Inverse Relationship of Internal Jugular Vein Narrowing and Increased Brain Volumes is Mitigated by Age in Healthy Individuals

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Target Audience: Vascular researchers and clinicans. Also researchers interested in the process of aging.

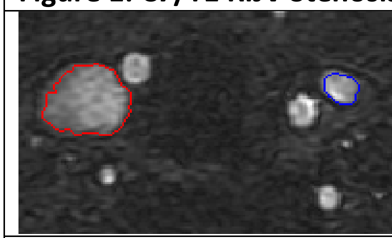
Background & Purpose / Hypothesis: Stenosis, or extracranial venous system narrowing, has been implicated in the pathology of many central nervous system diseases including multiple sclerosis.[1] Consequently, there is a need to: 1) identify, locate, and quantify typical and atypical internal jugular vein (IJV) diameters, 2) assess the prevalence of narrowing in healthy controls (HC) prior to any comparison with disease groups, and 3) determine the effect of narrowing location on brain volumes. We predicted that increased presence and severity of narrowing would correlate with worsened atrophy measures (reduced brain volumes).

Table 1: Demographic Information

Sex (M/F)	Total (N=131)	Male (N=43)	Female (N=88)	P-Value
Mean Age (SD)	42.2 (16.4)	38.1 (18.0)	44.1 (15.3)	.23
Pulmonary Disease	10	2	8	.50
Heart Disease	14	4	10	.94
Hypertension	19	6	13	.77
Smoking	41	9	32	.28
BMI (kg/m^2)	26.3 (5.5)	26.0 (4.6)	26.4 (5.87)	.41
Stenosis Present[1]	81	24	57	.32

Methods: 131 healthy individuals received 2-Dimensional Magnetic Resonance Venography (2D MRV) and structural MRI via an Inversion-Recovery Fast Spoiled Gradient Echo (IR-FSPGR) sequence at 3T. Java Image Manipulation Tool (JIM) version 5.0 was used for region of interest (ROI) analysis of the IJVs at C2/C3, C4, C5/C6, and C7/T1 and collateral veins at C2/C3 on the 2D MRV. The ROI was calculated on the slice in the given location with the smallest cross-sectional area (CSA). Brain volume measures were calculated using Structural Image Evaluation using Normalization of Atrophy (SIENAX) cross-sectional method.[2] Narrowing was defined as an IJV CSA less than 25 mm^2 at the levels of T1-C4, or less than 12.5 mm^2 at C2-C3, in line with previously published criteria[1]. Chi square analyses were performed for testing demographic differences and correlation analyses for association between CSA and brain volumes.

Figure 1: C7/T1 RIJV Stenosis



The LIJV (red) is of expected size, whereas the RIJV (blue) is significantly smaller.

Results: Basic cardiovascular risk factors are presented in Table 1. Narrowing was found across 82 individuals with 65 (48.5%) in the LIJV and 75 (56.3%) in the RIJV. Reduced CSA and larger grey matter and whole brain volumes strongly correlated when accounting for sex and cardiovascular risk factors as shown in Table 2. White matter volumes did not strongly correlate. Lower cervical locations (C7/T1) showed the strongest correlations, whereas higher (C2/C3) were weaker.

Discussion & Conclusions: Unexpectedly, the relationship between brain volumes and CSA was found to be opposite to our hypothesis, as the more the IJVs narrowed, the larger the brain volumes; this could be potentially indicative of edema, venous stasis or swelling of the brain parenchyma. These findings were not significant after adjusting for age differences, suggesting that the relationship between IJV CSA narrowing and brain volumes is mediated by age. A similar effect was found to a lesser extent in collateral vessels at the C2/C3 level. To our knowledge this is the largest assessment of narrowing in HC by MRV, and suggests that venous narrowing is common in healthy individuals (prevalence >45%). Further longitudinal studies are warranted to examine the temporal evolution of IJVs narrowing and changes of the brain volumes.

Table 2: IJV Cross Sectional Area Correlations with Brain Volumes

	C7/T1	C5/C6	C4	C2/C3	Collaterals
NGMV without Age	**-.300 (.004)**	**-.286 (.008)**	*-.256 (.01)*	*-.277 (.01)*	*-.278 (.01)*
NGMV with Age	-.101 (.56)	-.032 (.85)	-.074 (.66)	-.131 (.48)	-.250 (.19)
NWMV without Age	*-.203 (.04)*	-.094 (.37)	.007 (.95)	.023 (.83)	-.106 (.34)
NWMV with Age	-.130 (.19)	-.012 (.91)	.082 (.43)	.048 (.66)	-.048 (.67)
NWBV without Age	**-.314 (.003)**	*-.243 (.02)*	-.167 (.12)	-.198 (.07)	*-.247 (.02)*
NWBV with Age	-.169 (.22)	-.025 (.86)	.046 (.74)	-.009 (.95)	-.156 (.31)

NGMV=Normalized Grey Matter Volume; NWMV=Normalized White Matter Volume; NWBV=Normalized Whole Brain Volume. All correlations are corrected for sex pulmonary disease, heart disease, hypertension, smoking, and BMI; age is excluded as a covariate for "without Age" correlations, but including age as a covariate for "with Age" correlations. P-values less than 0.01 were considered significant, and are in bold. P-values less than 0.05 were considered trends, and are italicized.

References: [1] Haacke, E.M., et al., Patients with multiple sclerosis with structural venous abnormalities on MR imaging exhibit an abnormal flow distribution of the internal jugular veins. J Vasc Interv Radiol, 2012. 23(1): p. 60-8 e1-3. [2] Zivadinov, R., et al., *Preservation of gray matter volume in multiple sclerosis patients with the Met allele of the rs6265 (Val66Met) SNP of brain-derived neurotrophic factor.* Human molecular genetics, 2007. **16**(22): p. 2659-68