The Neuroscience of Sleep and its Disorders

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“I first noticed the wound upon the head before I alighted from my carriage, the pulsations of the brain being very distinct. The top of the head appeared somewhat like an inverted funnel, as if some wedge-shaped body had passed from below upward. Mr Gage, during the time I was examining this wound, was relating the manner in which he was injured...I did not believe [his] statement...Mr G got up and vomited; the effort of vomiting pressed out about half a teacupful of the brain, which fell upon the floor”

Phineas Gage, 1823-1860
“Sleep is of the brain, by the brain and for the brain”
– J’Allan Hobson

Many sleep disorders result from lesions of the brain
  Sometimes transient
  Sometimes functional
  Sometimes microscopic

Some sleep disorders lesion sleep and provide insights into the function(s) of sleep
Wake

Sleep

“Each day is a little life: every waking and rising a little birth, every fresh morning a little youth, every going to rest and sleep a little death”

Schopenhauer
Non-REM Parasomnias

- Spectrum of behaviours arising from slow-wave (N3) sleep
- Range from sleeptalking, confusional arousals, sleep terrors, sleep-eating, sexsomnias, sleep-walking
- Typically arise in first half of night
- Eyes usually open, complex speech or behaviours, directed with interaction with environment
- Amnesia for events, difficult to wake, occasional dream fragments or partial awareness
Figure 2: SPECT findings during sleepwalking after integration into the appropriate anatomical magnetic-resonance image
M Terzaghi et al, Sleep 2009, 32 (3): 409-412
Sleep is Not a Universal Brain State

- Slow-wave sleep
  - Motor cortex: Movements
  - Frontoparietal association cortex: Consciousness, Awareness, Judgement
  - Limbic cortices and amygdala: Reward, Emotions
  - Hippocampus: Memory

- Parasomnia episode
  - Complex motor behaviours
  - Absence of inhibitory control
  - Low consciousness
  - Expression of intense fear
  - Autonomic activation

- Wakefulness
  - Partial or complete amnesia
Wake
REM Sleep
NREM Sleep
Blurred Lines
The First Night Effect

Tamaki et al, 2016, Curr Biol 26 (9): 1190-1194
The Concept of Local Sleep

Brain recordings in rats show “silent areas” in the cortex
These increase in frequency and duration with wakefulness
Correlation with impairment of tasks

Other Examples of Blurred Lines?
REM Sleep Behaviour Disorder

- Estimated prevalence of <1%
- Usually towards latter half of night
- Lashing out, crying, swearing, shouting
- Eyes closed
- Speech usually unintelligible
- Pts do not leave bed, no purposeful interaction
- If woken may have dream recall
- Can occur every night, several times a night
- Injuries to self or bed partner a real risk
Muscle Paralysis in REM Sleep

Fig. 2. Polysomnographic record of an idiopathic RBD patient showing REM sleep with chin muscle atonia and excessive limb muscle twitches. LTA: thumb anterior.
RBD is a Herald of Brain Degeneration

Iranzo et al., 2014
So does Isolated RBD Exist?

- People with RBD have higher rates of:
  - Abnormalities in smell, bladder, gut and cardiovascular function
  - Higher rates of alpha-synuclein in a variety of tissue biopsies
  - Constipation, anosmia, subtle Parkinsonian signs, abnormal brain scans
  - Subtle problems with cognition
- Is RBD therefore really prodromal neurodegenerative disorder?
- Are patients with RBD candidates for disease-modifying drugs?
Origins of Narcolepsy?
What Causes This Loss?

Adapted from Rogers et al. Sleep 1994; 17:590
And Cataplexy?
Electrical Differences in Lucid Dreaming – Relevance to Insomnia?
What About Lesioning Sleep Itself?

• Wide range of conditions “lesion” sleep
  • Chronic Sleep Deprivation
  • Insomnia
  • Obstructive Sleep Apnoea
  • Periodic Limb Movement Disorder

• Sleep disorders associated with an array of neurological consequences
  • Cognitive and mood problems
  • Stroke
  • Dementia
Ehsan-Shokri et al, PNAS 2018, 115 (17).

Sleep Drives Metabolite Clearance from the Adult Brain

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Conclusions

Sleep is not a single brain state
Sleep is not even a global brain state
Sleep disorders provide important insights into the regulation and functions of sleep
Phenomena that we may all experience, even in good health, can be explained in these terms