Functional Imaging of Sleep Loss

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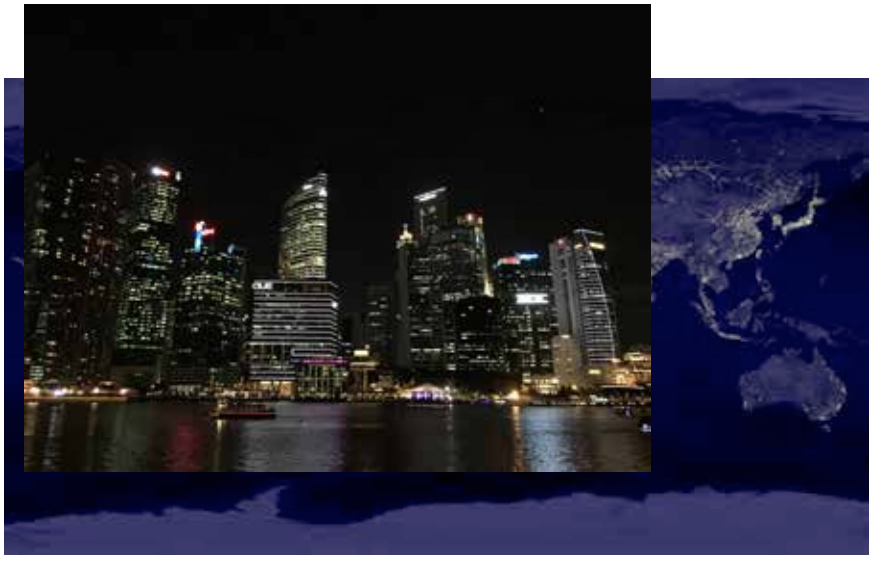


http://apod.nasa.gov/apod/ap001127.html

http://www.nytimes.com/2011/01/17/technology/17brain.html
Mathewingram.com/work

Outline

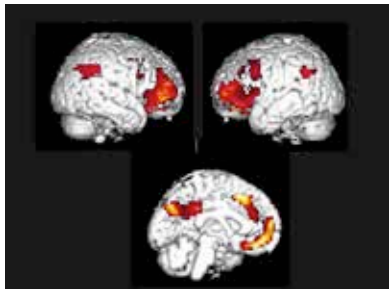
- Setting the stage
- Some relevant imaging features of sleep
- Task-related fMRI and behavioral alterations associated with sleep deprivation
  - Attention and information processing capacity
  - Negative emotional stimuli, economic decisions
  - Food stimuli
- Resting state connectivity in sleep deprived persons
- Summary and future directions

Setting the stage

	Task based fMRI	Task free fMRI
Time scale evaluated	Seconds (10-20)	Minutes unless DFC used
Brain regions surveyed	Reveals state differences in areas recruited by task only	Theoretically can examine entire connectivity infrastructure, simultaneously
Hypothesis driven?	Almost always so	Often exploratory

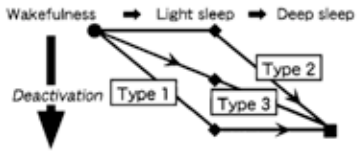
NREM Sleep results in decreased blood flow

- Brainstem
- Thalamus
- Basal forebrain
- Insula
- Anterior cingulate
- Fronto-parietal association cortices



Maquet 1996,1997

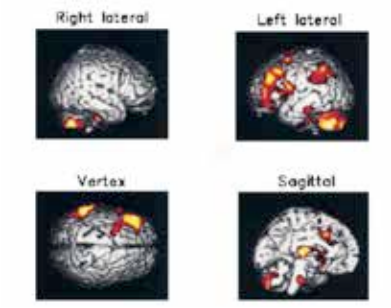
Changes are progressive across state (sampling frame minutes)



Type 1
- Left cerebellar hemisphere
- Right cerebellar hemisphere
- Left putamen
- Anterior cingulate gyrus
- Left inferior frontal gyrus
- Left medial frontal gyrus
- Left infrior parietal gyrus

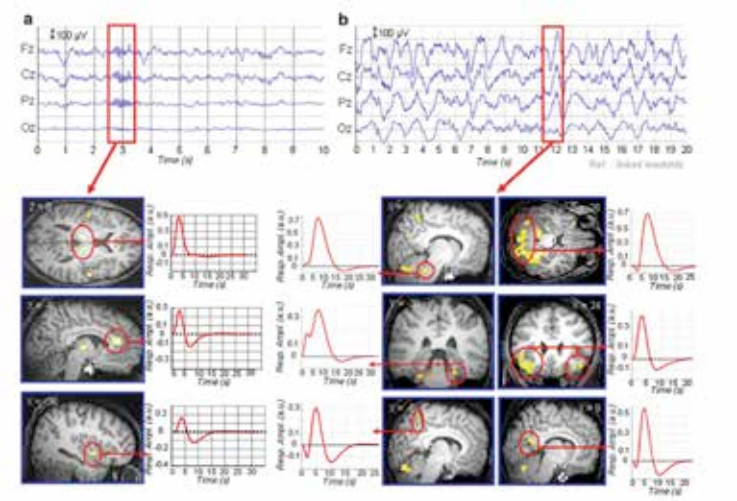
Type 2
- Midbrain
- Left caudate nucleus
- Right caudate nucleus
- Cerebellar vermis

Type 3
- Pons
- Left thalamus
- Right thalamus

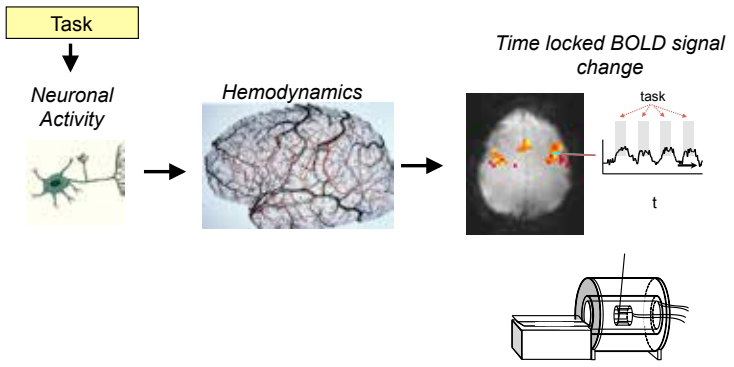


Kajimura N et al;. J Neurosci 1999

BOLD signal correlates of spindles and slow oscillations



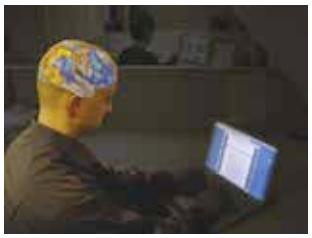
Thien Thanh Dang-Vu; PNAS 2007, 2008)



Task-related fMRI and behavior in sleep deprived persons

Attention: William James c. 1890

"Focalization, concentration of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others…"



Selection

Vigilance

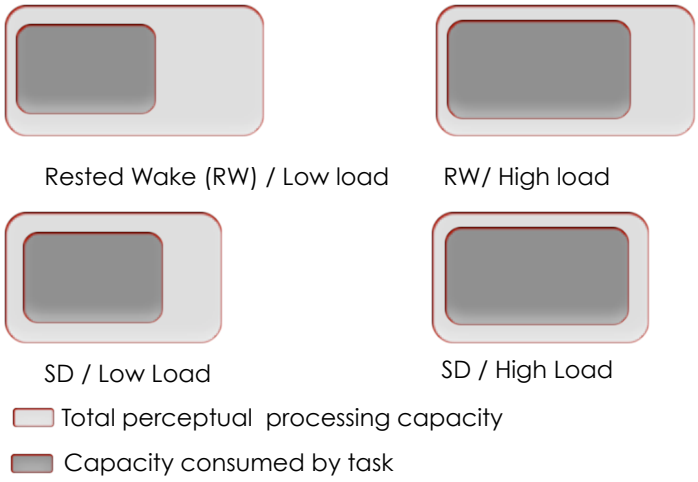
Processing capacity

Distractor suppression

Effects of SD on attention and perceptual processing

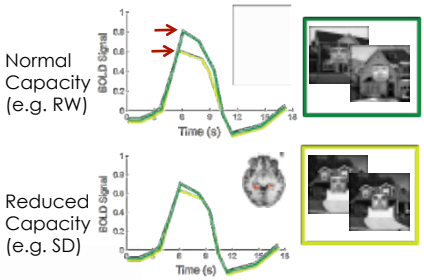
- **Altered divided attention** (Drummond 2001, Jackson 2011)
- ⬇ **selective attention** (Tomasi 2008, Chee 2010 a, b; Lim 2010)
- ⬇ **distractor suppression** (Kong 2012)
- ⬇ **preparatory activity** before stimulus appearance is affected (Chee 2012)
- ⬇ **capacity to respond to rapidly presented serial images** (Kong 2014)
- ⬇ **peripheral processing capacity** (Kong 2011)
- ⬇**Visual short term memory** capacity (Chee 2007, Chuah 2008)
- ⬆ **Time-on-task effects** (Asplund 2014)
- **Metanalysis of attention effects** (Ma 2015)

