Silent Brain Infarcts After CEA/CAS Really Matter And Affect Cognitive Changes: The Size And Number of DW MRI Defects Are Critical

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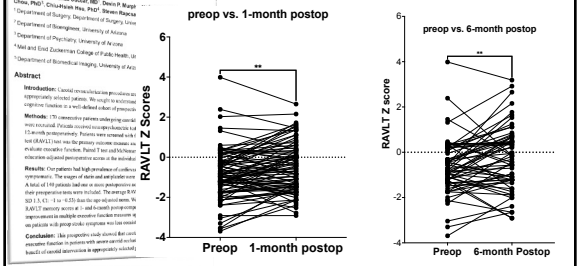
Carotid Intervention and Changes in Executive Function

Carotid Intervention Improves Cognitive Function in Patients with Severe Atherosclerotic Carotid Disease

	n	Preop Mean±SD(SE)	Postop Mean±SD(SE)	P-value	Cohen's d
Preop vs. 1 month postop					
WAISE III-Digit Span	133	10.38±2.76 (9.9-10.85)	10.65±2.72 (10.18-11.11)	*0.077*	0.154
WAISEIII-Letter/Number	104	8.45±3.44(7.78-9.12)	9.09±3.06(8.49-9.68)	***0.016***	0.240
TMT -A	132	7.74±3.09(7.21-8.27)	8.41±3.20(7.86-8.96)	***<0.001***	0.313
TMT- B	126	7.92±3.06(7.38-8.46)	8.54±3.04(8-9.08)	***0.003***	0.273
BNT	120	10.78±2.75(10.28-11.27)	10.28±2.86(9.77-10.80)	***0.001***	0.312
GDS	127	7.51±6.126(6.44-8.58)	6.72±6.13(5.65-7.80)	***0.015***	0.220
Preop vs. 6 months postop					
Digit Span	99	10.54±3.02(9.93-11.14)	11.12±2.81(10.50-11.68)	***0.011***	0.261
Letter/number	83	8.92±3.29(8.20-9.64)	9.59±3.00(8.94-10.25)	***0.028***	0.245
TMT -A	98	8.07±3.33(7.40-8.74)	8.94±3.40(8.26-9.62)	***0.001***	0.341
TMT- B	97	8.12±3.10(7.50-8.75)	8.86±2.90(8.27-9.44)	***0.005***	0.291
BNT	92	10.22±3.14(9.57-10.87)	10.95±3.06(10.31-11.58)	***<0.001***	0.410
GDS	97	7.42±6.20(6.17-8.67)	7.24±6.41(5.94-8.53)	*0.656*	0.045
Preop vs. 12 months postop					
Digit Span	87	10.39±3.26(9.70-10.96)	10.85±2.96(10.22-11.67)	***0.002***	0.345
Letter/number	63	8.52±3.47(7.65-9.40)	9.37±3.66(8.44-10.29)	***0.043***	0.260
TMT -A	81	7.79±3.02(7.12-8.46)	9.07±3.48(8.30-9.85)	***<0.001***	**0.576**
TMT- B	80	7.93±3.06(7.24-8.61)	8.68±3.37(7.92-9.43)	***0.016***	0.276
BNT	78	10.45±2.97(9.78-11.12)	11.26±2.66(10.66-11.86)	***<0.001***	0.436
GDS	82	7.73±5.81(6.45-9.01)	6.84±6.14(5.49-8.19)	*0.087*	0.191

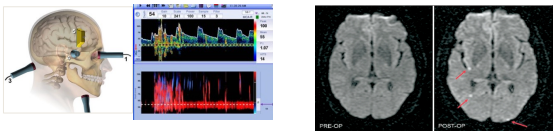
Carotid Intervention and Changes in Episodic Memory



Silent Brain Infarcts

- Subclinical microembolization →SBIs
- Common after carotid intervention
  - 20-70%

Al-Mubarak et al, Circulation 2001
Zhou et al, J of Vascular Surgery, 2012
Hitchner et al, J of Vascular Surgery 2016



J Stroke Cerebrovasc Dis. 2019 Sep;28(9):2376-2387. doi: 10.1016/j.jstrokecerebrovasdis.2019.03.036. Epub 2019 Jul 5.

Association Between Silent Brain Infarcts and Cognitive Function: A Systematic Review and Meta-Analysis.

Lei C[1], Deng Q[1], Li H[1], Zhong L[2].

MMSE

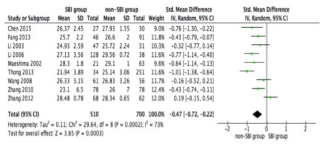


Figure 2. *Meta-analysis of continuous data on the relationship between SBI and Mini-Mental State Examination.*

Montreal Cognitive Assessment scales

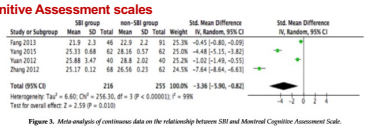


Figure 3. *Meta-analysis of continuous data on the relationship between SBI and Montreal Cognitive Assessment Scale.*

Challenges of Studying SBIs

- **SBIs are heterogenous**
  - Size, number, and location
  - Paucity of Information on size effects
- **Cognitive measures are heterogenous**
  - Various sensitivity
  - Practice effects
  - Timing

Cognitive domains	Neuropsychological tests
Executive function	Stroop Color and Word Test
	Trail-Making Test B (TMT-B)
	Montreal Cognitive Assessment (MOCA)
	Trail Making Test A (TMT-A)
	Working Memory Index (WMI)
	Letter-Number Span (WMS-III)
	Digit Span (WMS-III)
Memory	Rey's Auditory Verbal Learning Test
	The California Verbal Learning test
	Hopkins Verbal Learning Test
	MOCA
	Fuld Object Memory Evaluation
	Wechsler Memory Scale-Revised
Global cognition	Alzheimer Disease Assessment Scale-Cognitive Subtest
	MMSE
Language	Boston Naming Test
	Category Verbal Fluency
Visuospatial function	Rey-Osterrieth Complex Figure Test
	Clock Drawing Test

