Learning Objectives

1. Understand the role of sleep in the acquisition of motor skills and cognitive information

2. Consider how stroke changes sleep patterns and examine data showing how this relates to motor learning

Sleep

All mammals sleep but it is not entirely clear why

Recent work points to a role for sleep in the encoding and consolidation of memories

This is true for both cognitive and motor memories
Introduction

Sleep is important for motor learning and memory consolidation in young neurologically intact individuals.

The effect of sleep on motor learning is less clear for older adults and individuals with neuropathology.

Sleep: An overview

What is sleep?
1. Reduced motor activity
2. Decreased response to stimulation
3. Stereotypic posture (lying down, eyes closed)
4. Relatively easy reversibility

Rechtschaffen & Siegel, 2000

Why do we sleep?

One hypothesis is that sleep contributes to processes of memory and brain plasticity:
- Sleep dependent memory processing

Leaves open the questions of what kinds of memories rely on sleep.
Sleep is not a homogenous state

- Alternate between periods of rapid eye movement (REM) sleep and non-REM sleep through the night
- 4 phases of non-REM sleep (1-4)
  - Each stage contains progressively “deeper” sleep
- Deepest sleep non-REM stages 3 and 4; also known as slow wave sleep because of low-frequency cortical oscillations

### Sleep Stages

<table>
<thead>
<tr>
<th>Stage of Sleep</th>
<th>Characteristic Activity</th>
<th>Characteristic Wave Form</th>
<th>Time Spent (Young Adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REM</td>
<td>muscle atonic, rapid eye movements</td>
<td>low-voltage, mixed-frequency pattern, PGO spikes</td>
<td>20-25%</td>
</tr>
<tr>
<td>NREM Stage 1</td>
<td>Slow rolling of eyes</td>
<td>sinusoidal alpha wave activity (10Hz)</td>
<td>about 5%</td>
</tr>
<tr>
<td>NREM Stage 2</td>
<td>deep spindles (12-14 Hz) and K complexes</td>
<td>high-amplitude slow delta waves (0.5-2Hz)</td>
<td>50-60%</td>
</tr>
<tr>
<td>SWS (Stages 3 &amp; 4)</td>
<td>high-amplitude slow delta waves (0.5-2Hz)</td>
<td>15-20%</td>
<td></td>
</tr>
</tbody>
</table>

Each stage has a unique physiological mechanisms that impact memory consolidation

Across the night REM and NREM sleep cycle every 90 minutes

The ratio of REM to NREM shifts over the night:
- Early in the night stages 3 and 4 NREM dominate; later in the night REM and stage 2 NREM prevail
Sleep Stages and Aging

Young adults spend largest amount of sleep in:
- stage 2 (50-60%)
- REM (20-25%)
- SWS (stages 3 & 4; 15-20%)
- stage 1 (5%)

Sleep Stages and Aging

With age:
- total sleep time decreases
- percent of time in REM sleep decreases
- percent of time in SWS sleep decreases
- stage 2 sleep remains stable
- reduction in the numbers of sleep spindles

Sleep and Memory Processing

Role of sleep in motor learning likely depends on which stage of memory processing is being considered

Memory Processing:
1. **Encoding**: memory is initially formed into a representation in the brain
2. **Consolidation**: memory is taken from a labile form and made more permanent
Sleep and Memory Processing

**Consolidation:**

a) **Stabilization:** maintenance of motor skill performance, occurs simply through the passage of time, not dependent on sleep

b) **Enhancement:** improvement in performance of a skill; is dependent on sleep

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Sleep and Memory Processing

**Memory Processing:**

3. **Storage:** memory is maintained in the brain over time

4. **Recall:** motor memory brought out of storage for use

5. **Reconsolidation:** transfer a memory destabilized by recall back to a stable form

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The precise impact of sleep on learning and memory appears to depend on the type of memory being formed
Types of Memory

Explicit / Declarative
- Facts
- Events

Implicit / Non Declarative

- Priming
  - Skills & Habits
  - Associative Learning (e.g. Operant Conditioning)
  - Non Associative Learning (e.g. Habituation)

Learning and Stage of Sleep

- Unclear whether one stage of sleep or an ordered sequence of stages promotes learning
  - NREM and REM appear to be necessary for consolidation of memories
  - Declarative (explicit) memories appear to depend on SWS (stages 3 & 4) sleep
  - Procedural (implicit) memories appear to depend on stage 2 NREM and/or REM sleep

Sleep and Memory Processing

- Sleep may differentially affect each stage of motor memory processing
- **Encoding** relies on prefrontal cortex
- Reductions in prefrontal activity are evident after sleep deprivation
- Encoding is disrupted by pre training sleep deprivation
  - Altered activity in prefrontal and medial temporal cortices noted
Sleep Deprivation and Encoding

- Sleep deprived for 36 hours
- Encoded emotional and non-emotional declarative memories
- Tested after 2 nights “recovery sleep”

