Neuroimaging Of Circuit-Specific Protein Synthesis In Human Subjects During Sleep-Dependent Memory Consolidation

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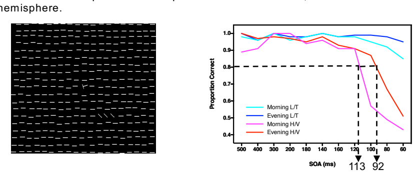
1) Introduction

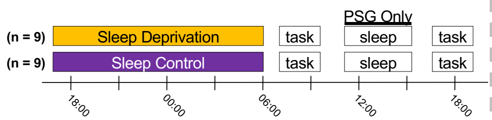
The notion that memory consolidation depends on protein synthesis is based on demonstrations that protein synthesis inhibitors prevent consolidation. We sought to demonstrate directly that protein synthesis is affected during sleep-dependent memory consolidation. We used L-[1-^{11}C]leucine positron emission tomography (PET) to measure circuit-specific rates of cerebral protein synthesis (rCPS) during a daytime nap opportunity with simultaneous polysomnography (PSG).

2) Texture Discrimination Task

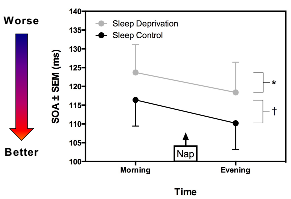
Subjects completed the texture discrimination task before and after the nap opportunity. The retinotopic specificity of this task allows the local state to vary. The trained hemisphere was compared to the contralateral, untrained hemisphere.



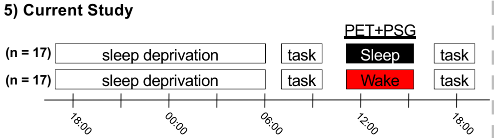
3) Behavior-Only Pilot Study (McWhirter, 2015)



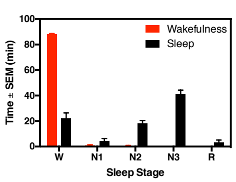
4) No Effect of Sleep Deprivation on Encoding



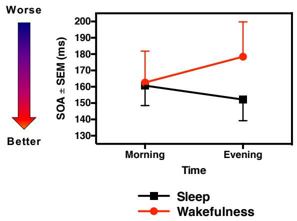
5) Current Study



6) Sleep Results



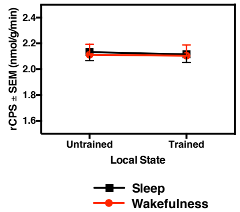
7) Memory



2 (Ss/Condition) × 2 (Time) mixed-model two-way analysis of variance. Condition (wakefulness, sleep) was the between-subjects variable and time (morning, evening) was the within-subjects variable.

Condition:
$F(1,31) = 0.36$, $p = 0.55$, $f^2 = 0.01$ (small)
Time:
$F(1,31) = 0.41$, $p = 0.53$, $f^2 = 0.01$ (small)
Condition x Time:
$F(1,31) = 4.55$, $p = 0.04$, $f^2 = 0.15$ (medium)

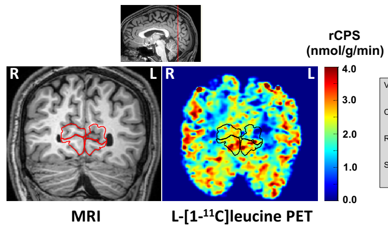
8) Protein Synthesis: Primary Visual Cortex



2 (Ss/Condition) × 2 (Local State) mixed-model two-way analysis of variance. Condition (wakefulness, sleep) was the between-subjects variable and local state (untrained, trained) was the within-subjects variable.

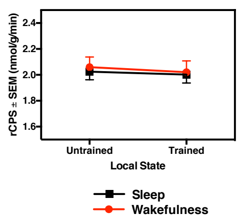
Condition:
$F(1,32) = 0.02$, $p = 0.88$, $f^2 = 0.0007$ (small)
Local State:
$F(1,32) = 0.47$, $p = 0.50$, $f^2 = 0.0100$ (small)
Condition x Local State:
$F(1,32) = 0.07$, $p = 0.79$, $f^2 = 0.0020$ (small)

9) Protein Synthesis: Primary Visual Cortex (n = 1)



Visual field trained:
Left
Change in threshold SOA:
41.8 ms
REM during 90-min scan:
4.0 min
SWS during 90-min scan:
40.0 min

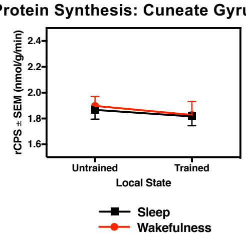
10) Protein Synthesis: Cuneate Gyrus



2 (Ss/Condition) × 2 (Local State) mixed-model two-way analysis of variance. Condition (wakefulness, sleep) was the between-subjects variable and local state (untrained, trained) was the within-subjects variable.

