Gait and Falls in Cerebral Amyloid Angiopathy

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BACKGROUND

- Cerebral amyloid angiopathy (CAA) is characterized by vascular amyloid deposition.
- Gait is a complex motor task requiring coordinated efforts of different regions of the brain[1].
- While gait is known to decline in age-related diseases, little is known about the gait profile of CAA[2].

HYPOTHESES

- Gait:
  - Gait will be impaired in CAA compared to NC
- Falls:
  - Greater number of falls and fear of falling will be associated with greater impairment in gait

METHODS

- Participants were selected from the Functional Assessment of Vascular Reactivity study (n=91):
  - **NC** (n=44): Determined normal based on clinician impression and MoCA score
  - **MCI** (n=24): Diagnosis of MCI based on NIA-AA core clinical criteria
  - **CAA** (n=31): Diagnosis of probable CAA based on Revised Boston Criteria
  - **AD** (n=16): Diagnosis of AD based on NIA-AA Diagnostic Criteria

- **Gait assessments** conducted using ProtoKinetics Zeno Walkway (ProtoKinetics LLC, Havertown, PA)
  - 6-metre electronic walkway that can detect footfalls, allowing for collection of information regarding gait and balance.
- Accompanying ProtoKinetics Movement Analysis Software (PKMAS) records data on pressure, time, and space, allowing for many gait-related measurements to be calculated.

- Participants completed the following walks down the length of the walkway:
  - Preferred pace walk
  - 3 dual task walks, wherein participants walked at their preferred pace while engaging in once of the following cognitive tasks:
    - **Serial 1's**: Count backwards from 100 by ones
    - **Naming Animals**: Name as many different animals as possible
    - **Serial 7's**: Count backwards from 100 by 7's
  - Groups were compared via general linear model, adjusting for age, sex, and height

- Participants completed **Falls and Balance** questionnaire indicating:
  - Number of falls over the past 12 months
  - Fear of falling on a scale of 1-10
  - We investigated the associations between these and gait domain scores via logistic regression, controlling for age and sex

RESULTS – Demographic Information

	All Participants	NC	MCI	CAA	AD	p-value*
N	116	47	24	29	16	-
Male (%)	56 (48.3)	13 (27.7)	15 (62.5)	17 (58.6)	11 (68.8)	**<0.01**
Age	71.8 (7.3)	70.0 (6.3)	72.8 (8.3)	75.1 (7.7)	69.8 (6.2)	**0.01**
Height	168.5 (10.3)	165.8 (9.7)	170.0 (9.8)	171.0 (10.8)	169.7 (11.2)	0.14
Years of Education	15.3 (3.5)	15.8 (3.2)	15.5 (4.2)	13.9 (3.3)	16.0 (3.4)	0.09
MoCA	23.3 (4.9)	26.9 (1.9)	23.2 (2.9)	20.5 (5.7)	18.1 (4.0)	**<0.001**
Osteoarthritis (%)	54 (47.0)	28 (60.9)	9 (37.5)	13 (44.8)	4 (25.0)	0.06
WMH Volume	12.9 (16.9)	5.5 (5.8)	11.7 (15.9)	29.1 (22.1)	7.2 (8.2)	**<0.001**
CMB Count	21.3 (114.7)	0.2 (0.6)	0.9 (3.0)	84.1 (220.3)	0.1 (0.3)	**<0.01**

Note: Values represent means (standard deviation) for continuous variables and count (percent) for categorical variables. Bolded values indicate significant difference (p<0.05) between study groups based on ANOVA and chi square as appropriate. *comparisons are between individual groups (i.e., NC, MCI, CAA, and AD).

