Comparison of IVIM MRI measures of brain fluid transport against contrast-enhanced MRI in the setting of sleep deprivation

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[1]Swati Rane, [2]Carla Vanderweerd, [2]Mitchell Roberts, [3]Tarandeep Singh, [3]Alejandro Corbellini, [1]Cole Anderson, [4]Juan Piantino, [4]Miranda M. Lim, [3]Paul Dagum, [3]Jeffrey Iliff
[1]University of Washington , [2]University of Florida, [3]Applied Cognition, [4]Oregon Health& Science University

MAIN FINDINGS

- Contrast MRI and non-contrast MRI markers of the glymphatic system measure different aspects of solute and fluid transport. Hence, they are not strongly correlated with each other.
- Both contrast and non-contrast MRI markers of glymphatic function are associated with sleep physiology

MOTIVATION

The glymphatic system supports the perivascular exchange of cerebrospinal fluid (CSF) and brain interstitial fluid (ISF) during sleep, facilitating the clearance of solutes including amyloid beta, tau and alpha synuclein. The current gold-standard to assess solute transport is to measure MRI signal enhancement following intrathecally and intravenously administered Gadolinium-based contrast agent (GBCA).

Gadolinium contrast-based MRI has limited utility due to its invasive nature, semi-quantitative measurements, long waits between scans, inapplicability across all individuals and diseases due to safety concerns. Non-invasive, quantitative approaches are yet to be devised for studying the glymphatic system.

In an attempt to address this scientific gap, we present intravoxel incoherent motion (IVIM) diffusion to study slow CSF movement in the subarachnoid space. We compared IVIM measures to late contrast enhancement after an IV Injection of Gadolinium and tested both measures for association with sleep parameters.

SLEEP STUDY SETUP

Demographics: 15 cognitively normal participants (ages = 60±5 yrs. old, 7M/8F)

Experiment: Participants were scanned under 2 conditions: night of normal sleep and a night of sleep deprivation at University of Florida/Lakeview Medical Imaging. Evening and morning scans were performed at 1900 and 0700 hrs. respectively for each condition.

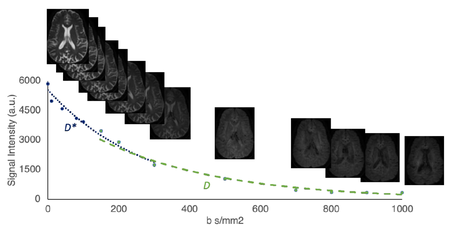
AD measurements: Plasma amyloid levels ($A\beta_{42}$/ $A\beta_{40}$) and presence of E4 allele was assessed

Sleep measurements: Sleep architecture was measured using an investigational medical device developed by Applied Cognition. Sleep stages N1, N2, N3, REM, slow wave (SW) durations, spindle durations and number were recorded. Sleep quality measures were derived from this data.

Due to the high intercorrelatedness between all the measures sleep measure, only those parameters where correlations <0.7 were selected.

Cognitive measurements: UDS 3.0 battery, and sleep-sensitive psychomotor vigilance test (PVT).

Imaging: IVIM: The diffusion weighted IVIM protocol used 12 b-values (10 - 1000 s/mm^2), 6 directions and one b=0 s/mm^2, resolution = 1x1x5 mm^3, slices = 30 , TR/TE = 3000/62 ms. The IVIM MRI was processed to calculate fluid fraction, *f*, diffusion coefficient, *D,* and pseudo-diffusion coefficient, *D**, as a measure of slow diffusion occurring over long distances in the SAS.



IV contrast enhancement: Contrast was only administered n the morning at both visits. A standard 3 T1 MRI was acquired before and 4-hours after Gadolinium injection. To assess glymphatic transport of Gd we used (1) ratio of the contrast signal in the sinuses (sink) to that in carotid arteries (source) as a measure of GBCA clearance through the brain, (2) delayed enhancement in the hippocampus (HFe) as a AD-vulnerable region and the earliest entry point for intrathecally administered GBCA, and (3) delayed enhancement in the SAS.

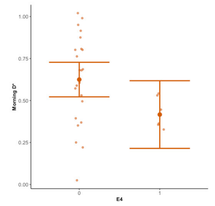
Analysis: We performed the following analyses:

1. A correlation analyses to test relation between contrast MRI and IVIM measures
2. A linear regression analyses to test association of all MRI measures with AD markers, sleep measurements, and cognitive measurements after adjusting for demographic variables.

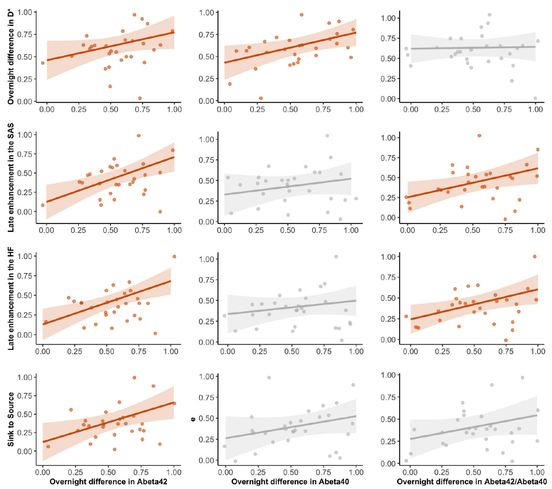
RESULTS

No association was detected between contrast and. non-contrast MRI measures

AD measurements: Only morning *D** was significantly different in E4 carriers compared to non-carriers..



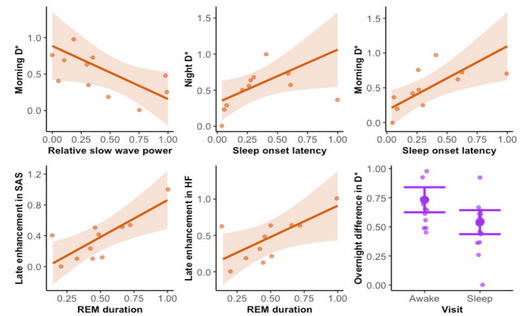
Multiple associations were detected between all the MRI measures and plasma amyloid levels ($A\beta_{42}$/ $A\beta_{40}$)



No association detected between contrast or. non-contrast MRI measures with PVT

Association with overnight sleep condition: Only overnight differences in *D** were different based on whether the participants underwent a night of normal sleep or a night of sleep deprivation. The reduction in *D** in the morning after a night of sleep deprivation was greater than that observed after a night of normal sleep

Association with sleep architecture and objective measures of sleep: As with plasma amyloid levels, multiple association were detected between all the MRI measures and various sleep metrics.



CONCLUSIONS

- Contrast MRI and non-contrast MRI markers measure different aspects of solute transport. Contrast MRI measures GBCA transport and is most similar to the solute exchange facilitated by the glymphatic system. The non-contrast MRI measures focus on CSF movement or fluid movement in the SAS.
- Higher amyloid (especially $A\beta_{40}$) levels in the plasma were associated with lower *D** in the morning compared to night, greater enhancement in the SAS and hippocampus, and greater enhancement in the venous system compared to the arterial inputs.
- Higher overnight REM duration was associated with greater enhancement in the SAS and hippocampus.
- Greater overnight slow wave power is associated with lower lower *D**.
- Longer sleep onset latency was associated with both higher night and morning measures of *D**.
- Reduction in *D** in the morning after a night of sleep deprivation was greater than that after a night of normal sleep.

CONTACT INFORMATION

Paul Dagum, MD PhD
CEO and Co-founder, Applied Cognition
1629 Main Street, Redwood City, CA 94063
[redacted]