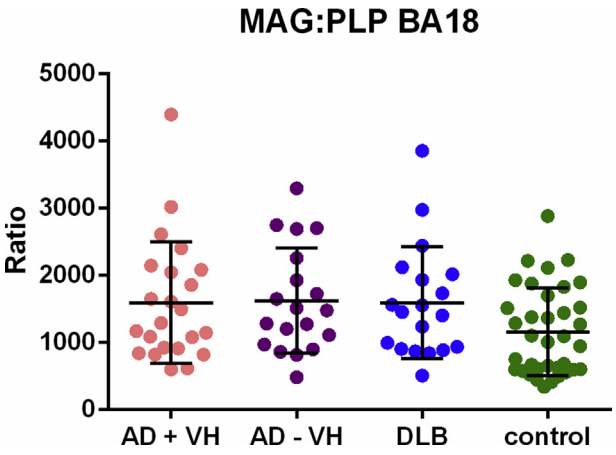
	AD + visual hallucinations		AD without visual hallucinations		dementia with Lewy Bodies		Controls			P with age as covariate
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Statistical evidence	
Age (y)	76.7	9.0	79.3	9.0	81.0	7.0	82.1	6.3	ANOVA p=0.065	
Post mortem interval (h)	36.7	21.1	41.8	16.3	33.3	18.1	36.5	15.5	ANOVA p=0.533	
Age at onset of dementia (y)	66.9	10.4	68.3	9.8	73.0	6.9	N/A	N/A	Kwallis p=0.1518 X2=3.770	
Duration of dementia (y)	9.7	4.2	11.1	3.3	7.6	4.6	N/A	N/A	ANOVA p=0.0357	p=0.0397
Mean Braak stage	5.5	0.5	5.3	0.9	3.1	1.5	2.0	0.8	X2=109.9, p <0.001	
Total CAA (cerebral amyloidosis score)										
0	3		3		9		25		X2=31.37, p=<0.001	
1	7		3		3		3			
2	7		8		2		3			
3	6		5		5		3			
Occipital small vessel disease score										
0	2		2		3		8		X2=8.07, p=0.527	
1	11		6		5		11			
2	6		4		1		6			
3	0		2		1		1			
VEGF concentration BA18 (ng/ml)	0.762	1.071	1.013	0.637	1.009	1.071	0.824	0.889	ANOVA p=0.148	P=0.176
VEGF concentration BA19 (ng/ml)	0.564	0.344	0.869	0.525	0.197	0.513	0.723	0.380	ANOVA p=0.0496	p=0.089
MAG concentration BA18 (ng/ml)	404.9	119.8	417.3	101.8	361.3	127.3	401.4	106.6	ANOVA p=0.450	P=0.482
MAG concentration BA19 (ng/ml)	308.6	87.8	307.6	65.0	283.5	58.3	336.6	89.1	ANOVA p=0.170	P=0.139
MAG:PLP1 ratio BA18	1586.8	904.7	1620.4	784.0	1585.1	835.1	1154.0	649.3	ANOVA=p.0.022	p=0.034
MAG:PLP1 ratio BA19	1233.2	589.8	1038.1	506.8	1089.1	614.0	1309.6	913.4	ANOVA p=0.534	P=0.541
PLP1 concentration BA18 (ng/ml)	0.321	0.182	0.34	0.264	0.313	0.23	0.494	0.329	KWallis p=0.087, X2=6.579	
PLP1 concentration BA19 (ng/ml)	0.302	0.154	0.341	0.125	0.327	0.173	0.329	0.161	ANOVA p=0.796	P=0.785
Von Willebrand Factor concentration BA18 (arbitrary units)	14.472	8.013	14.025	3.859	12.151	4.315	13.229	3.182	ANOVA p=0.550	P=0.514
Von Willebrand Factor concentration BA18 (arbitrary units)	9.682	3.539	10.161	2.997	8.362	3.099	8.298	2.467	ANOVA p=0.092	p=0.051
ChAT activity BA18 (pmol/min/mg)	441.205	295.378	721.512	565.730	627.203	405.569	509.002	298.864	ANOVA p=0.151	p=0.151
ChAT activity BA19 (pmol/min/mg)	764.023	444.436	812.124	644.481	710.934	619.500	750.413	605.677	Kwallis p=0.895, X2=6.06	

