

SUPPLEMENTAL MATERIAL

Longitudinal progression of MRI markers and cognition in Dutch type hereditary Cerebral Amyloid Angiopathy (D-CAA)

Suzanne E. van Dijk, MSc¹; Jeroen van der Grond, PhD¹; Jessie Lak, MSc¹; Annette van den Berg-Huysmans, MSc¹; Gerda Labadie, BSc¹; Gisela M. Terwindt, MD, PhD²; Marieke J.H. Wermer, MD, PhD²; M. Edip Gurol, MD³; Mark A. van Buchem, MD, PhD¹; Steven M. Greenberg, MD, PhD³; Sanneke van Rooden, PhD¹

¹ Department of Radiology, Leiden University Medical Center, Leiden, The Netherlands

² Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands

³ Department of Neurology, Massachusetts General Hospital, Boston, U.S.A

Corresponding author:

Suzanne E. van Dijk

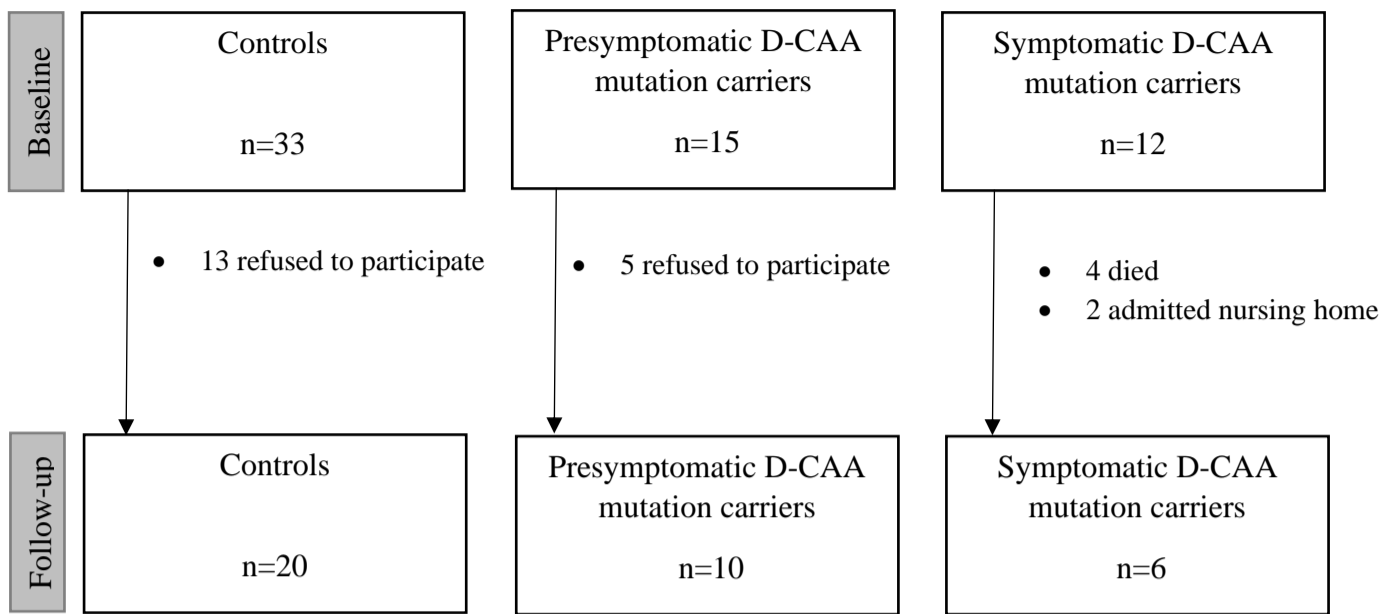
Department of Radiology, C3-Q, Leiden University Medical Center

