

Hematocrit explains variability in Arterial Spin Labeling MRI-derived cerebral blood flow across sexes and cohorts



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Background

Arterial spin labeling (ASL)-MRI is a non-invasive method for assessing cerebral blood flow (CBF) and has been instrumental in demonstrating reduced perfusion and cognitive function in cerebrovascular studies of Alzheimer's Disease (AD).

Hematocrit is the proportion of blood containing red blood cells and is an important methodological confounder in ASL-MRI measurements. This makes hematocrit critical when applying ASL-MRI to groups with known hematocrit differences, such as anemic vs. non-anemic, men vs. women, and pre vs. post-menopausal women.

Objective

To assess the effect of hematocrit on CBF and relation between sex and CBF on ASL-MRI in one local cohort and another from Alzheimer's Disease Neuroimaging Initiative (ADNI).

Methods

- **Participants:** Local: n=403, ADNI: n=119
- **Imaging:**
 - Cortical CBF quantified using ASL-MRI.
 - Sex differences assessed with t-test.
 - Multiple regression models assessed age, sex, and hematocrit as predictors of CBF.

Results

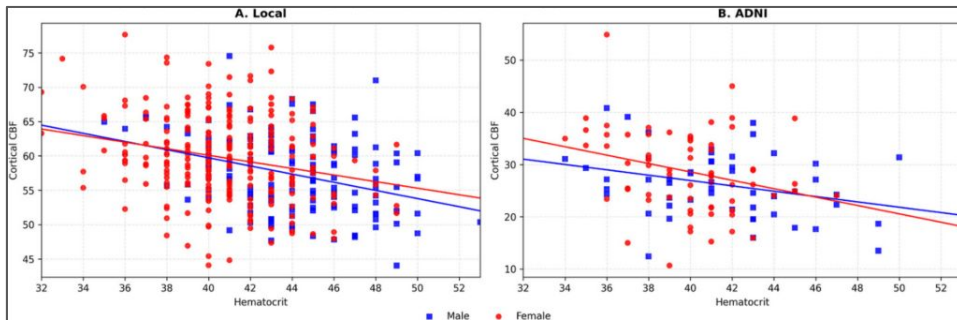


Figure 1: Inverse correlation between hematocrit and cortical cerebral blood flow using two different ASL-MRI methods in men and women.

A. LOCAL		Men (n=151)	Women (n=252)	P-value for sex difference
	Mean age in years (sd); [range]	69.9 (6.39); [52.0, 84.0]	68.2 (7.44); [50.0, 91.0]	0.015
	Mean hematocrit (sd); [range]	44.0 (3.24); [35.0, 53.0]	40.8 (3.02); [32.0, 49.0]	<0.001
	Mean relative cortical CBF ml/100g/minute (sd); [range]	57.4 (5.46); [44.0, 74.6]	59.7 (6.07); [44.1, 77.7]	<0.001
B. ADNI		Men (n=52)	Women (n=67)	P-value for sex difference
	Mean age in years (sd); [range]	71.8 (7.26); [56.0, 85.0]	71.7 (6.42); [58.0, 84.0]	0.938
	Mean hematocrit (sd); [range]	41.5 (3.74); [34.0, 50.0]	39.8 (2.72); [34.0, 47.0]	0.008
	Mean cortical CBF in ml/100g/minute (sd); [range]	26.2 (6.25); [12.4, 40.8]	28.7 (7.88); [10.7, 54.9]	0.052

Table 1: Participant Characteristics.

Without adjusting for Hct, women appeared to have higher cortical CBF in both datasets and was the only significant predictor in multiple regression in the local dataset ($\beta=0.186$) and trending in ADNI ($\beta=0.175$). However, once added, Hct became the strongest and only predictor of CBF (local: $\beta=-0.306$, ADNI: $\beta=-0.275$), with sex no longer significant. Hematocrit reduced AIC by 30.62 (local) and 7.27 (ADNI), explaining substantial variance in CBF.

Conclusion

Hematocrit significantly affects ASL-MRI-measured CBF calculations through blood T1 and physiological (rheology and vasodilation) effects and must be considered when comparing groups with differing hematocrit.

Implications

This project is relevant especially to studies of age and menopause, which is associated with increased hematocrit due to cessation of menstruation. Since female sex and postmenopausal status are AD risk factors, accounting for hematocrit is essential when using ASL-MRI to investigate how both influence brain perfusion, function and vulnerability to AD.

Limitations

Key limitations include a restricted age range (>50, local, >55, ADNI) and lack of menopause information.

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