Condition:
$F(1,32) = 0.07$, $p = 0.79$, $f^2 = 0.002$ (small)
Local State:
$F(1,32) = 1.25$, $p = 0.27$, $f^2 = 0.040$ (medium)
Condition x Local State:
$F(1,32) = 0.09$, $p = 0.76$, $f^2 = 0.003$ (small)

11) Protein Synthesis: Cuneate Gyrus (Most-Anterior Third)



2 (Ss/Condition) × 2 (Local State) mixed-model two-way analysis of variance. Condition (wakefulness, sleep) was the between-subjects variable and local state (untrained, trained) was the within-subjects variable.

Condition:
$F(1,32) = 0.04$, $p = 0.84$, $f^2 = 0.001$ (small)
Local State:
$F(1,32) = 1.61$, $p = 0.21$, $f^2 = 0.050$ (medium)
Condition x Local State:
$F(1,32) = 0.04$, $p = 0.84$, $f^2 = 0.001$ (small)

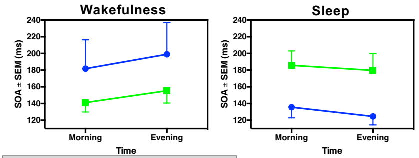
12) Discussion (Planned Analyses)

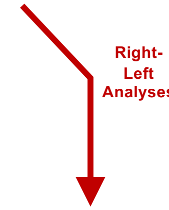
This may indicate that sleep-dependent memory consolidation depends on processes other than protein synthesis such as synaptic renormalization.

It may also indicate that our assumption that the protein synthesis response would take place in the same locale as the known sensory response is not correct. Also, we assume that it is the visual response that is being trained, but it may be selective visual attention, which would have a neural substrate outside the primary visual cortex.

The remaining analyses are exploratory analyses, and thus must be viewed with caution.

13) Memory

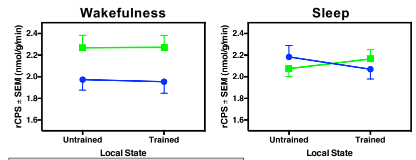




Condition (C) x Time (T) x Visual Field Trained (V)	
C:	$F(1,29) = 0.322$, $p = 0.575$, $f^2 = 0.0111$ (small)
T:	$F(1,29) = 0.371$, $p = 0.547$, $f^2 = 0.0128$ (small)
V:	$F(1,29) = 0.054$, $p = 0.818$, $f^2 = 0.0019$ (small)
C x T:	**$F(1,29) = 4.232$, $p = 0.049$, $f^2 = 0.1459$ (medium)**
C x V:	**$F(1,29) = 4.357$, $p = 0.046$, $f^2 = 0.1502$ (medium)**
T x V:	$F(1,29) = 0.007$, $p = 0.936$, $f^2 = 0.0002$ (small)
C x T x V:	$F(1,29) = 0.121$, $p = 0.731$, $f^2 = 0.0042$ (small)

Visual Field Trained
Right
Left

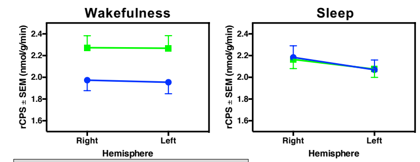
14a) Protein Synthesis: Primary Visual Cortex



Condition (C) x Local State (L) x Visual Field Trained (V)	
C:	$F(1,30) = 0.004$, $p = 0.950$, $f^2 = 0.0001$ (small)
L:	$F(1,30) = 0.440$, $p = 0.510$, $f^2 = 0.0147$ (small)
V:	$F(1,30) = 2.314$, $p = 0.139$, $f^2 = 0.0771$ (medium)
C x L:	$F(1,30) = 0.030$, $p = 0.860$, $f^2 = 0.0010$ (small)
C x V:	$F(1,30) = 2.509$, $p = 0.124$, $f^2 = 0.0836$ (medium)
L x V:	**$F(1,30) = 14.90$, $p = 0.001$, $f^2 = 0.4966$ (large)**
C x L x V:	**$F(1,30) = 9.079$, $p = 0.005$, $f^2 = 0.3026$ (medium)**

Visual Field Trained
Right
Left

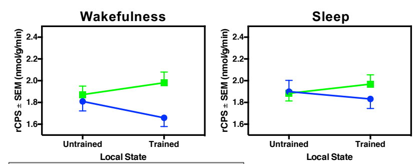
14b) Protein Synthesis: Primary Visual Cortex



Condition (C) x Hemisphere (H) x Visual Field Trained (V)	
C:	$F(1,30) = 0.004$, $p = 0.950$, $f^2 = 0.0001$ (small)
H:	**$F(1,30) = 14.90$, $p = 0.001$, $f^2 = 0.4966$ (large)**
V:	$F(1,30) = 2.314$, $p = 0.139$, $f^2 = 0.0771$ (medium)
C x H:	**$F(1,30) = 9.079$, $p = 0.005$, $f^2 = 0.3026$ (medium)**
C x V:	$F(1,30) = 2.509$, $p = 0.124$, $f^2 = 0.0836$ (medium)
H x V:	$F(1,30) = 0.441$, $p = 0.512$, $f^2 = 0.0147$ (small)
C x H x V:	$F(1,30) = 0.030$, $p = 0.863$, $f^2 = 0.0010$ (small)