PO Box 9600, 2300 RC Leiden, The Netherlands

Phone: +31-71-5263476

Email: S.E.van_Dijk.RADI@lumc.nl

Supplementary figure I. Patient flow diagram



Supplementary table I. MRI markers at baseline and follow up in healthy controls

Controls (n=20)						
		Baseline		Follow-up		<i>P</i> value Baseline vs follow- up
		Prevalence	Mean (SD; range)	Prevalence	Mean (SD; range)	
Hemorrhagic markers	Microbleeds – Lobair, n	5% (1/20)	0.1 (0.2; 0 - 1)	20% (4/20)	0.3 (0.6; 0 - 2)	0.104
	ICHs, n	0% (0/20)	0 (0; 0 - 0)	0% (0/20)	0 (0; 0 - 0)	–
	Convexity SAH, n	0% (0/20)	0 (0; 0 - 0)	0% (0/20)	0 (0; 0 - 0)	–
	cSS Focal Disseminated	0% (0/20) (0/20) (0/20)	–	0% (0/20) (0/20) (0/20)	–	–
Non- hemorrhagic markers	WMHs volume (cm3)	–	2.5 (3.1; 0.2 - 14.1)	–	3.8 (5.4; 0.3 - 25.3)	0.021
	DPVS-CSO	–	2.0 (0.8; 1 – 3)	–	2.3 (0.9; 1 – 4)	0.046
	DPVS-BG	–	1.9 (0.5; 1 – 3)	–	2.0 (0.5; 1 – 3)	0.317
	Lacunar infarcts, n	30% (6/20)	0.3 (0.5; 0 -1)	35% (7/20)	0.4 (0.5; 0 - 1)	0.330
	Fazekas	–	0.9 (0.5; 0.5 – 2.5)	–	1.0 (0.5; 0.5 – 2.5)	0.564
SVD in CAA	Total SVD in CAA	–	0.4 (0.6; 0 – 2)	–	0.6 (0.7; 0 – 2)	0.083
Perfusion	CBF frontal lobe (ml/100gr/min)	–	39.7 (7.9; 25.4 – 53.8)	–	37.9 (8.9; 21.4 – 52.8)	0.139
	CBF occipital lobe (ml/100gr/min)	–	42.1 (7.2; 25.4 – 56.2)	–	39.1 (7.9; 20.4 – 53.8)	0.001
	CBF parietal lobe (ml/100gr/min)	–	41.8 (7.6; 27.0 – 56.7)	–	40.2 (8.4; 23.3 – 52.9)	0.106
	CBF temporal lobe (ml/100gr/min)	–	32.6 (5.2; 22.4 – 42.0)	–	31.6 (5.5; 19.9 – 40.8)	0.157
	CBF total cortical gray matter (ml/100gr/min)	–	39.1 (6.9; 25.2 – 52.3)	–	37.3 (7.5; 21.6 – 48.9)	0.069

Supplementary table II. MRI markers at baseline and follow-up in presymptomatic D-CAA mutation

Presymptomatic mutation carriers (n=10)						
		Baseline		Follow-up		P value Baseline vs follow- up
		Prevalence	Mean (SD; range)	Prevalence	Mean (SD; range)	
Hemorrhagic markers	Microbleeds – Lobair, n	20% (2/10)	3.6 (10.1; 0 - 32)	40% (4/10)	10.6 (25.6; 0 - 82)	0.191
	ICHs, n	10% (1/10)	0.8 (2.5; 0 - 8)	10% (1/10)	2.2 (7.0; 0 - 22)	0.343
	Convexity SAH, n	10% (1/10)	0.1 (0.3; 0 - 1)	10% (1/10)	0.1 (3.1; 0 - 1)	–
	cSS Focal Disseminated	10% (1/10) (0/10) (1/10)	–	10% (1/10) (0/10) (1/10)	–	–
Non-hemorrhagic markers	WMHs volume (cm ³)	–	5.3 (6.0; 1.1 - 21.4)	–	7.3 (10; 1.3 - 33.1)	0.236
	DPVS-CSO	–	2.5 (1.3; 1 - 4)	–	2.7 (1.3; 1 - 4)	0.157
	DPVS-BG	–	1.8 (0.4; 1 - 2)	–	1.8 (0.4; 1 - 2)	–
	Lacunar infarcts, n	30% (3/10)	0.5 (0.9; 0 - 2)	30% (3/10)	0.5 (0.9; 0 - 2)	–
	Fazekas	–	1.3 (0.7; 0.5 - 2.5)	–	1.4 (0.8; 0.5 - 3)	0.157
SVD in CAA	Total SVD score in CAA	–	1.3 (1.9; 0 - 6)	–	1.6 (2.2; 0 - 6)	0.180
Perfusion	CBF frontal lobe (ml/100gr/min)	–	43.7 (6.1; 33.5 - 56.5)	–	44.5 (6.6; 35.0 - 57.9)	0.718
	CBF occipital lobe (ml/100gr/min)	–	40.7 (4.8; 31.0 - 48.4)	–	44.2 (7.8; 34.7 - 55.8)	0.152
	CBF parietal lobe (ml/100gr/min)	–	44.9 (5.7; 34.1 - 55.9)	–	45.7 (5.4; 37.5 - 54.1)	0.686
	CBF temporal lobe (ml/100gr/min)	–	32.0 (4.3; 22.6 - 39.7)	–	33.6 (4.3; 27.2 - 40.8)	0.243
	CBF total cortical gray matter (ml/100gr/min)	–	41.1 (5.1; 31.2 - 51.4)	–	42.4 (5.5; 34.1 - 52.4)	0.472