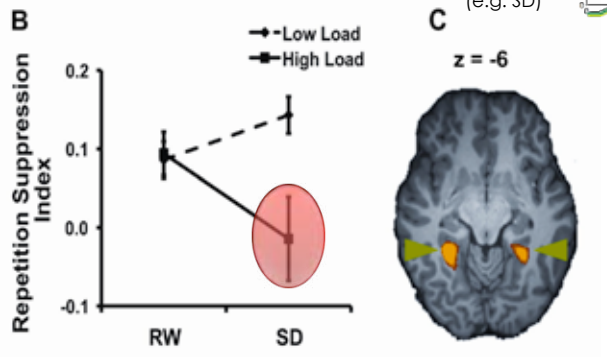
Lavie's Perceptual Load Theory of Attention: Indirectly inferring processing capacity



Lavie N; J Exp Psychol Hum Percept Perform (1995)

Residual processing capacity is reduced following SD

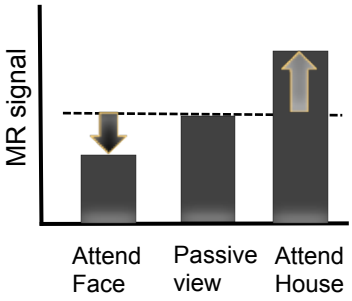


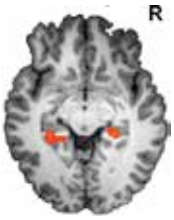


Repetition Suppression Index:
(**PE** Non Repeat – **PE** Repeat) / **PE** Non Repeat

Kong et al;, Neuroimage (2011)

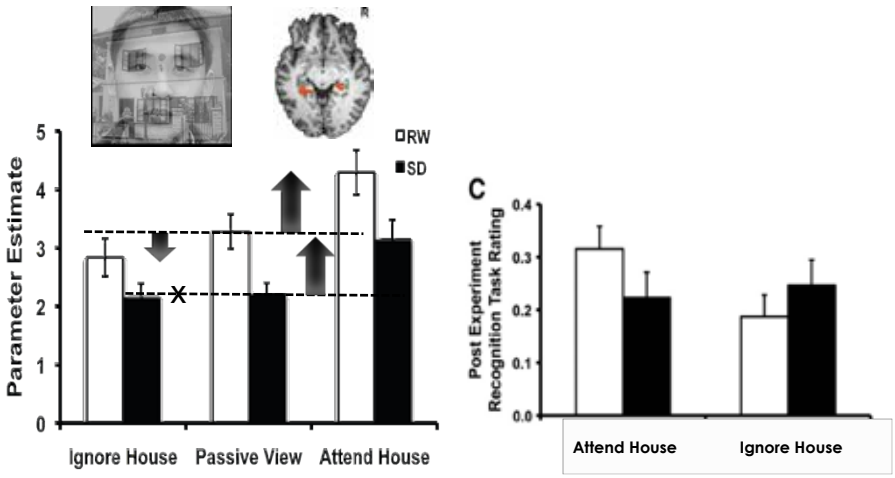
Object selective attention: probing target enhancement & distractor suppression





Kong et al; Neuroimage 2012

SD: preserved target-related enhancement, impaired distractor suppression

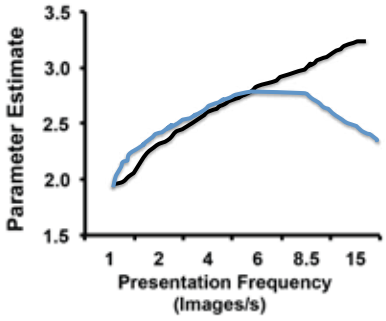


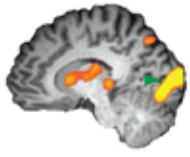
Kong et al; Neuroimage 2012

Evaluating speed of object processing – Rapid Serial Visual Processing (RSVP)

Kong et al;, NeuroImage (2014)

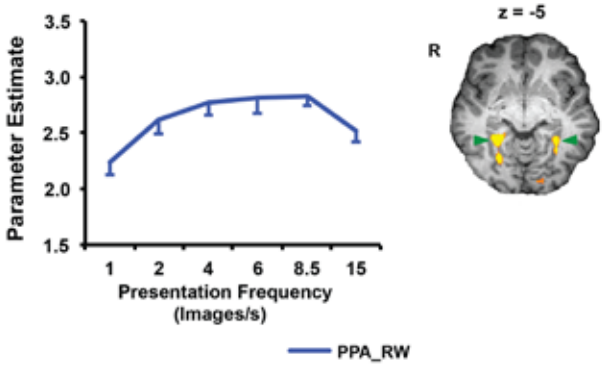
Contrasting activation profiles in early visual areas and PPA: where is the speed bottleneck?





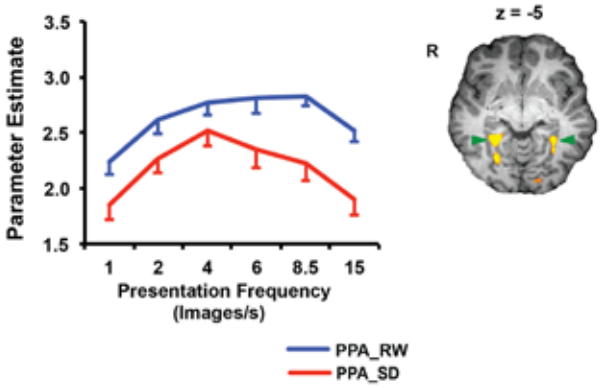
Kong et al;, NeuroImage (2014)

Activation in PPA peaks at ~ 7 images/s in rested wake state



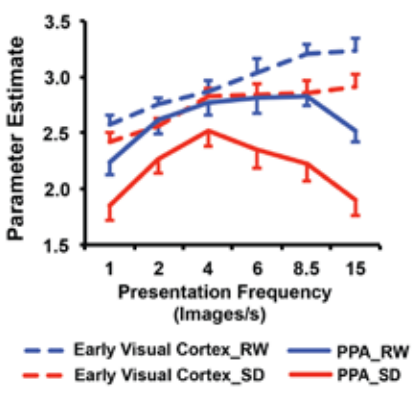
Kong et al;, NeuroImage (2014)

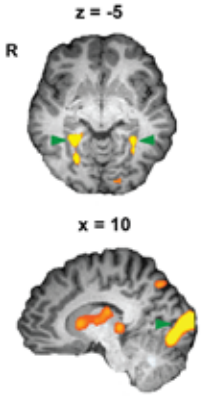
Activation peaks at ~4 images/s in SD: Slower processing speed



Kong et al;, NeuroImage (2014)

Dissociation between higher and early visual cortex responses to presentation rate

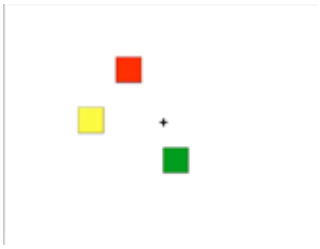




Kong et al;, NeuroImage (2014)

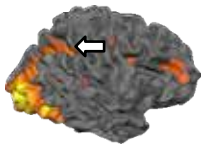
Testing visual short term memory …

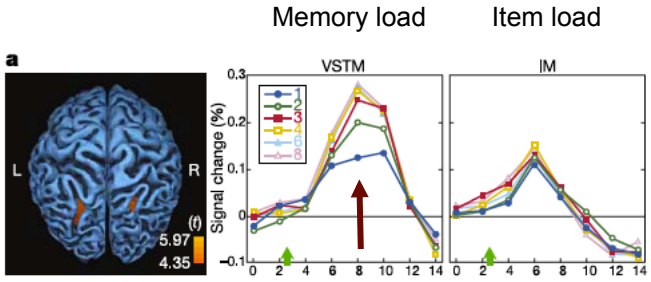
- Visual Short Term Memory
  - 1 to 8 coloured squares are presented
  - Respond to whether the probe square was presented earlier
- Visual Item Load Control
  - 1 to 8 coloured squares are presented
  - Respond to whether or not there is a coloured square in the centre of the array



Todd & Marois: Nature (2004) Chee & Chuah: PNAS(2007); Chuah & Chee; J Neurosci (2008)