Visual Field Trained
Right
Left

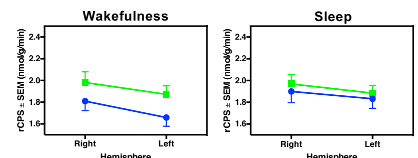
15a) Protein Synthesis: Parietal Cortex



Condition (C) x Local State (L) x Visual Field Trained (V)	
C:	$F(1,30) = 0.59$, $p = 0.449$, $f^2 = 0.020$ (small)
L:	$F(1,30) = 0.09$, $p = 0.763$, $f^2 = 0.003$ (small)
V:	$F(1,30) = 2.19$, $p = 0.149$, $f^2 = 0.073$ (medium)
C x L:	$F(1,30) = 0.59$, $p = 0.450$, $f^2 = 0.020$ (small)
C x V:	$F(1,30) = 0.59$, $p = 0.448$, $f^2 = 0.020$ (small)
L x V:	**$F(1,30) = 29.5$, $p < 0.001$, $f^2 = 0.983$ (large)**
C x L x V:	$F(1,30) = 2.01$, $p = 0.167$, $f^2 = 0.067$ (medium)

Visual Field Trained
Right
Left

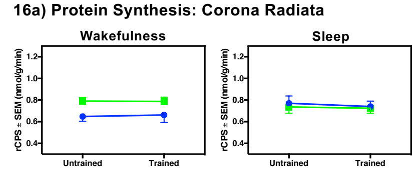
15b) Protein Synthesis: Parietal Cortex



Condition (C) x Hemisphere (H) x Visual Field Trained (V)	
C:	$F(1,30) = 0.59$, $p = 0.449$, $f^2 = 0.020$ (small)
H:	**$F(1,30) = 29.5$, $p < 0.001$, $f^2 = 0.983$ (large)**
V:	$F(1,30) = 2.19$, $p = 0.149$, $f^2 = 0.073$ (medium)
C x H:	$F(1,30) = 2.01$, $p = 0.167$, $f^2 = 0.067$ (medium)
C x V:	$F(1,30) = 0.59$, $p = 0.448$, $f^2 = 0.020$ (small)
H x V:	$F(1,30) = 0.09$, $p = 0.763$, $f^2 = 0.003$ (small)
C x H x V:	$F(1,30) = 0.59$, $p = 0.450$, $f^2 = 0.020$ (small)

Visual Field Trained
Right
Left

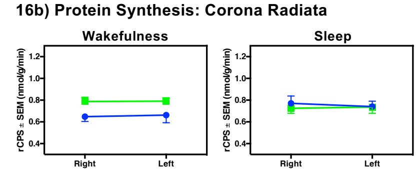
16a) Protein Synthesis: Corona Radiata



Condition (C) x Local State (L) x Visual Field Trained (V)	
C:	$F(1,30) = 0.183$, $p = 0.67$, $f^2 = 0.00609$ (small)
L:	$F(1,30) = 0.152$, $p = 0.70$, $f^2 = 0.00506$ (small)
V:	$F(1,30) = 1.203$, $p = 0.28$, $f^2 = 0.04009$ (medium)
C x L:	$F(1,30) = 0.414$, $p = 0.53$, $f^2 = 0.01380$ (small)
C x V:	$F(1,30) = 2.585$, $p = 0.12$, $f^2 = 0.08617$ (medium)
L x V:	$F(1,30) = 0.001$, $p = 0.98$, $f^2 = 0.00002$ (small)
C x L x V:	$F(1,30) = 0.191$, $p = 0.67$, $f^2 = 0.00636$ (small)

Visual Field Trained
Right
Left

16b) Protein Synthesis: Corona Radiata



Condition (C) x Hemisphere (H) x Visual Field Trained (V)	
C:	$F(1,30) = 0.183$, $p = 0.67$, $f^2 = 0.00609$ (small)
H:	$F(1,30) = 0.001$, $p = 0.98$, $f^2 = 0.00002$ (small)
V:	$F(1,30) = 1.203$, $p = 0.28$, $f^2 = 0.04009$ (medium)
C x H:	$F(1,30) = 0.191$, $p = 0.67$, $f^2 = 0.00636$ (small)
C x V:	$F(1,30) = 2.585$, $p = 0.12$, $f^2 = 0.08617$ (medium)
H x V:	$F(1,30) = 0.152$, $p = 0.70$, $f^2 = 0.00506$ (small)
C x H x V:	$F(1,30) = 0.414$, $p = 0.53$, $f^2 = 0.01380$ (small)

Visual Field Trained
Right
Left

17a) Discussion (Untrained-Trained Analyses)

This may indicate that each hemisphere has inherent properties requiring either reduced or elevated protein synthesis for memory consolidation to occur during sleep.

17b) Discussion (Right-Left Analyses)

Regardless of visual field trained, sleep after training may lead to higher protein synthesis in the right hemisphere.