Supplementary table III. MRI markers at baseline and follow-up in symptomatic D-CAA mutation

Symptomatic mutation carriers (n=6)						
		Baseline		Follow-up		P value baseline vs follow-up
		Prevalence	Mean (SD; range)	Prevalence	Mean (SD; range)	
Hemorrhagic markers	Lobar microbleeds, n	100% (6/6)	103 (179.1; 20 - 468)	100% (6/6)	155.5 (193.2; 34 - 528)	0.064
	ICHs, n	100% (6/6)	18.3 (12.0; 7 - 35)	100% (6/6)	36.5 (19.8; 6 - 58)	0.007
	Convexity SAH, n	83.3% (5/6)	2.3 (2.9; 0 - 8)	83.3% (5/6)	4.0 (4.3; 0 - 12)	0.042
	cSS Focal Disseminated	100% (5/5) (2/5) (3/5)		100% (6/6) (0/6) (6/6)		0.157
Non- hemorrhagic markers	WMHs volume (cm3)	–	48.7 (24.7; 10.8 - 82.4)	–	67.8 (29.7; 20.3 - 107.1)	0.061
	DPVS-CSO	–	4.0 (0.0; 4 - 4)	–	4.0 (0.0; 4 - 4)	–
	DPVS-BG	–	2.2 (0.4; 2 - 3)	–	2.3 (0.5; 2 - 3)	0.317
	Lacunar infarcts, n	0% (0/6)	0 (0 - 0)	16.7% (1/6)	0.2 (0.4; 0 - 1)	0.363
	Fazekas	–	2.9 (0.2; 2.5 - 3)	–	3.0 (0.0; 3 - 3)	0.317
SVD in CAA	Total SVD score in CAA	–	5.6 (0.5; 5 - 6)	–	6.0; 0.0; 6 - 6)	0.157
Perfusion	CBF frontal lobe (ml/100gr/min)	–	35.6 (9.8; 18.7 - 42.7)	–	28.3 (7.9; 17.3 - 36.3)	0.025
	CBF occipital lobe (ml/100gr/min)	–	33.0 (11.3; 13.3 - 41.4)	–	28.9 (9.7; 11.0 - 35.4)	0.101
	CBF parietal lobe (ml/100gr/min)	–	36.7 (12.9; 15.1 - 46.6)	–	28.8 (9.3; 12.3 - 39.7)	0.012
	CBF temporal lobe (ml/100gr/min)	–	27.5 (9.2; 11.9 - 35.4)	–	22.5 (6.3; 12.9 - 29.4)	0.053
	CBF total cortical gray matter (ml/100gr/min)	–	33.9 (10.5; 16.0 - 41.5)	–	27.5 (7.3; 14.7 - 34.6)	0.011

Supplementary table IV. Cognitive and neuropsychiatric function at baseline and follow-up