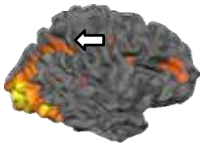
The parietal area tracks VSTM capacity

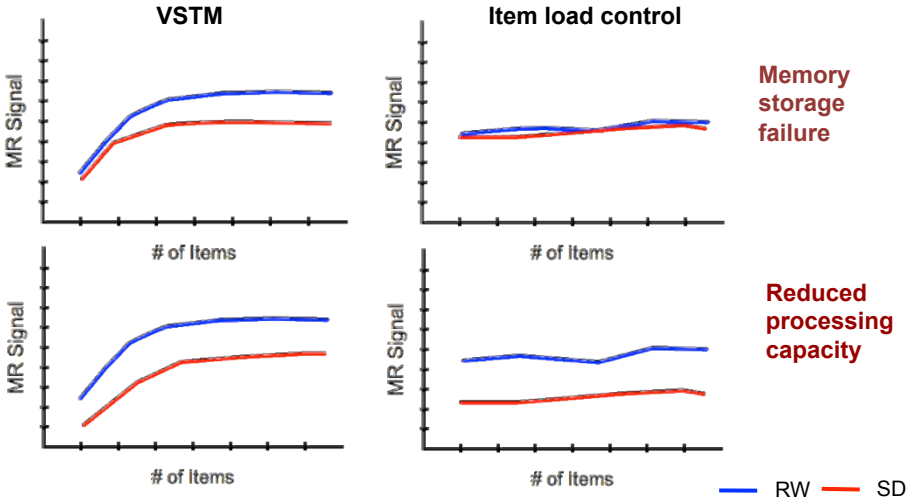




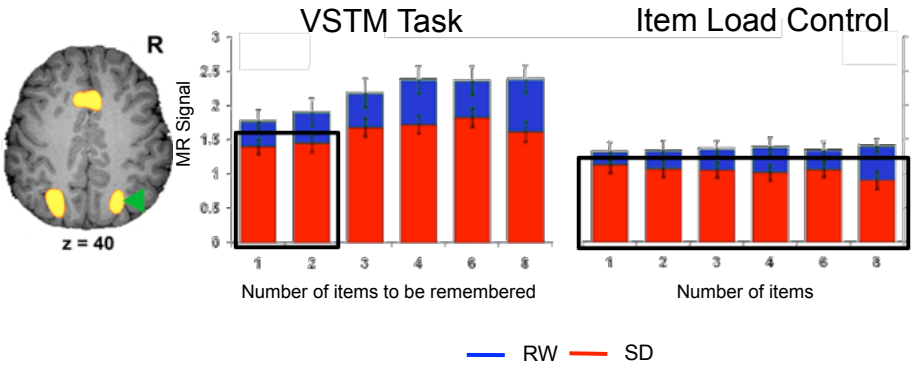
Todd & Marois: Nature (2004)

Parietal activation: memory storage vs. attention deficit accounts of performance reduction





Sleep deprivation reduces parietal activation even when memory capacity is not taxed



Chee & Chuah: PNAS (2007); Chuah & Chee; J Neurosci (2008)

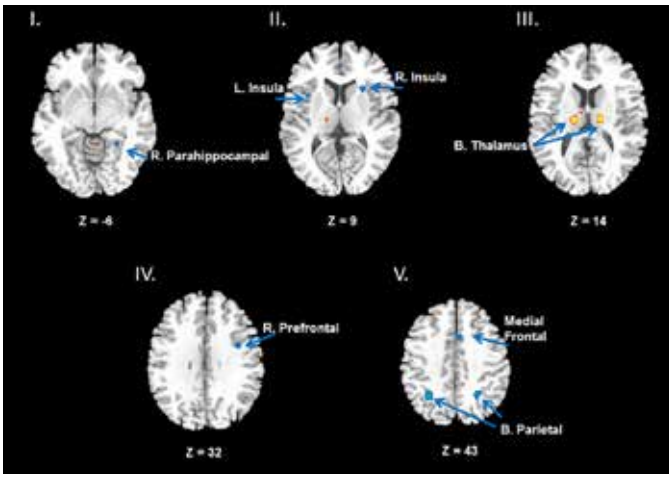
Metanalysis of 11 studies of attention in sleep deprived persons

	Publication	Journal	Number of Participants	Waking Hours	Type of Attention Task*
1	Chee et al., 2008[10]	J Neuroscience	17	24	Selective
2	Chee et al., 2010[11]	Neuroimage	26	24	Selective
3	Chee and Tan, 2010[12]	Neuroimage	20	24	Selective
4	Czisch et al., 2012[51]	Front Neurology	14	36	Selective
5	Drummond et al., 2001[49]	J Sleep Research	13	35	Divided
6	Jackson et al., 2011[50]	Brain Imaging Behav	12	27	Divided
7	Kong et al., 2011[13]	Neuroimage	18	24	Selective
8	Kong et al., 2012[14]	Neuroimage	22	24	Selective
9	Lim et al., 2010[15]	PlosOne	23	24	Selective
10	Mander et al., 2008[52]	Brain Research	6**	34–36	Orienting
11	Tomasi et al., 2009[53]	Cerebral Cortex	14	24	Orienting

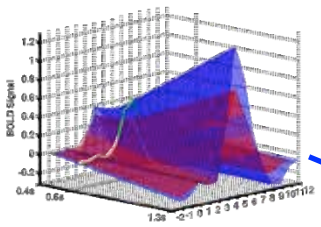
*There were no qualified studies involving only sustained attention performance. **In Mander et al., 2008 study, there were total 7 participants, but only 6 involved in fMRI experiment.

Ma N et al;. Sleep (2015)

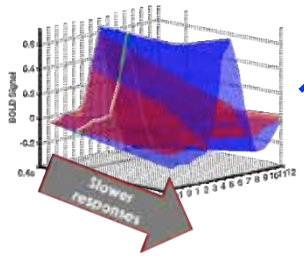
Metanalysis of 11 studies of attention in sleep deprived persons

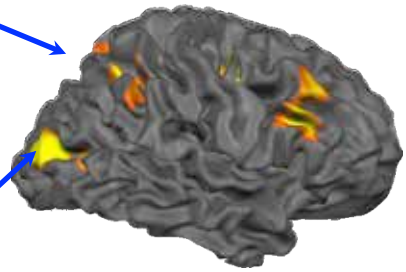


Ma N et al;. Sleep (2015)

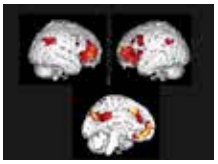


Reduced activation in regions mediating top-down control of attention during SD



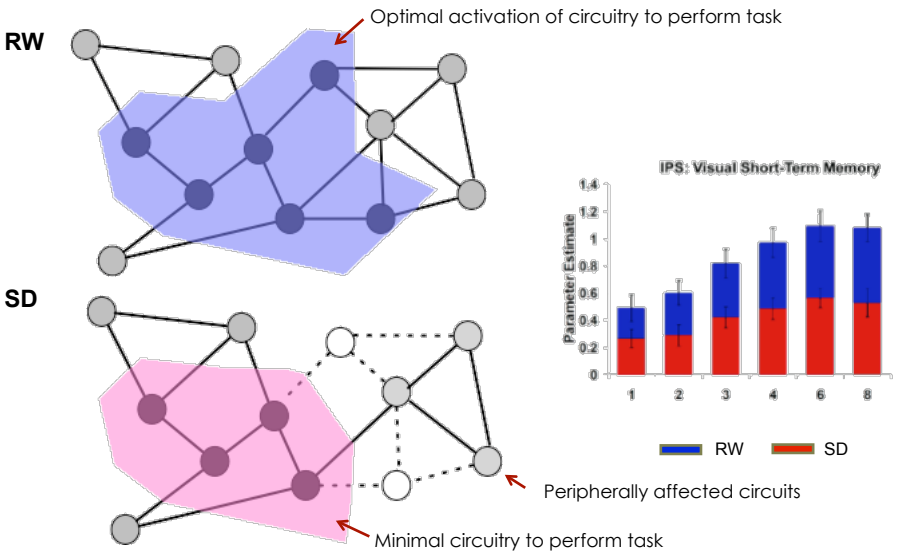


Affects sensory cortex activation



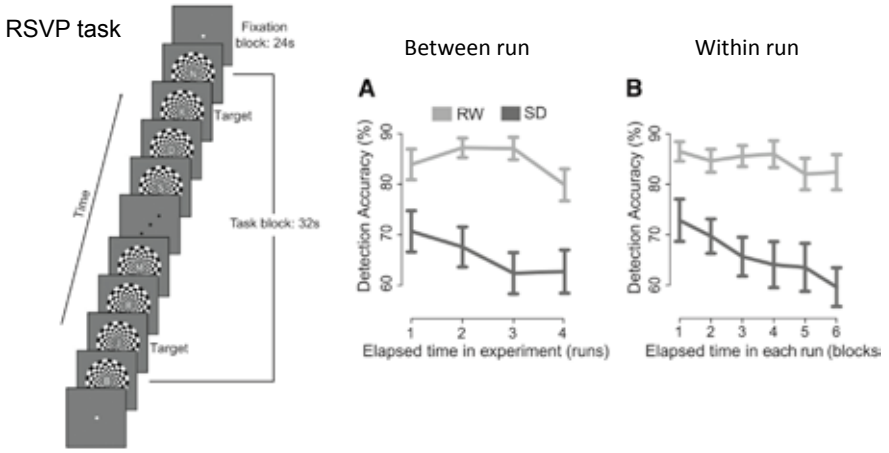
Chee MW; J Neurosci (2008)

