casper de Boer⁴, Neva Coello⁵, Alankar Atreya⁶, Pauline Conde², Holger Fröhlich⁷, Margarita Grammatikopoulou⁸, Chris Hinds⁶, Ioulietta Lazarou⁸, Manuel Lentzen⁷, Vaibhav A Narayan⁹, Rouba Kozak¹⁰, Spiros Nikolopoulos⁸, Srinivasan Vairavan¹¹, Pieter Jelle Visser⁴, Gayle M. Wittenberg¹¹, Dag Aarsland^{1,12}, on behalf of the RADAR-AD Consortium

(1) King's College London, United Kingdom; (2) University Hospital of Old Age Psychiatry, University of Bern, Switzerland; (3) Novartis Institutes for Biomedical Research, Switzerland; (4) Alzheimer Center Amsterdam, the Netherlands; (5) Biostatistics and Pharmacometrics, Novartis Pharma AG, Basel; (6) University of Oxford, UK; (7) Fraunhofer Institute for Algorithms and Scientific Computing SCAL, Germany; (8) Centre for Research & Technology Hellas, Greece; (9) Davos Alzheimer’s Collaborative, USA; (10) Novartis, Cambridge, MA, USA ; (11) Janssen Neuroscience Research & Development, USA; (12) Stavanger University Hospital, Norway. *Shared first authors



Scan the QR code to learn more about the RADAR-AD study

BACKGROUND

- Gait is a complex everyday activity and abnormal gait has been associated with an increased risk of institutionalisation and death
- As cognition declines, the interaction and competition for neuronal resources during motor-cognitive dual-tasking (e.g., walking while talking) might be a sensitive measure of functional impairments in early Alzheimer’s disease (AD)

AIM OF THE STUDY

- Identify gait deficits due to neuronal competition during cognitive-motor dual-tasking across the AD spectrum in RADAR-AD

STUDY DESIGN

- We attached three inertial measurement units (accelerometer and gyroscope) to both feet and one hip to assess dual task effects (DTE)
- To determine DTE we assessed gait performance with/without concurrent serial subtraction-by-1 task in the four study groups

PARTICIPANTS

GROUP	AMYLOID	CDR	MMSE
HC	Negative	0	>=28
PreAD	Positive	0	>=27
ProAD (MCI)	Positive	0.5	24 - 26
MildAD	Positive	>=1	18 - 23

Table 1. Group specification.

	HC	PreAD	ProAD	MildAD	p-value
N	58	31	51	44	
Female, N(%)	31(53%)	20(65%)	20(39%)	20(46%)	0.134
Age (Mn±Sd)	67.1 ± 7.9	70.4 ± 5.7	69.0 ± 7.9	70.1 ± 9.0	0.156
BMI (Mn±Sd)	25.9 ± 3.2	25.2 ± 4.2	25.2 ± 3.6	24.1 ± 3.5	0.086
Education (Mn±Sd)	14.7 ± 3.5	15.5 ± 2.9	14.7 ± 4.5	13.6 ± 4.3	0.241
GDSS (Mn±Sd)	0.9 ± 1.6	1.8 ± 2.0	3.2 ± 2.7	2.4 ± 1.8	<.001
ADCS-ADL (Mn±Sd)	75.9 ± 3.0	76.0 ± 2.8	72.2 ± 6.1	61.5 ± 13.0	<.001
MMSE (Mn±Sd)	29.3 ± 0.8	29.2 ± 1.1	26.6 ± 2.4	21.8 ± 3.2	<.001
CDR (0/0.5/1/2)	57/0/0/0	29/2/0/0	2/48/0/0	0/5/31/8	<.001

Abbreviations: ADCS-ADL: Alzheimer’s Disease Cooperative Study - Activities of Daily Living Inventory; BMI: Body-mass-index; CDR: Clinical Dementia Rating; GDSS: Geriatric Depression Scale; MMSE: Mini-Mental State Examination; Mn: Mean; SD: Standard deviation; p-values <.05 indicate significant group differences.

Table 2. Demographic information.