endothelial growth factor (VEGF, a marker of tissue hypoxia), myelin-associated glycoprotein:proteolipid protein 1 (MAG:PLP1) ratio (a measure of tissue oxygenation relative to metabolic demand) and α-synuclein were quantified by ELISA, Von Willebrand factor (a marker of endothelial cell content) by dot blot and α-synuclein also by immunohistochemistry, as in our previous studies. Choline acetyl-transferase activity was quantified by chemiluminescence. Routine neuropathological data were also available. Data was analysed using parametric statistical tests wherever possible, with the MAG:PLP ratio as the primary outcome. **Results:** The MAG:PLP ratio was reduced in controls compared to the dementia groups in BA18 (p=0.034) and unchanged in BA19. There was no strong evidence of a between group difference in ChAT activity, VEGF or vWF. **Conclusions:** Our results do not support chronic hypoperfusion of visual processing areas in the occipital cortex as a cause of VH in those with dementia. The ChAT data require further investigation by additionally measuring AChE and BChE.



P3-208 **THE OXYTOCIN RECEPTOR AND VASCULAR COGNITIVE IMPAIRMENT: POTENTIAL AS A NOVEL THERAPEUTIC TARGET**

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Background: Vascular cognitive impairment (VCI), defined as a decline in cognition resulting from stroke or subclinical vascular brain injury, is one of the leading causes of cognitive impairment and dementia worldwide. Currently, beyond rapid-response treatments to resolve the vascular lesion, effective therapies to protect or restore cognitive function are lacking. Motivated by this need, we sought to identify a novel mechanism differentially expressed in cases of VCI compared to incidences of Alzheimer's disease (AD) and no dementia. **Methods:** We used Agilent microarray technology to quantify gene expression in frozen frontal cortex tissue obtained postmortem from University of Michigan AD Center subjects who died with VCI (of the multi-infarct subtype), moderate AD, or without dementia. qPCR and western blotting were used to validate microarray results. Immunohistochemistry was also performed using paraffin embedded frontal cortex tissue from the same cases. **Results:** We identified a previously unreported upregulation of the oxytocin receptor (OXTR) in the frontal cortex of VCI subjects compared to AD and no dementia controls (log fold change = 1.86, FDR adjusted $p < 0.04$). OXTR upregulation in VCI was confirmed via qPCR (one-way ANOVA [F=3.886, p=0.0329]) and western blotting (Kruskal-Wallis [$\chi 2$=7.07, p=0.0292]). Immunohistochemical analysis revealed widespread OXTR expression in frontal cortex, with notable co-localization of the receptor with tomato lectin, a vascular endothelial cell marker. **Conclusions:** Given the established role of oxytocin in anti-inflammatory, antioxidant, and angiogenic signaling, we posit that OXTR upregulation in VCI is indicative of a vascular localized compensatory response that could be harnessed therapeutically to ameliorate the pathologic aspects of ischemic or hemorrhagic injury, promote cell survival, and improve cognitive outcomes. We are testing this hypothesis mechanistically in a novel rodent model of VCI and in vascular cell cultures subjected to hypoxia.

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COGNITIVE IMPAIRMENT IS ASSOCIATED WITH PREMATURE ARTERIAL STIFFENING, AORTIC WALL FIBROSIS AND INCREASED BLOOD PRESSURE: A NOVEL RAT MODEL OF AGE-DEPENDENT VASCULAR DEMENTIA

Olga V. Fedorova, Yulia Grigorova, Madeleine Hagood, Jeffrey Long, Ross McDevitt, Rebecca McPherson, Akshay Naraine, Ondrej Juhasz, Wen Wei, Valentina Zernetkina, Nataliya Petrashevskaya, Kenneth W. Fishbein, Richard G. Spencer, Peter R. Rapp, Edward G. Lakatta, *National Institute on Aging/National Institutes of Health (NIA/NIH), Baltimore, MD, USA. Contact e-mail: FedorovO@grc.nia.nih.gov*