Reduction in active circuits during SD



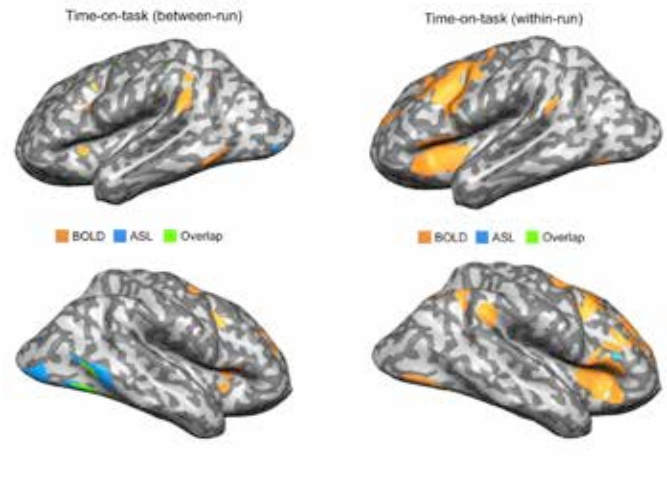
Chee MW et al;, Neuroimage 2011

Performance accuracy shows time-on-task effects that are greater in SD



Asplund CA; NeuroImage (2013)

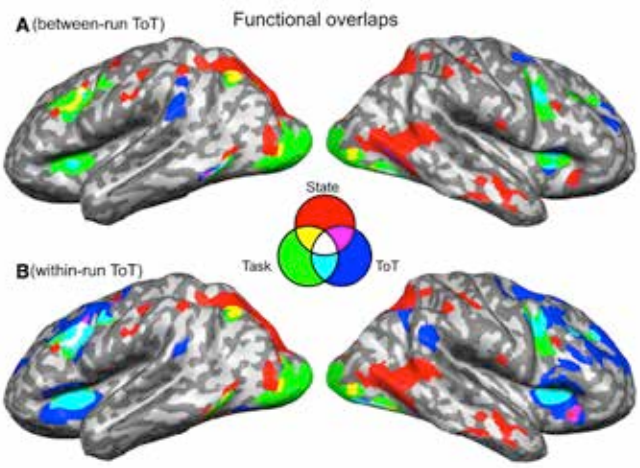
Between vs. **Within** Run Time-On-Task Effects



Between Run **Within Run**

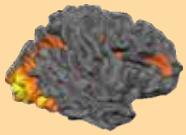
Asplund CA; NeuroImage (2013)

Overlap between task, state and ToT effects



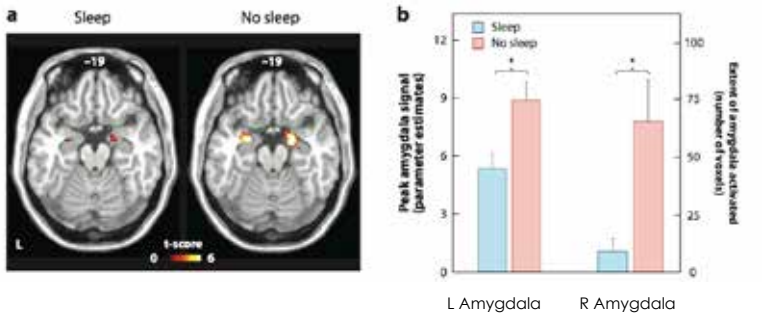
Asplund CA; NeuroImage (2013)

Total Sleep Deprivation:



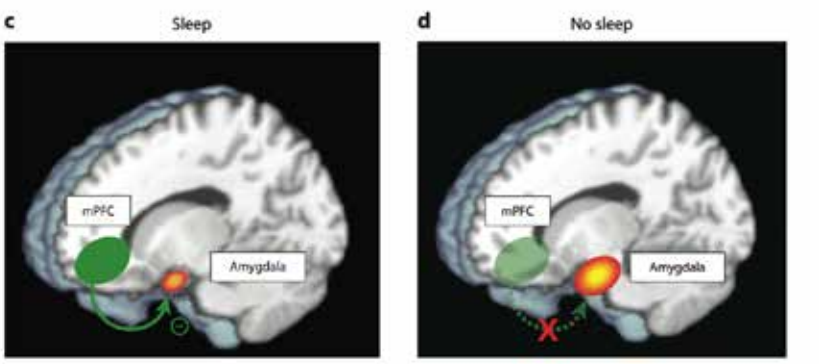
- Reduces task-related activation of fronto-parietal areas mediating cognitive control
- Concurrently reduced top-down biasing of extrastriate (less / no effect on primary) visual cortex activation
- Behavioral consequences:
  - Reduced selectivity
  - Decreased inhibition of distractors
  - Reduced capacity to process visual information
    - Rate of visual object processing
    - Peripheral processing of irrelevant stimuli
  - Accentuated time on task effects

Increased amygdala activation to negative pictures after a night of TSD



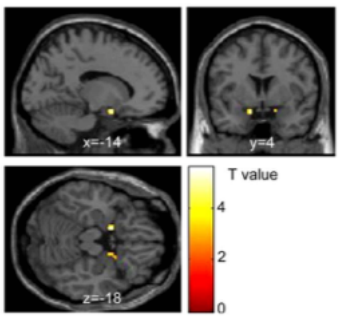
Yoo SS et al;. Nat Neurosci (2007)

Reduced functional connectivity between amygdala and mPFC

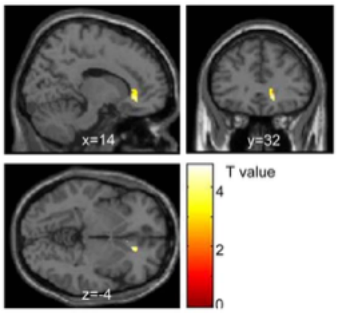


Yoo SS et al;. Nat Neurosci (2007)

Similar patterns of amygdala activation and connectivity change after 5 nights of PSD



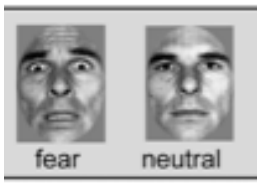
Excess activation to negative faces in PSD

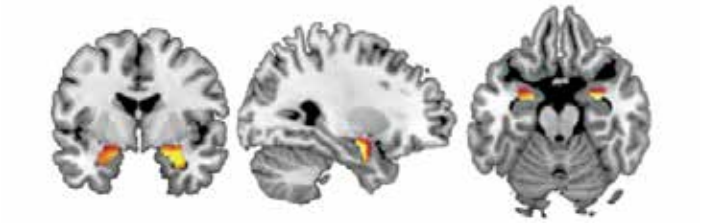


Reduced functional connectivity with L amydala seed in PSD condition

Motomura et al. PloS One (2013)

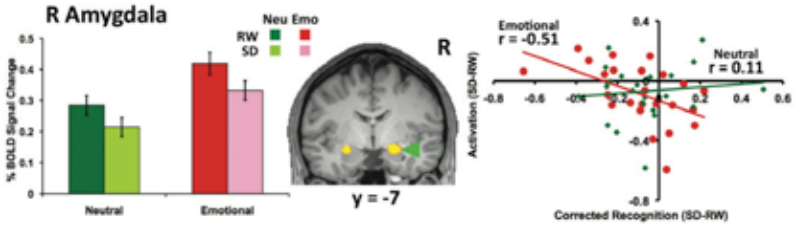
Subjective poor sleep quality also affect amygdala activation and connectivity





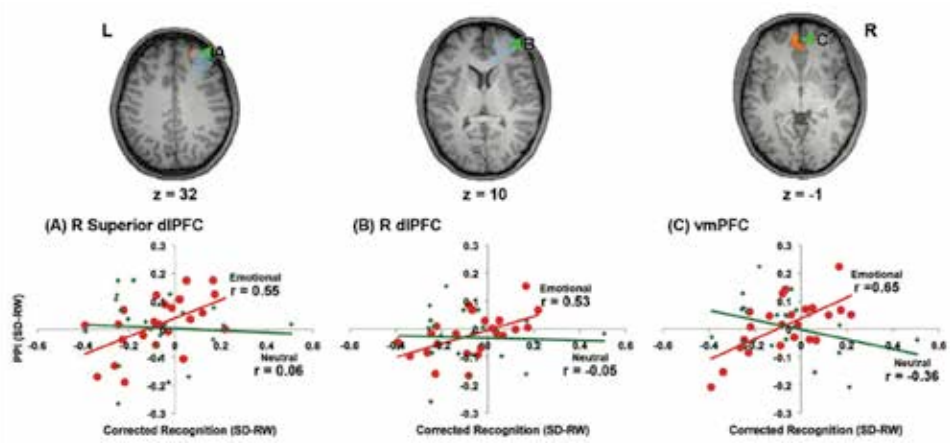
Prather AA, Psychosom Med (2013)