Experimental Models

Microembolism infarcts lead to delayed changes in affective-like behaviors followed by spatial memory impairment

Behav Brain Res, 2012

Microemboli Composed of Cholesterol Crystals Disrupt the Blood-Brain Barrier and Reduce Cognition

Joseph H. Rapp, MD; Xian Mang Pan, MD; Melanie Neumann, PhD; Michelle Hong, BS; Kelsy Hollenbeck, BS; Jialing Liu, PhD

Stroke, 2008

Atheroemboli to the brain: Size threshold for causing acute neuronal cell death

Joseph H. Rapp, MDa, Xian M. Pan, MDa, Frank R. Sharp, MDb, Dhiraj M. Shah, MDc, Gregory A. Wille, MDd, Pauline M. Velez, MDe, Aaron Troyer, BAa, Randall T. Higashida, MDf, David Saloner, PhDf

JVS, 2000

Experimental animal models: Infarct size correlates to neuronal damage and cognitive outcome

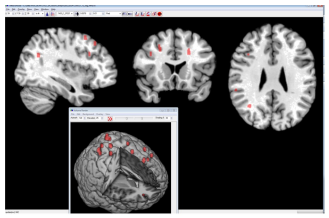
A NIH-sponsored prospective study of peri-procedure subclinical embolization

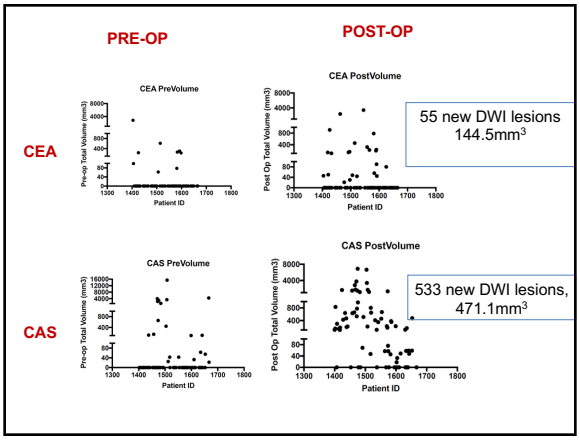
Homogenous population: severe carotid disease undergoing interventions

SBI quantification: DWI lesions that have shown radiographic impacts on MRI

Minimize practice effects: Parallel forms

Avoid anesthetic effects: Cognitive testing at 1, 6 month, and 12 postop





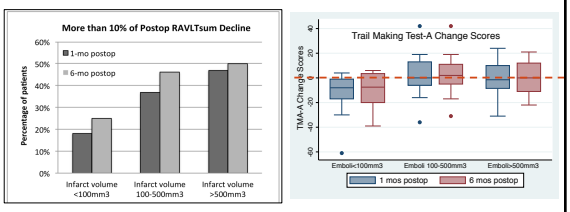
Size Effects in CAS Cohort

Patients Characteristics		<100mm3 N= 18	100-500mm3 N=23	>500mm3 N=19	P values
Age (Mean, years)		69	72	70	0.38
Diabetes		10 (56%)	10 (43%)	10 (53%)	0.82
SBP >140		6 (33%)	12 (52%)	3 (16%)	0.05*
Obesity		6 (33%)	8 (35%)	10 (53%)	0.4
COPD		3 (17%)	3 (13%)	3 (16%)	0.94
Coronary artery disease		9 (50%)	14 (61%)	12 (63%)	0.73
Atrial fibrillation		0 (0%)	2 (1%)	2 (10%)	0.54
Chronic renal insufficiency		4 (22%)	11 (48%)	6 (32%)	0.22
Anti-platelets		8 (44%)	17 (74%)	12 (63%)	0.73
Contralateral occlusion/stenosis		3 (17%)	4 (18%)	5 (26%)	0.78
Pre-op symptoms		32 (46%)	8 (35%)	9 (47%)	0.68
Baseline memory scores	RAVLTsum	32	33	35	0.57
	RAVLT SD	5.1	6.3	6.5	0.13
	RAVLT LD	5.7	6	6.5	0.7

Size Effects in CAS Cohort

>10% Decline in Memory

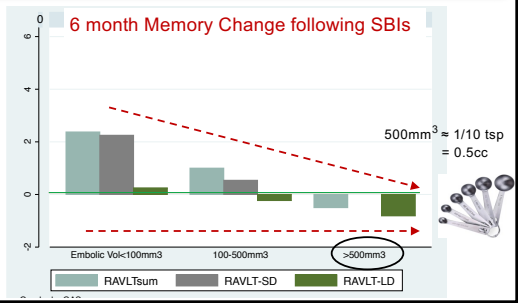
Change in Psychomotor Speed (Timed test)



Volume of subclinical embolic infarct correlates to long-term cognitive changes after carotid revascularization

Wei Zhou, MD,[ab] Brittanie D. Baughman, MS,[a] Salil Soman, MD,[c] Max Wintermark, MD,[d] Laura C. Lazzeroni, PhD,[e] Elizabeth Hitchner, MS,[a] Jyoti Bhat, MS,[f] and Allyson Rosen, PhD,[ef] *Palo Alto and Stanford, Calif; and Cambridge, Mass*

JVS2017



Size Matters

- Silent brain Infarcts after carotid intervention affect cognitive changes
- The size of SBIs significantly influences cognitive outcome short-term and long-term