Dual Task Effect	Df	Sum Sq	Mean Sq	F value	p-value
Peakswing (cv)	3	36.850	12.284	8.136	<.0001***
Speed (cv)	3	26.800	8.934	6.602	<.001***
Double support (avg)	3	19.722	6.574	4.711	.004**
Swing (cv)	3	23.297	7.766	3.875	.012*
Push off rate (cv)	3	27.998	9.333	6.039	<.001***
Stance (cv)	3	20.386	6.795	5.839	<.001***
Foot flat rate (avg)	3	20.697	6.899	3.616	.017*
Path length (avg)	3	11.077	3.692	3.164	.026*
Cadence (cv)	3	7.926	2.642	2.706	.048*
Toe off angle (cv)	3	20.775	6.925	5.095	.002**
Stride length (avg)	3	13.914	4.638	4.983	.003**
Stride length (cv)	3	22.821	7.607	4.778	.005**
Swing width (avg)	3	34.838	11.613	7.642	<.001***
Gate cycle time (avg)	3	29.558	9.853	4.295	.008**
Gate cycle time (cv)	3	21.918	7.306	5.122	.002**
Gait cycles (n)	3	0.669	0.223	2.953	.035*

Table 3. ANCOVA results.

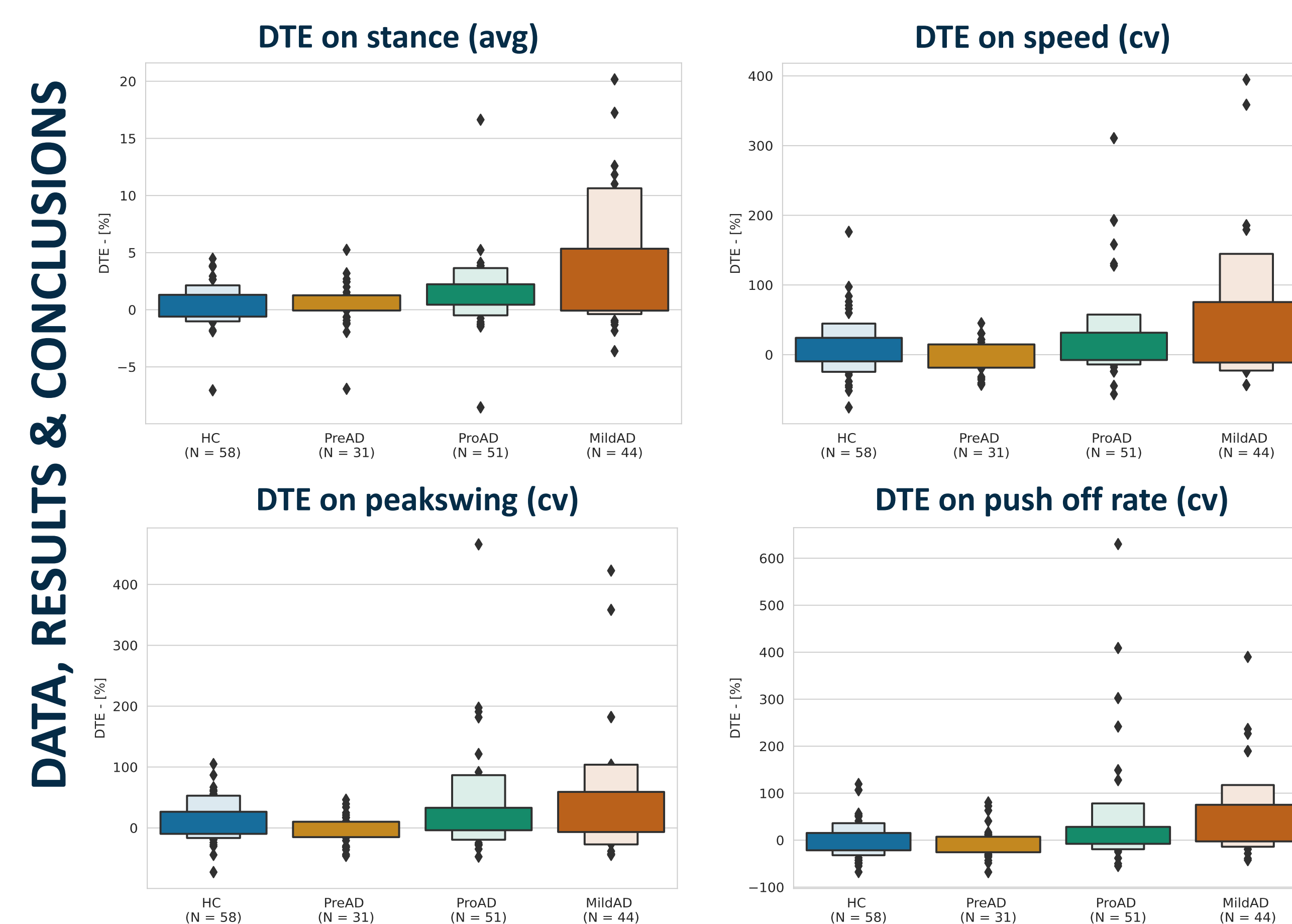


Fig 1. Distribution of dual task effects with significant group effects (ANOVAs with group effects p<.001).