Amygdala activation to emotional distracters in SD affects working memory



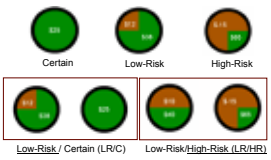
Chuah L Sleep (2010)

Functional connectivity between amygdala and frontal regions correlates with less interference of memoranda by negative pictures

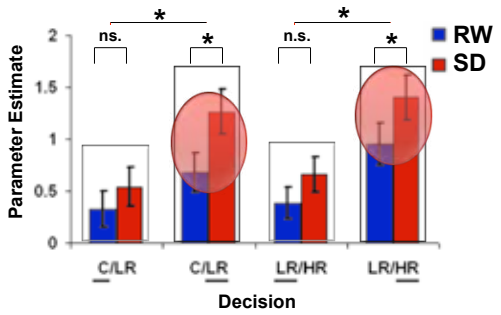


Riskier economic decisions activate the nucleus accumbens; and more in SD

- Significant main effect of risk (see also McKenna; 2007)
  - C certain/LR (low risk) > C/LR
  - LR/HR (High Risk) > LR/HR
- **Riskier decisions in SD elevated NA activation**

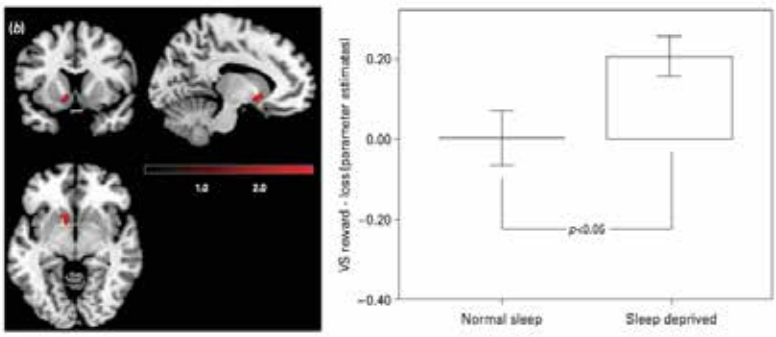


Right Nucleus Accumbens



Venkatraman; Sleep (2007)

Greater ventral striatal responses to win-loss trials in SD

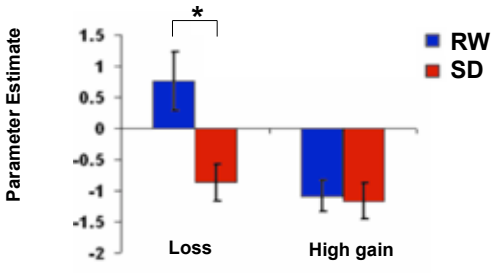


Mullin BC; Psychosom Med (2013)

SD attenuates activation in insula following losses

- Suggests reduced emotional response towards losses following sleep deprivation
- Insula related to loss averse behavior (Paulus et al., 2003; Kuhnen and Knutson, 2005; Venkatraman et al., 2009)

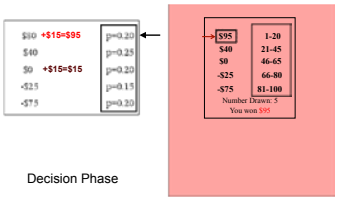
Left Anterior Insula

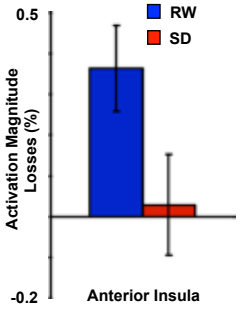


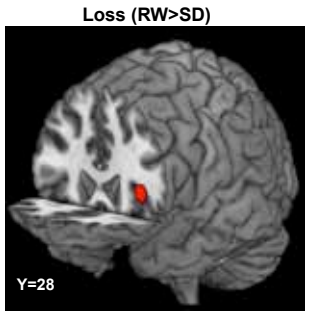
Venkatraman; Sleep (2007)

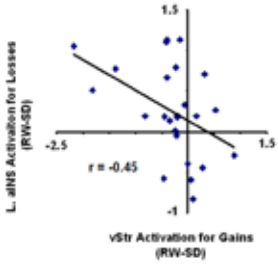
SD decreased sensitivity to receipt of losses in anterior insula

Multiple outcome gamble →









(Outcome phase data)

Venkatraman et al 2011

Selection of negative studies related to decision making in SD

- No change in **relative valuation of rewards** (Libedinsky 2011)
- No increase in **impulsivity** (Libedinsky 2013)
- **Intact detection of temporal distribution** of rewards (Massar J Sleep Res 2015 - accepted)
- **Mixed results** with Iowa Gambling Task (Killgore 2006, 2007, 2012)
- **No effect on risk** (Menz 2012)

Affective processing and economic decision-making summary:

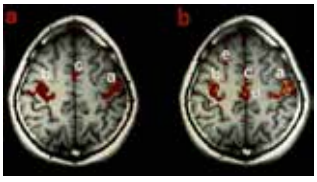
- Increased amygdala activation to negative stimuli
- Amygdala-frontal connectivity alterations differ across persons; correlate with behavioral shifts
- Neural signatures for increased propensity to take higher risk and desensitization to loss under some test paradigms
- **No obvious changes in impulsivity, evaluation of temporal distribution information or valuation**
- State shifts not as clear-cut as with attention

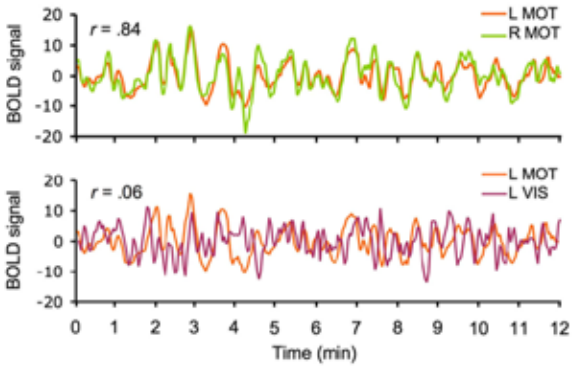
Effects on appetite:

Author	TSD/PSD	Duration	N	Stimulus	Variables of interest	Imaging
Greer (2013)	TSD	1N	23	Desirability of food pictures	Sleepiness predicted desire for higher calorie foods	↓ Ant. Insula, ant cingulate, orbitofrontal, ↑ amygdala*
St. Onge(2012)	PSD	6N/ 4h/ night	**30**	Blocked food vs. non-food pictures	No behavioral measure	↑ Ant insula, thalamus, putamen, IFG,OFC (food>non-food) +PSD-Ctrl
Benedict (2012)	TSD	1N	12	High vs. Low Cal food pictures	↑ Self reported hunger ratings after TSD	↑ mid ACC
Fang (2015)	TSD	1N	**46**	Resting state - Salience network - dACC (ROI seed)	Macronutrient content in food a day after SD; ↑ fat but not carb intake	↑↑ fC in Salience network (dACC-putamen, ant insula); corrl with incr fat calorie intake

Resting state connectivity in SD

Intrinsic correlation of low frequency oscillations in BOLD signal





Biswal B et al; (1995), Dijk KRA (2010)

Correspondence of the brain's functional architecture during activation and rest

Stephen M. Smith[a,1], Peter T. Fox[b], Karla L. Miller[a], David C. Glahn[b,c], P. Mickle Fox[b], Clare E. Mackay[a], Nicola Filippini[a], Kate E. Watkins[a], Roberto Toro[d], Angela R. Laird[b], and Christian F. Beckmann[a,e]