(Walker, 2006)

Sleep Deprivation and Encoding

- Appears that REM sleep is key for encoding of new memories
- Noted when REM sleep is disrupted pre-training encoding is not as efficient
- Encoding appears to be largely mediated by prefrontal cortex and hippocampus (medial temporal lobe)
- Impairs long-term potentiation and reduces levels of brain derived neural growth factor (BDNF)
- Sleep deprivation does not impact encoding for fear-conditioning tasks (mediated by amygdala)

(McDermott, 2003)

Sleep and Memory Processing

- Sleep may differentially affect each stage of motor memory processing
  - Consolidation appears to be the stage most impacted by sleep
  - Consolidated memory trace is fairly stable across time until recalled from memory for task practice and reconsolidated (which may also be sleep dependent)
Sleep and Memory Consolidation

• Declarative (explicit) memories appear to be supported by sleep
  – Significant increases in post-training REM sleep after successful intensive language training (Konick, 1989)
  – Both REM and SWS contribute to consolidation of complex, emotionally salient memories

Sleep and Memory Consolidation

Procedural (implicit) memories are less well linked with sleep

(Fisher et al. 2006)
Motor skill improvement is related to sleep but not time

Motor skill improvement is related to sleep but not time (Walker, 2006)

Sleep and Brain Plasticity

- Patterns of brain activity shown during practice of a serial reaction time task re-emerge during REM sleep (Maquet, 2000)
- Extent of change during awake practice is related to the magnitude of reactivation during sleep (Peigneux, 2003)
  - Amount of SWS reactivation in the hippocampus is proportional to the amount of next-day improvement

Sleep changes brain activity

Compared to before sleep, more activity noted in
- Primary motor cortex
- Prefrontal cortex
- Hippocampus
- Cerebellum

(Walker et al., 2005)
### Aging and stroke change the time spent in different phases of sleep

<table>
<thead>
<tr>
<th>Type of Sleep</th>
<th>Characteristic Activity</th>
<th>Characteristic Measurements (from Electroencephalography)</th>
<th>Young Adults</th>
<th>Older Adults</th>
<th>Stroke With Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-REM sleep</td>
<td>None detected, rapid eye movements</td>
<td>Low voltage, low frequency, fast moving beta waves</td>
<td>19.2±1.1</td>
<td>16.7±1.7</td>
<td>16.3±3.2</td>
</tr>
<tr>
<td>Stage 1</td>
<td>Slow rolling of eyes</td>
<td>Increased alpha wave activity  (9-12 Hz)</td>
<td>3.7±2.1</td>
<td>1.5±1.5</td>
<td>0.5±0.5</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Sleep spindles (12-14 Hz) and K complexes</td>
<td>40-55</td>
<td>30-45</td>
<td>25-30</td>
<td>20-25</td>
</tr>
<tr>
<td>Non-REM sleep</td>
<td>None detected, rapid eye movements</td>
<td>Low voltage, low frequency, fast moving beta waves</td>
<td>19.2±1.1</td>
<td>16.7±1.7</td>
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</tbody>
</table>

After stroke percent of REM sleep maintained, amount of stage 2 (and sleep spindles) increases

(Siengsukon & Boyd, 2009)

### Failure to benefit from sleep with aging

Age related changes in the impact of sleep may related to alterations in both patterns of sleep and memory formation

(Siengsukon & Boyd, 2009)
The effect of sleep on motor learning in:
- Older adults: unclear
- Middle aged adults: unclear
- Individuals with stroke: unknown

Sleep and Stroke
After Stroke
- 20-40% of people have sleep-wake disorders (insomnia, excessive daytime sleepiness, fatigue, hyper-somnia)
- Can be attributed to depression, sleep-disordered breathing, medications, complications from stroke
- 54% of people post stroke show differences in sleep characteristics from age-matched controls

Purpose
To examine the role of sleep and instruction in motor skill learning and memory consolidation in individuals following stroke

Participants
40 individuals chronic (>6 mo) post-stroke (ST) pseudo-randomized into:
1. sleep/implicit,
2. sleep/explicit,
3. no-sleep/implicit,
4. no-sleep/explicit groups

37 neurologically intact individuals (CT) sex and age-matched (+/- 5 years).