Background: An age-associated central arterial wall stiffening and increased blood pressure (BP) have been linked to cognitive impairment in human epidemiologic studies. A premature increase in BP and aortic stiffening occur in Dahl salt-sensitive rats (Dahl-S) on a normal salt intake. Because a novel pro-hypertensive and pro-fibrotic steroid marinobufagenin (MBG) is implicated in BP increases in Dahl-S, we hypothesized that associated with MBG BP increase and the arterial wall stiffening in aged Dahl-S will lead to a cognitive decline. **Methods:** Male Sprague-Dawley rats (S-D; normotensive control) and Dahl-S were maintained on a normal diet (n=8-14/group). Systolic BP (SBP), aortic pulse wave velocity (aPWV; an index of aortic wall stiffening), urine MBG, collagen

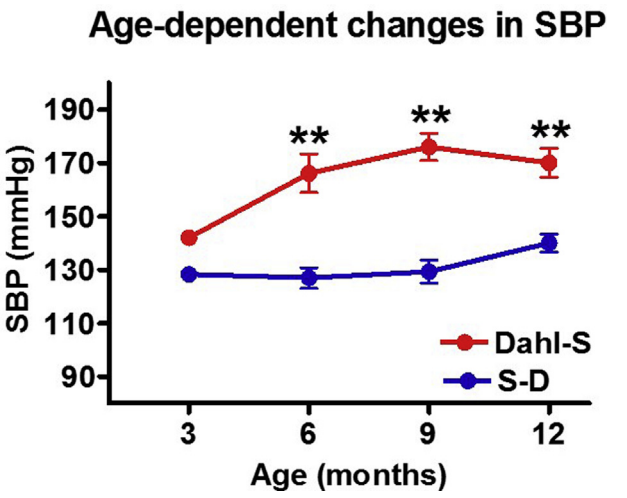

Figure 1. Systolic blood pressure (SBP) changes in Sprague-Dawley rats (S-D) and Dahl-S rats

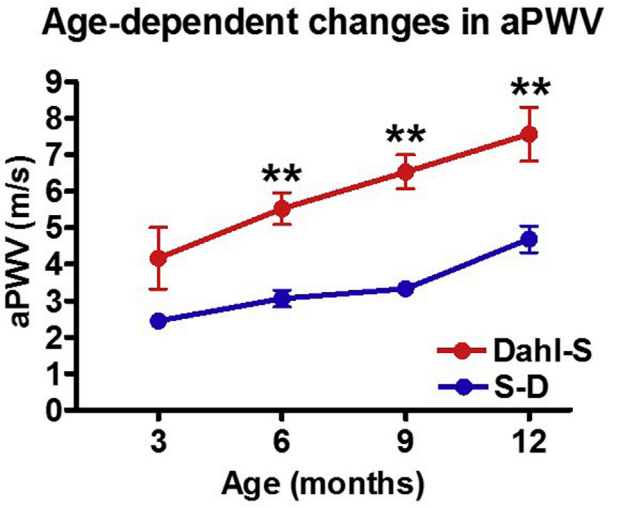

Figure 2. Aortic pulse wave velocity (aPWV) changes in Sprague-Dawley rats (S-D) and Dahl-S rats

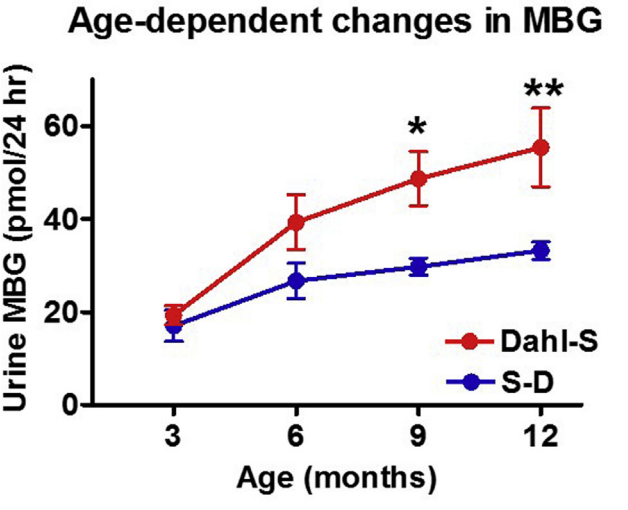

Figure 3. Marinobufagenin (MBG) changes in Sprague-Dawley rats (S-D) and Dahl-S rats