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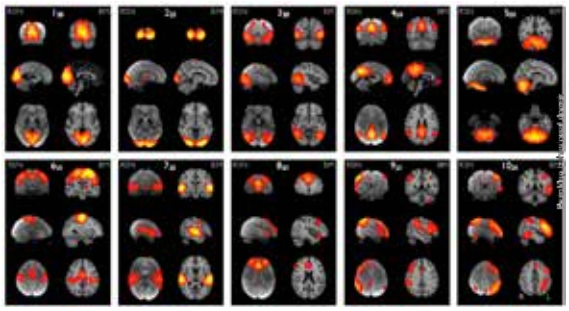
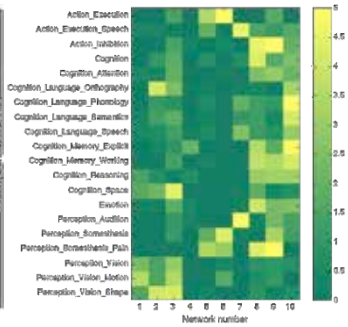
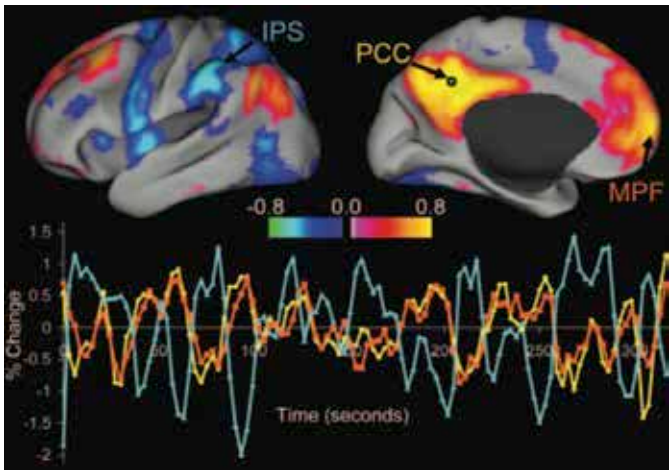
Edited by Marcus E. Raichle, Washington University School of Medicine, St. Louis, MO, and approved June 12, 2009 (received for review May 13, 2009)





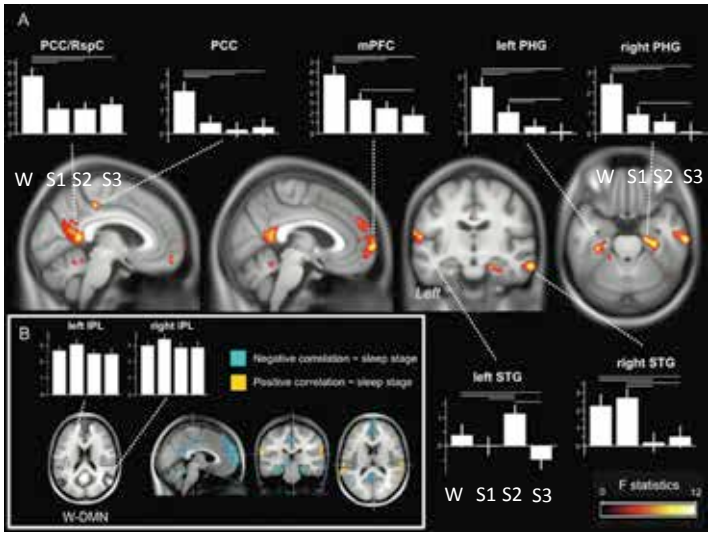
Smith SM (2009) Proc Nat Acad Sci USA

Low frequency oscillations and anti-correlated functional networks



Fox et al; PNAS (2005)

Change in DMN FC from wake to deep sleep

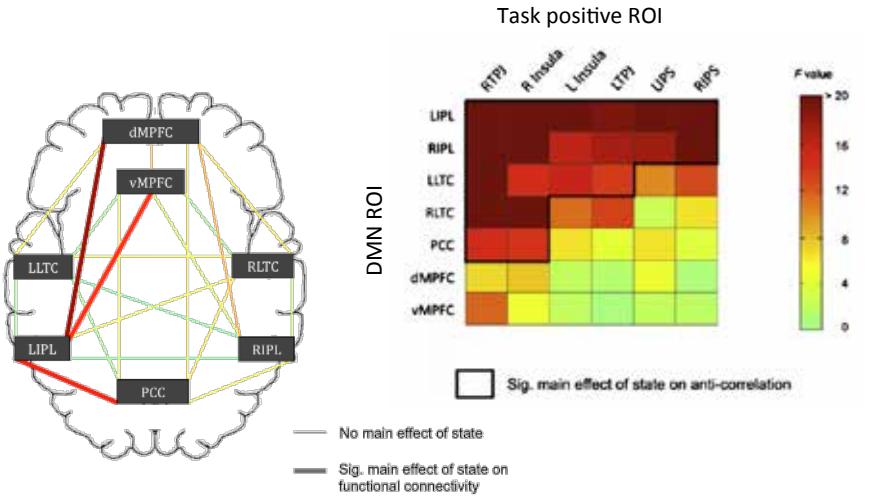


Sämann PG (2011); Horovitz SG (2009)

Resting state fMRI in SD:

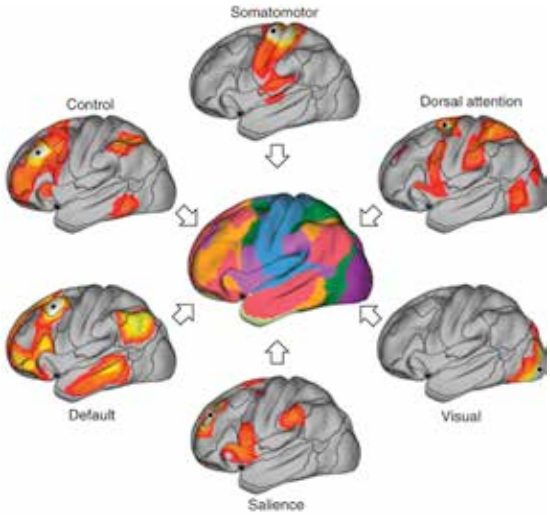
Author	TSD/PSD	N	Duration / TR	Global Signal Regression	Seed	Main findings
Samaan (2010)	PSD/ 1N	14	6min TR 2s	Yes	Multiple DMN and ACN	⬇DMN correlation; ⬇anti-correlation % DMN and ACN
De Havas (2012)	TSD/ 1N	26	8min TR1.5s	Yes	Multiple DMN and ACN seeds	⬇DMN correlation; ⬇anti-correlation % DMN and CAN
Bosch (2013)	PSD/ 1N	12	8min TR 2.5s	Yes	PCC	⬇PCC and ACC; ⬇anti-correlation: PCC & DLPFC (reported as ⬆correlation)
Shao (2013)	TSD/1N	14	6.5 min TR 2s	Yes	Thalamus R/L	⬇thalamo-PHG, MTG, SFG
Yeo (2015)	TSD	68	24min RW/ 12min SD; TR 2s	Yes + No	ICA/ Template	⬇DMN correlation; ⬇anti-correlation % DMN and ACN; ⬇anticorrelation in RW predicts vulnerability to vigilance decline
Ong (2015)	TSD	24	12 min TR 2	Yes + No	ICA/ Template	Accentuated SD changes within DMN and DAN connectivity with eye-closure in SD

Reduced DMN connectivity and decreased anti-correlation between DMN and task-positive ROI



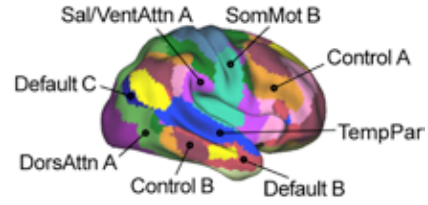
de Havas; NeuroImage (2012)

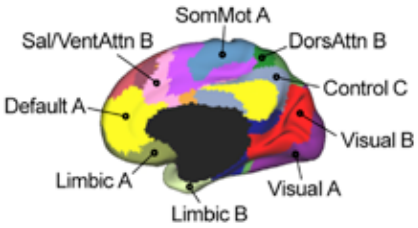
Intrinsically connected brain networks



Buckner, Krienen, Yeo (2013)

17-network resting state parcellation



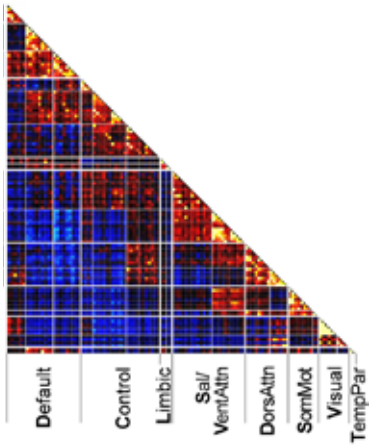


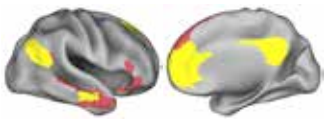
Segregation into 8 functional groups

Default
Salience/Ventral Attention
Dorsal Attention
Control
Visual
Somatomotor
Limbic
Temp Par

Yeo BT; J Neurophysiol (2011)