Introduction
• 20-40% of people with stroke have sleep-wake disorders
• 53% of chronic stroke individuals demonstrate abnormal sleep EEG
• Past work has not considered the impact of sleep on people with stroke
• Past work has only used relatively simple motor tasks (SRTT)
Task

- Continuous tracking task practiced in evening (sleep groups) or in morning (no-sleep groups)
- 10 blocks of 10 trials per block; each trial 1 random and 1 repeated segment in counterbalanced order
- Retention test 12 hrs later (+/- 1 hour); 1 block

Group Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Time post-stroke (month)</th>
<th>Fugl-Meyer</th>
<th>Orgiagton</th>
<th>Side of Lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke Sleep</td>
<td>87.56 (10.5)</td>
<td>43 (16.3)</td>
<td>2.56 (.88)</td>
<td>3 Left; 0 Right</td>
</tr>
<tr>
<td>Stroke No-sleep</td>
<td>68.78 (45.5)</td>
<td>48.21* (35)</td>
<td>2.63 (.81)</td>
<td>3 Left; 0 Right</td>
</tr>
</tbody>
</table>

First Experiment: after stroke are implicit and explicit learning differentially impacted by sleep?

- Half of groups explicitly taught a 10-element sequence of colors (explicit)
- Half of groups physically practice 10-element sequence of colors without knowledge of the existence of the repeating pattern (implicit)
- Half tested after sleep (sleep)
- Half tested after 12 hours awake (no-sleep)
Sleep associated improvements in tracking error for the implicit and explicit stroke group

Off-Line Learning: None of the control groups demonstrated sleep related off-line learning at retention

Off-Line Learning: Both the stroke sleep groups (Implicit and Explicit) demonstrated sleep related off-line motor learning at retention
Recall...
In young healthy people, sleep aides the formation of explicit but not implicit memories

Second Experiment: To determine the effect of sleep on components of the learned continuous motor task

Time Series Analysis

Accurate motor performance can relate to improved spatial or temporal accuracy
Time Lag of Tracking

Individuals with stroke show improvements in the time lag of tracking after sleep (-60 msec); older adults do not.

Time lag a Cerebellar function.

Spatial accuracy of Tracking

Individuals with stroke show improvements in spatial accuracy of tracking after sleep; older adults do not.

Spatial accuracy mediated by hippocampus and basal ganglia.

**Group Descriptives:** No difference in

- age ($p=0.875$)
- Stanford Sleepiness Scale at practice ($p=0.179$) or retention ($p=0.252$) (1=wide awake, 7=sleep soon)
- MMSE ($p=.131$)
- Pittsburgh sleep quality scale ($p=.776$)
- Geriatric Depression Scale (.270)
- average sleep ($p=0.458$) 7 hours
- time-post stroke ($p=.911$)
- Orpington ($p=.920$)
- UEFM ($p=.630$)
Discussion

Sleep enhances both explicit and implicit skill learning in post-stroke individuals.

Its impact on both time lag (cerebellum) and spatial accuracy (hippocampus and basal ganglia) suggest a widespread effect across distinct brain regions.

Discussion

Control participants did not benefit from sleep to promote skill learning and memory consolidation.

- Provide concurrent evidence that healthy older adults are not reliant on sleep for motor memory consolidation.

Why does sleep benefit individuals with stroke?
Aging and stroke change the time spent in different phases of sleep (Siensuukon & Boyd, 2009)

<table>
<thead>
<tr>
<th>Type of Sleep</th>
<th>Characteristic Activity</th>
<th>Characteristic Movement/Function Changes</th>
<th>Young Adults</th>
<th>TIA</th>
<th>Acute Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-rapid eye movement</td>
<td>See text</td>
<td>Low voltage, slow frequency, theta, alpha activity is absent</td>
<td>7.25</td>
<td>12.25</td>
<td>17</td>
</tr>
<tr>
<td>Stage 1</td>
<td>See text</td>
<td>Inconsistent sleep-wake cycle</td>
<td>2.5</td>
<td>7.12</td>
<td>13</td>
</tr>
<tr>
<td>Stage 2</td>
<td>See text</td>
<td>No delta waves, low voltage, irregular</td>
<td>10.62</td>
<td>20.62</td>
<td>30</td>
</tr>
<tr>
<td>Non-REM sleep</td>
<td>See text</td>
<td>High-frequency, low voltage theta activity</td>
<td>19.23</td>
<td>25.16</td>
<td>5</td>
</tr>
</tbody>
</table>

After stroke percent of REM sleep maintained, amount of stage 2 (and sleep spindles) increases

Why does sleep benefit individuals with stroke?

- Likely relate to differences in the content of sleep rather than the quantity of sleep
- However, was a moderate correlation between magnitude of improvement in tracking error and amount of total hours of sleep (r=.23)

Why does sleep benefit individuals with stroke?

- Shifts in percentage of sleep in REM and stage 2 SWS suggest that after stroke the brain is re-positioned to optimize learning
- Large increases in sleep spindles noted
- Speculate that these changes parallel others showing changes in synaptic plasticity associated with learning (ie. altered GABA and glutamate regulation)
Conclusions & Implications

These data should lead to:

Reorganization of rehabilitation and recovery to prioritize sleep
• An emphasis on the need for sleep between therapy sessions
• Efforts to address any underlying sleep disorders as rapidly and effectively as possible

Final Thought

“It’s practice, with sleep, that makes perfect”

(Walker, 2006)

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