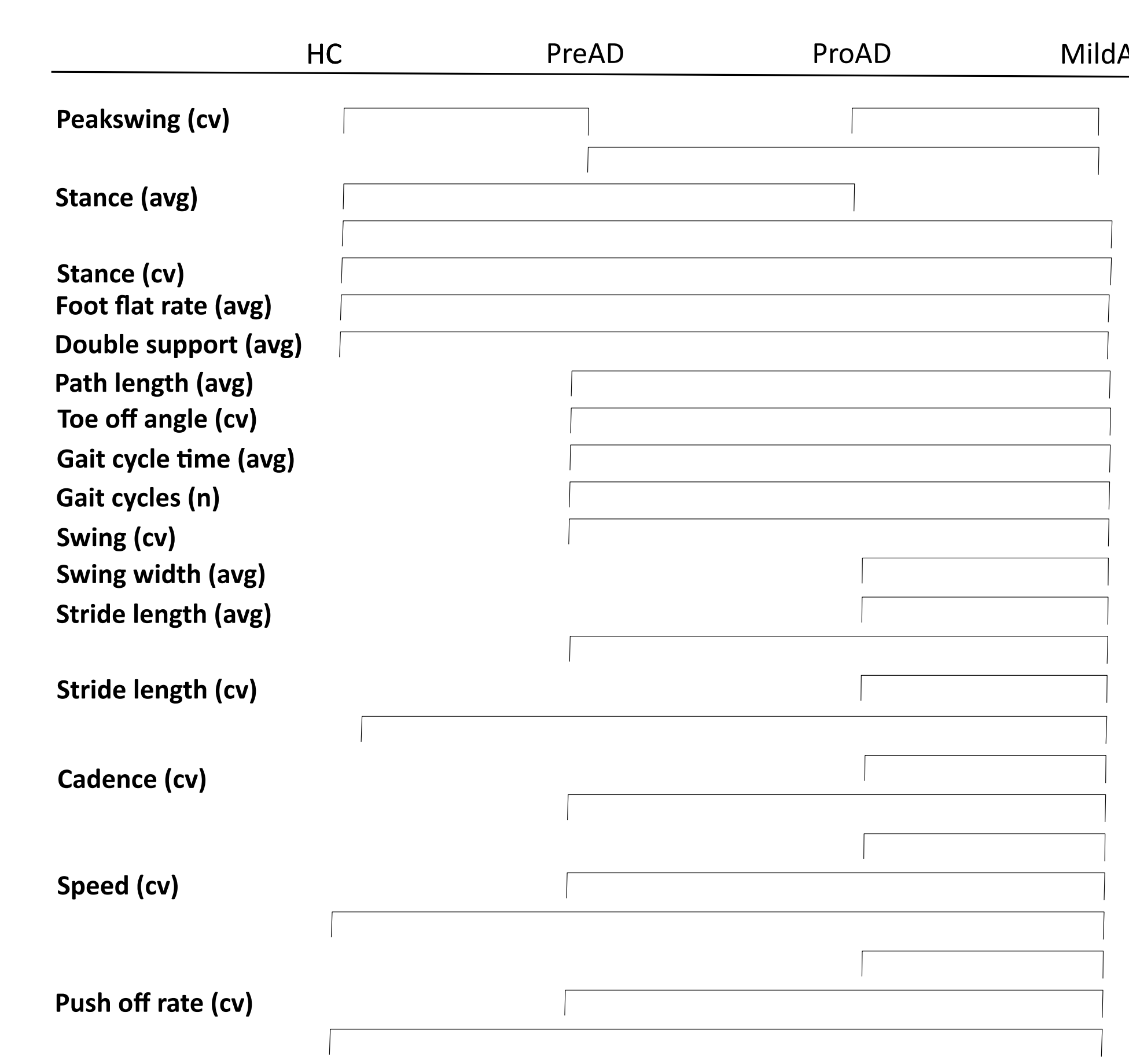


Fig 2. Significant dual task effects between groups (Tukey HSD, p<.05).

CONCLUSIONS

- Neuronal competition as assessed with motor-cognitive dual-tasking can be used to detect early impairments not captured by cognitive or motor tests alone
- Possible applications: predict and monitor changes in gait and use to prevent falls and hospitalisations in later stages of the disease
- Future studies should implement an adaptive cognitive load to improve sensitivity/specificity



Single task

Dual task



Walking



Counting & Walking

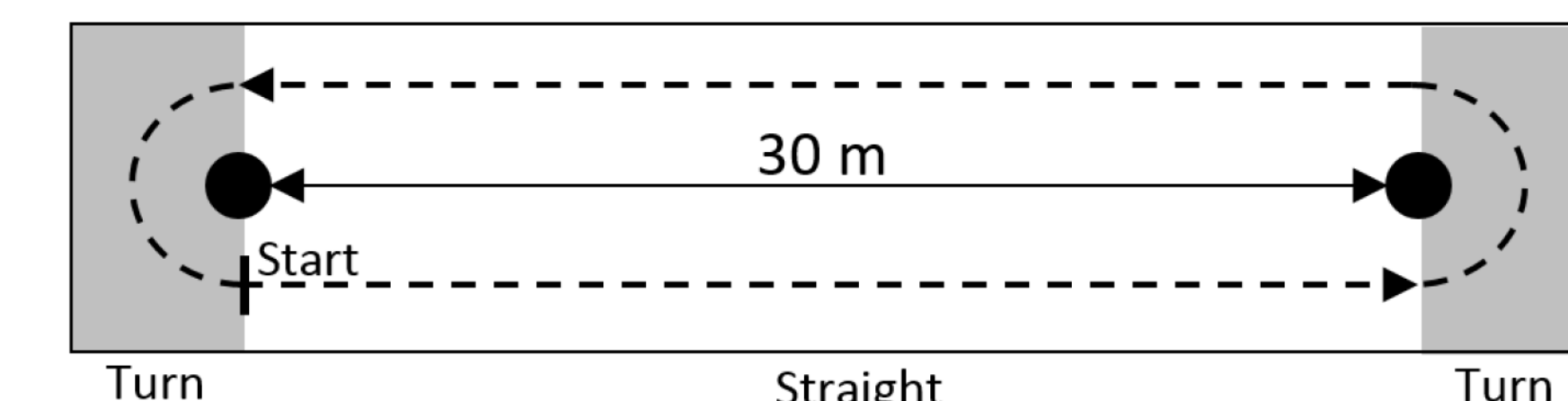


Fig 3. Dual tasking setup: inertial measurement unit sensors are placed on both feet and one on the right side of the hip. During the *single task*, they are instructed to walk at a comfortable pace. During the *dual task*, they are instructed the repeat the walking while loudly counting backwards from 100.

RESULTS

- Cognitive impairment affects a range of gait features, with significant changes mostly emerging in the later stages
- DTE on stance was significantly different between HC and ProAD
- DTE of variability (peakswing, swing, toe-off-angle, cadence, speed, and push-off-rate) and averages (path length, gait cycle time, gait cycles) differed significantly between PreAD and MildAD