Cognitive/ Neuropsychiatric domain	Test/questionnaire	Controls (n=20)			Presymptomatic mutation carriers (n =10)			Symptomatic mutation carriers (n=6)		
		Baseline	Follow-up	<i>P</i> value baseline vs follow- up	Baseline	Follow-up	<i>P</i> value baseline vs follow-up	Baseline	Follow-up	<i>P</i> value baseline vs follow-up
		Mean (SD; range)	Mean (SD; range)		Mean (SD; range)	Mean (SD; range)		Mean (SD; range)	Mean (SD; range)	
Global cognitive function	MMSE	29.5 (0.6; 28 - 30)	29.5 (0.7; 28-30)	0.710	29.9 (0.3; 29 - 30)	29.5 (0.7; 28 - 30)	0.046	26.7 (5.3; 16 - 30)	25.3 (7.2; 11 - 29)	0.109
Memory	WMS	125.3 (10.3; 105 - 143)	131.2 (12.4; 101 - 143)	0.043	123.1 (12.1; 103 - 137)	125.1 (12.3; 103 - 143)	0.525	121.5 (28.4; 72 - 143)	114.6 (20.9; 92 - 143)	0.071
	HVLT immediate recall	28.5 (4.8; 16 - 35)	29.3 (3.3; 24 - 34)	0.565	27.9 (3.0; 24 - 32)	27.6 (4.1; 19 - 31)	0.785	24.5 (9.0; 9 - 31)	21.0 (9.9; 9 - 33)	0.315
	HVLT delayed recall	10.7 (2.6; 6 - 19)	9.6 (2.9; 0 - 12)	0.130	10.0 (1.7; 7 - 12)	9.5 (2.4; 5 - 12)	0.397	7.8 (4.1; 0 - 11)	4.3 (5.4; 0 - 11)	0.124
Psychomotor speed	TMT A, sec	31.4 (11.2; 15 - 52)	25.6 (10.6; 13 - 51)	0.014	27.1 (9.3; 16 - 44)	24.3 (8.6; 13 - 40)	0.317	49.4 (22.7; 29 - 88)	70.2 (37.1; 26 - 107)	0.257
Executive function	TMT B, sec	59.6 (21.8; 30 - 105)	64.7 (39.7; 25 - 159)	0.419	54.9 (14.7; 39 - 85)	51.5 (16.4; 29 - 74)	0.258	132.2 (58.1; 74 - 228)	171.5 (119.2; 65 - 329)	0.283
	DSST	77.5 (16.3; 51 - 110)	75.0 (20.4; 38 - 113)	0.163	85.9 (10.6; 70 - 101)	82.2 (13.3; 60 - 104)	0.192	51.2 (13.5; 30 - 63)	42.0 (19.3; 19 - 64)	0.061
	Clock drawing (median points)	3.0 (0.2; 2 - 3)	3.0 (0.4; 2 - 3)	0.317	3.0 (0.3; 2 - 3)	3.0 (0.0; 3 - 3)	0.317	2.0 (0.5; 2 - 3)	3.0 (0.9; 1 - 3)	0.564
Language	Letter fluency	33.3 (10.2; 13 - 50)	33.2 (11.8; 9 - 48)	0.544	33.1 (11.52; 19 - 54)	30.1 (10.8; 13 - 44)	0.175	27.7 (7.7; 19 - 38)	20.8 (11.1; 7 - 34)	0.039
	Category fluency	20.5 (4.1; 14 - 29)	22.2 (4.0; 15 - 31)	0.280	24.1 (5.9; 14 - 32)	24.7 (4.7; 16 - 30)	0.756	15.2 (6.6; 3 - 21)	12.0 (6.0; 2 - 18)	0.087
	BNT	28.7 (1.1; 27 - 30)	28.7 (1.0; 26 - 30)	0.853	28.2 (1.1; 26 - 30)	27.5 (1.8; 23 - 29)	0.209	25.6 (1.8; 23 - 28)	24.0 (4.4; 19 - 29)	0.450
Apathy	Apathy scale of Starkstein	9.0 (3.9; 2 - 14)	7.2 (3.3; 2 - 12)	0.024	7.6 (4.1; 2-17)	5 (2.7; 1 - 11)	0.040	6.5 (3.8; 2-13)	6.0 (2.8; 2 - 10)	0.597
Anxiety	HADS subscale anxiety	3.4 (2.4; 0 - 9)	3.2 (3.9; 0 - 14)	0.787	3.8 (2.7; 0 - 9)	3.2 (2.9; 0 - 9)	0.595	5.2 (3.2; 0 - 8)	4.2 (3.0; 1 - 9)	0.849
Depression	HADS subscale depression	1.5 (1.6; 0 - 5)	1.6 (1.6; 0 - 6)	0.685	0.9 (1.6; 0 - 5)	1.5 (2.6; 0 - 8)	0.546	3.7 (3.3; 0 - 8)	6.4 (3.0; 2 - 9)	0.259