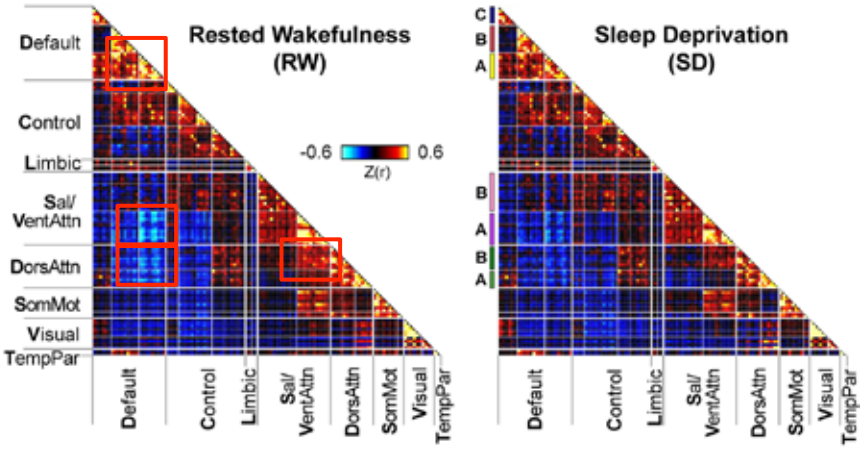
Depiction of resting state functional connectivity (n=68)





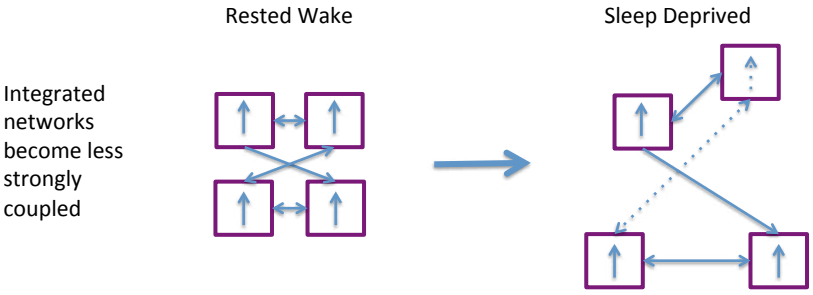
Yeo BT; NeuroImage (2015)

Comparison of functional connectivity – RW vs. SD

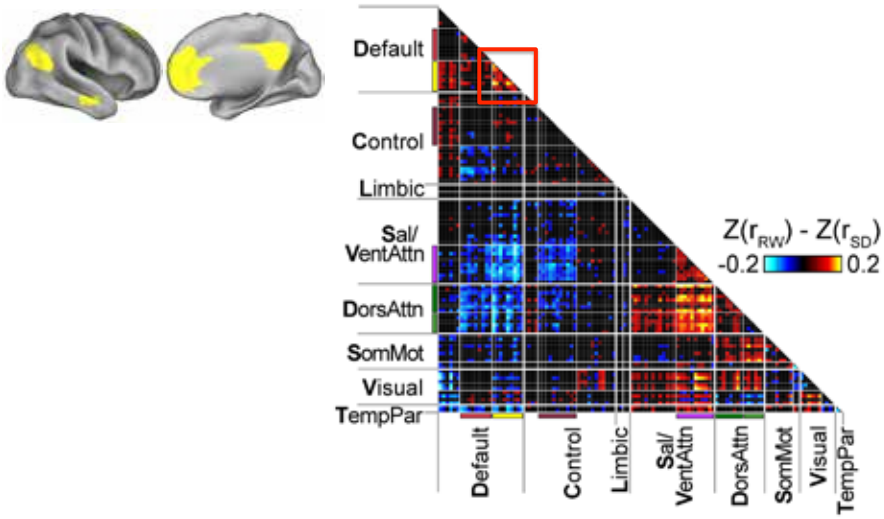


Yeo BT; NeuroImage (2015)

A simplified way of interpreting state changes in functional connectivity

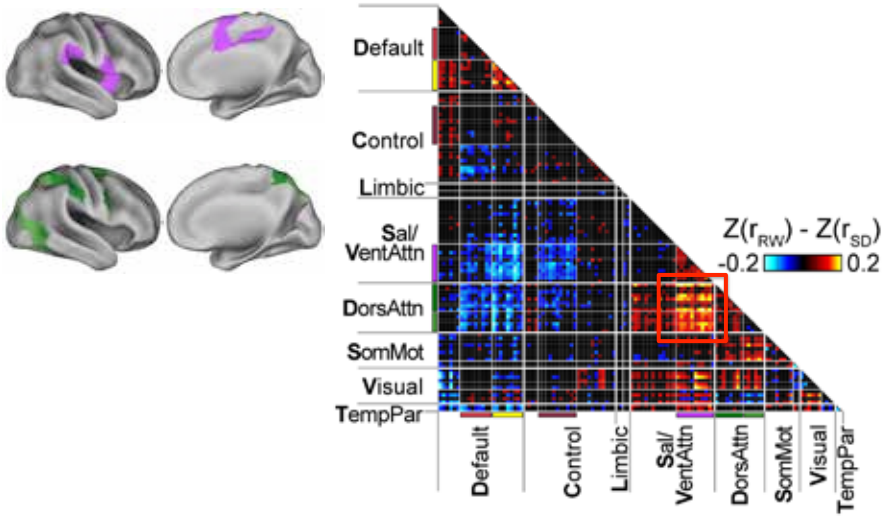


I. SD: Reduced positive correlation within Default *A* network



Yeo BT; NeuroImage (2015)

II. SD: Reduced positive correlation between Salience *A* vs. Dorsal Attention *A* networks



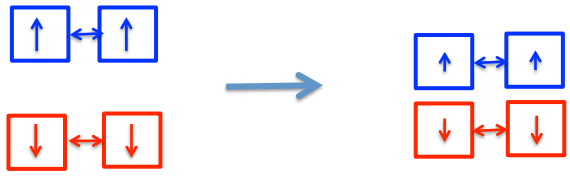
Yeo BT; NeuroImage (2015)