RESULTS – Group Comparisons on Individual Walks

	NC	MCI	CAA	AD
Preferred Pace				
Rhythm	-	-0.28 (-1.03, 0.48)	**-1.33 (-2.08, -0.58)[a,b]**	**-1.10 (-1.97, -0.24)[a]**
Pace	-	-0.33 (-1.05, 0.39)	**-1.23 (-1.95, -0.52)[a,b]**	**-1.01 (-1.84, -0.18)[a]**
Postural Control	-	-0.22 (-0.56, 0.12)	-0.01 (-0.35, 0.33)	-0.04 (-0.44, 0.35)
Variability	-	-0.54 (-1.27, 0.18)	**-1.08 (-1.80, -0.35)[a]**	**-1.45 (-2.29, -0.61)[a,b]**
Serial 1's				
Rhythm	-	-0.66 (-1.55, 0.24)	**-1.71 (-2.60, -0.82)[a,b]**	**-1.85 (-2.88, -0.82)[a,b]**
Pace	-	-0.42 (-1.13, 0.28)	**-1.42 (-2.12, -0.72)[a,b]**	**-1.18 (-1.99, -0.37)[a]**
Postural Control	-	-0.15 (-0.64, 0.34)	0.13 (-0.35, 0.62)	-0.00 (-0.56, 0.56)
Variability	-	-0.48 (-1.58, 0.62)	**-1.67 (-2.76, -0.58)[a,b]**	**-1.35 (-2.61, -0.09)[a]**
Naming Animals				
Rhythm	-	-0.66 (-1.56, 0.25)	**-1.35 (-2.27, -0.44)[a]**	**-2.04 (-3.08, -0.99)[a,b]**
Pace	-	-0.44 (-1.15, 0.26)	**-1.35 (-2.06, -0.63)[a,b]**	**-1.45 (-2.26, -0.64)[a,b]**
Postural Control	-	0.12 (-0.38, 0.62)	0.01 (-0.50, 0.51)	0.11 (-0.47, 0.68)
Variability	-	-0.18 (-1.49, 1.13)	-0.86 (-2.18, 0.47)	**-2.09 (-3.60, -0.58)[a,b]**
Serial 7's				
Rhythm	-	-0.27 (-1.07, 0.53)	-0.75 (-1.57, 0.06)	**-1.00 (-1.92, -0.09)[a]**
Pace	-	-0.27 (-0.92, 0.39)	**-1.20 (-1.87, -0.53)[a,b]**	**-1.12 (-1.87, -0.37)[a,b]**
Postural Control	-	-0.03 (-0.61, 0.55)	0.08 (-0.51, 0.67)	-0.18 (-0.84, 0.48)
Variability	-	-0.41 (-1.67, 0.85)	-1.25 (-2.53, 0.03)	**-1.58 (-3.02, -0.14)[a]**

Notes: Differences between disease groups (MCI, CAA, and AD) and control group (NC). Values represent mean (95% CI) standardized scores adjusted for age, sex, and height. Bolded values indicate significant differences between groups (p<0.05), using Tukey-Kramer method post hoc to adjust for multiple comparisons. [a]significant difference (p<0.05) compared to NC. [b]significant difference (p<0.05) compared to MCI.

RESULTS – Associations between Gait and Falls Characteristics

	Number of Falls				Fear of Falling			
	Model 1		Model 2		Model 1		Model 2	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
CAA								
Rhythm	0.88 (0.46, 1.68)	0.70	0.88 (0.48, 1.59)	0.66	0.98 (0.58, 1.64)	0.93	1.09 (0.60, 1.97)	0.77
Pace	1.30 (0.61, 2.79)	0.50	1.10 (0.47, 2.59)	0.82	**4.17 (1.26, 13.82)**	**0.02**	3.20 (0.92, 11.1)	0.07
Postural Control	0.22 (0.03, 1.61)	0.14	0.23 (0.02, 2.23)	0.20	0.59 (0.15, 2.35)	0.46	0.86 (0.19, 3.99)	0.85
Variability	1.08 (0.53, 2.19)	0.83	0.96 (0.39, 2.40)	0.93	**2.33 (1.08, 5.00)**	**0.03**	1.99 (0.79, 4.99)	0.15
All Participants								
Rhythm	0.89 (0.62, 1.28)	0.54	0.93 (0.62, 1.39)	0.71	0.99 (0.74, 1.31)	0.92	1.31 (0.93, 1.85)	0.12
Pace	0.96 (0.63, 1.46)	0.86	0.96 (0.61, 1.49)	0.84	**2.47 (1.59, 3.84)**	**<0.001**	**2.61 (1.59, 4.29)**	**<0.001**
Postural Control	0.65 (0.27, 1.53)	0.32	0.68 (0.27, 1.71)	0.42	0.96 (0.46, 2.00)	0.92	1.59 (0.70, 3.61)	0.27
Variability	1.11 (0.75, 1.65)	0.59	1.17 (0.77, 1.77)	0.47	**1.49 (1.07, 2.08)**	**0.02**	**1.64 (1.10, 2.44)**	**0.01**

Notes. Odds ratio (95% confidence interval) based on Preferred Pace walks. Bolded values indicate significance (p<0.05) ; OR = odds ratio; Model 1: Unadjusted; Model 2: Adjusted for age and sex.

DISCUSSION/ CONCLUSIONS

- Gait:
  - Rhythm and pace were impaired in CAA during preferred pace and dual task conditions, to a similar degree as in AD (Table 2).
- Falls:
  - Gait domains were not associated with number of falls (Table 3).
  - In CAA participants and the full study sample, better scores on pace and variability were associated with less fear of falling (Table 3).
- Conclusions:
  - Gait is impaired in CAA compared to NC and to a similar extent in AD and is associated with greater fear of falling.
  - Further research is needed to establish the underlying causes and other consequences of gait impairment in CAA.

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REFERENCES

1. Mirelman, A. et al. (2018). *Handb Clin Neurol.*, 159, 119-134.
2. McArdle, R. et al. (2019). *Alzheimer's Dement.*, 15(10), 1367-1377.

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