The Effect of Sex-Differences on the Relationship Between White Matter Hyperintensity, Cerebrovascular Reactivity, and Fluid Biomarkers

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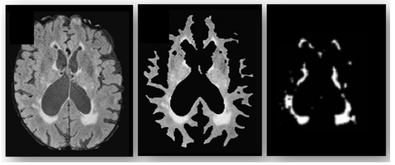
INTRODUCTION

Alzheimer's disease (AD), vascular cognitive impairment, and dementia (VCID) are the dominant types of dementia in older adults, associated with memory loss and cognitive deficits. White matter hyperintensities (WMH) are linked to both AD and VCID. Astrocytes play a crucial role in WM integrity, encompassing functions like neuroinflammation, oxidative stress, and Aβ clearance. Poorly reactive astrocytes could lead to implications, like WMH or vascular damage. This study aims to explore the sex-differences effect on the correlation between fluid biomarkers, WMH, and cerebrovascular reactivity(CVR).

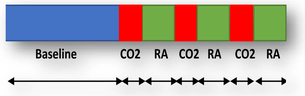
METHODS



White Matter Hyperintensity segmentation

METHODS

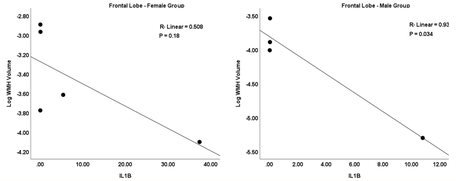
Twenty-seven participants (mean age 76.8±6.4 years, Female=15) preliminary data were collected from UK-ADRC/MarkVCID cohorts. A correlation test was employed to examine sex differences based on the correlation of fluid inflammatory (GFAP, IL6, IL8, IL10), angiogenic (TDP-43, and PIGF)biomarkers, and Aβ40 and 42, to global and regional CVR and WMH.



Cerebrovascular Reactivity (CVR)

RESULTS

We observed several sex differences: the female group showed a significant correlation between WMH at the occipital lobe and IL6, IL10, and GFAP (P-values, 0.031, 0.036, and 0.037, respectively), while the male group only showed a significant correlation between Aβ42 and WMH at the occipital lobe (P-value = 0.039).



RESULTS

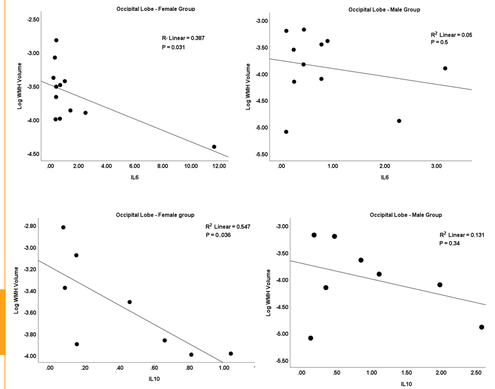


Table 1 shows CVR in the female group exhibited a strong correlation at the rt-side parietal lobe and IL8 and Aβ40, and between Aβ40 and CVR at the Rt-side temporal lobe. The male group showed a significant correlation between IL6 and CVR at the occipital lobe and a critical correlation between PIGF and WMH at the occipital lobe. Generally, the female group shows higher mean values for all biofluids except for IL10 and PIGF, but only significant at GFAP and TDP43. However, adjusted for age and sex showed that TDP-43 significantly correlated with WMH volumes in the temporal (P=0.04), occipital (P=0.02), and parietal lobes (P=0.02). GFAP displayed a significant correlation only with WMH volume in the frontal lobe (P=0.01).

RESULTs (CON.)

CVR: Female	AB40	AB42	F_IL6	F_IL8	F_IL10	F_PIGF	F_GFAP
WholeBrain	0.06	0.07	0.77	0.16	0.62	0.68	0.96
Frontal-L	0.18	0.19	0.99	0.13	0.43	0.11	0.52
Frontal-R	0.059	0.17	0.89	0.085	0.41	0.43	0.9
Parietal-L	0.077	0.32	0.71	0.21	0.7	0.27	0.68
Parietal-R	**0.038**	0.084	0.66	**0.037**	0.50	0.30	0.98
Temporal-L	0.075	0.054	0.52	0.11	0.43	0.82	0.92
Temporal-R	**0.021**	0.054	1.00	0.13	0.38	0.64	0.47
Occipital-L	0.066	0.133	0.47	0.12	0.83	0.68	0.94
Occipital-R	0.073	0.116	0.97	0.10	0.89	0.58	0.99
CVR: Male							
WholeBrain	0.28	0.31	0.12	0.92	0.21	0.11	0.86
Frontal-L	0.32	0.33	0.17	0.92	0.35	0.16	0.93
Frontal-R	0.39	0.41	0.2	0.97	0.42	0.22	0.87
Parietal-L	0.75	0.8	0.45	0.57	0.68	0.48	0.8
Parietal-R	0.4	0.39	0.14	0.98	0.46	0.25	0.4
Temporal-L	0.21	0.21	0.14	0.92	0.33	0.09	0.59
Temporal-R	0.24	0.24	0.31	0.77	0.56	0.12	0.84
Occipital-L	0.31	0.31	**0.012**	0.84	0.09	0.13	0.70.6
Occipital-R	0.2	0.2	0.1	0.53	0.24	**0.049**	0.97

CONCLUSIONS

Despite the small sample size, which warrants expansion in future studies, we observed interesting findings of sex differences in specific brain regions in relation to fluid biomarkers. These biomarkers may arise, in part, from reactive astrocytes, commonly found near many brain lesions, including WM pathology. Further studies are needed to gain deeper insight into astrocyte activities in diseases associated with WMH and CVR, like AD.

REFERENCES

Bahrani AA, Smith CD, Barber JM, et al. Development of a protocol to assess within-subject, regional white matter hyperintensity changes in aging and dementia. J Neurosci Methods 2021;360:109270.

Liu P, JB De Vis, Lu H. Cerebrovascular reactivity (CVR) MRI with CO2 challenge: A technical review. Neuroimage. 2019;187:104-115.

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