A simplified way of interpreting state changes in functional connectivity

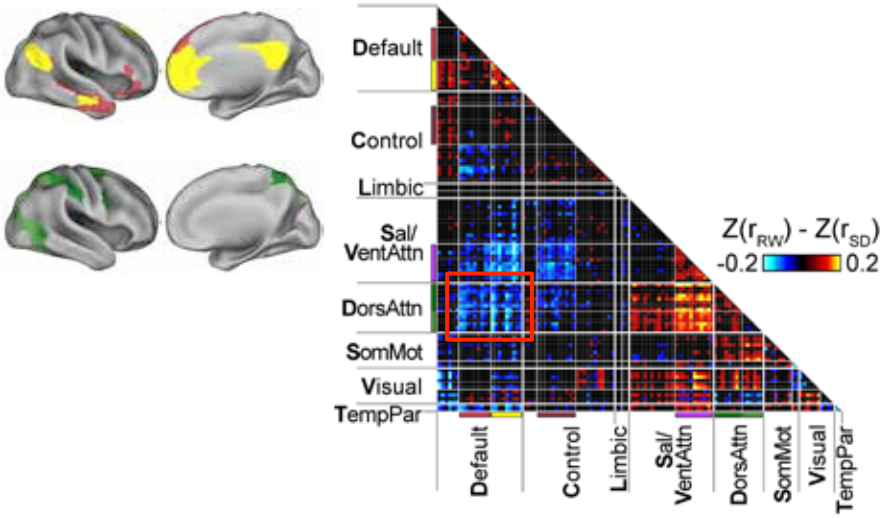
Rested Wake

Sleep Deprived

Segregated Networks become less segregated

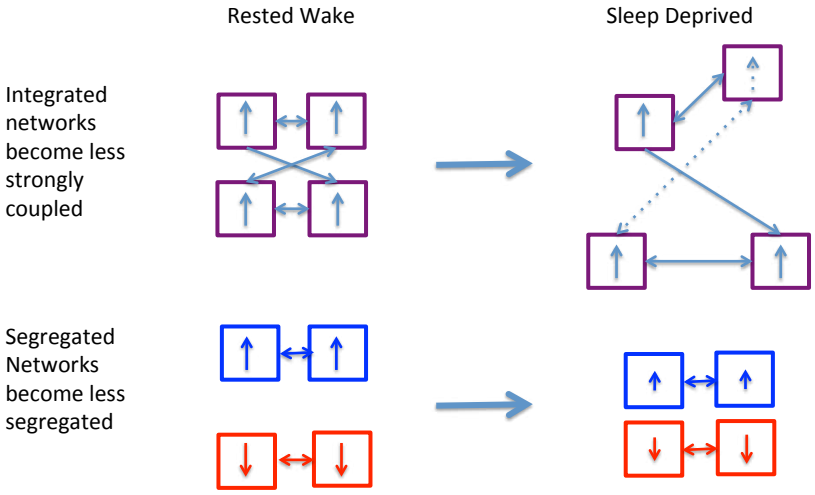


IV. SD: Reduced anti-correlation between Default A&B and Dorsal Attention A Networks

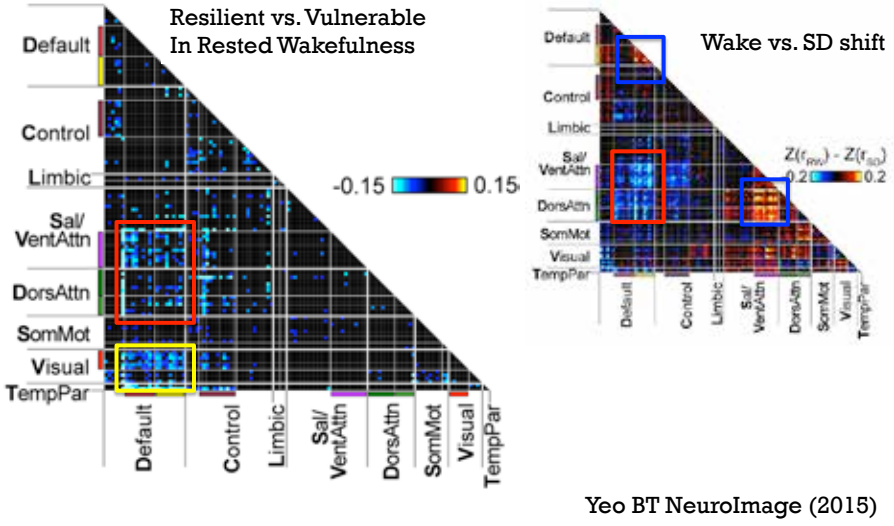


Yeo BT; NeuroImage (2015)

A simplified way of interpreting state changes in functional connectivity

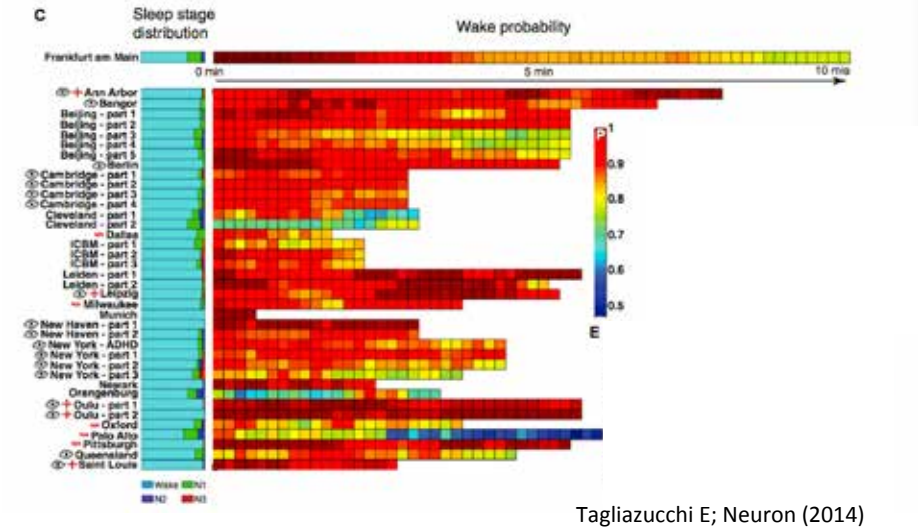


Predicting resilience to SD with connectivity:



Yeo BT NeuroImage (2015)

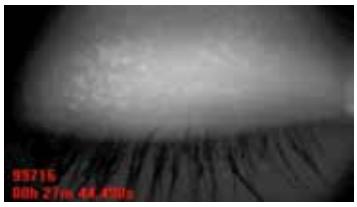
A third of long'resting state' scans during 'wakefulness' contain sleep!



Tagliazucchi E; Neuron (2014)

Spontaneous eye closures in SD

ES = 1



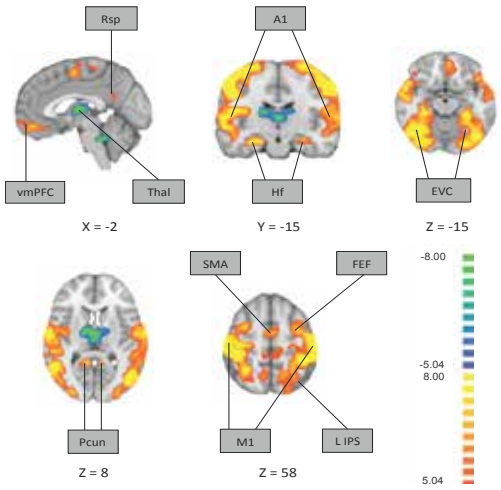
ES = 9

ES = 5

- Eye videos: 2 sec video clips around each auditory event
- Eyescores (ES) from 1 (fully closed) to 9 (fully opened) by 2 independent raters

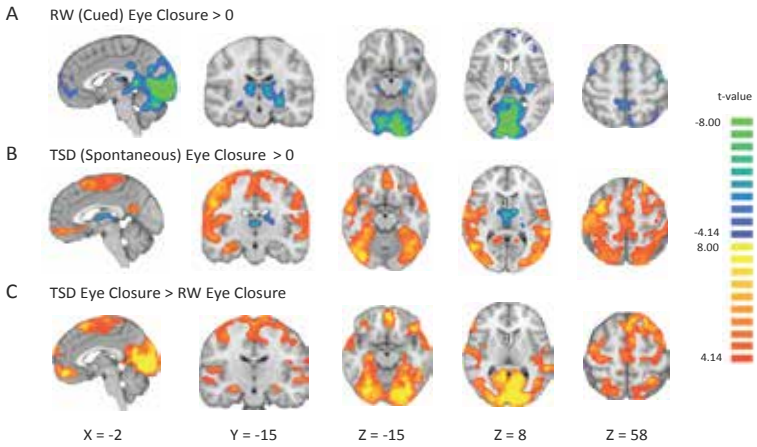
(Ong JL Sleep 2014; Ong JL NeuroImage 2015)

Co-activation and deactivation associated with spontaneous eye-closures in SD



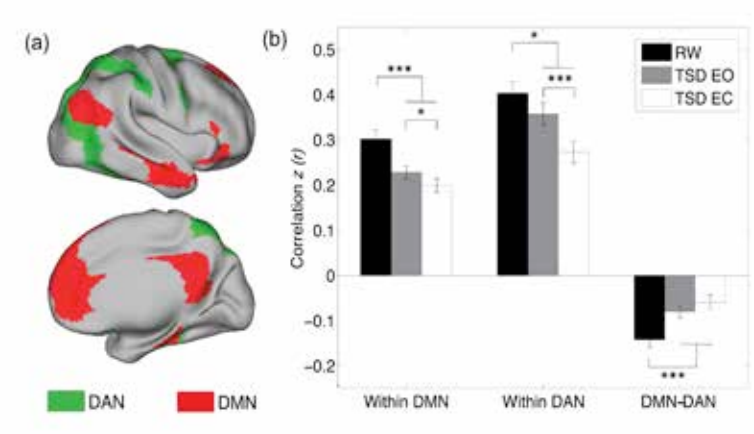
(Ong JL NeuroImage 2015)

Differences in BOLD signal elicited by cued eye closures in RW & SD compared to spontaneous eye closures in SD



(Ong JL NeuroImage 2015)

Decrease in functional connectivity associated with spontaneous eye-closures in SD



(Ong JL NeuroImage 2015)

Resting state fMRI changes in SD

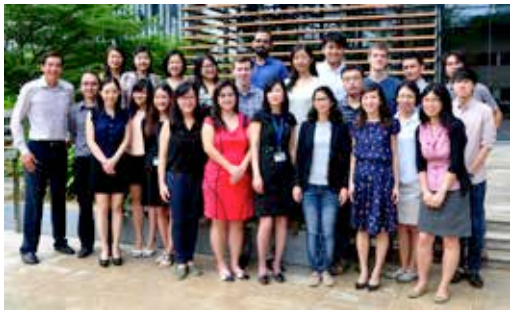
- All 'awake' resting state studies should monitor for sleep!
- ⬇connectivity within Default Mode Network (DMN)
- ⬇ anti-correlation between DMN and Task-Positive Network (ACN- anticorrelated networks); = increased correlation beween these
- Changes accentuated during eye closures
- Degree of anti-correlation in the rested state may predict vigilance changes in SD

Future directions

- Predictive marker for persons vulnerable to negative consequences of sleep deprivation
- Evaluating microstates in the sleep deprived condition using dynamic functional connectivity
- Uncover markers for long-term consequences of sleep loss or poor sleep quality on cognition / risk of cognitive decline or impairment
- Translation of these novel paradigms into studies involving insomnia, OSA patients

Acknowledgements

- *National Medical Research Council: STaR Award*



http://www.cogneuro-lab.org

Presentation available from website

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