Just sleep on it:
The role of sleep in recovery of motor function after stroke

Lara Boyd, PT, PhD

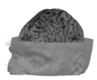
Assistant Professor, Dept. of Physical Therapy
& Brain Research Centre, University of British Columbia

Canada Research Chair, Neurobiology of Motor Learning

Michael Smith Foundation for Health Research Scholar

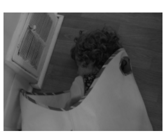
lara.boyd@ubc.ca

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

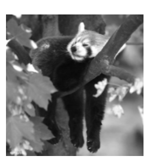


Sleep

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

Rechstchaffen & Siegal, 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

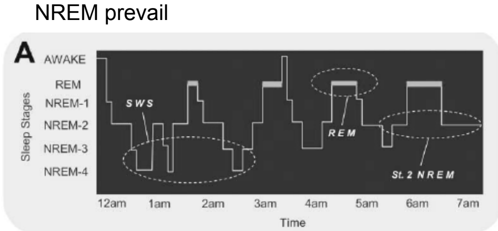
Stage of Sleep	Characteristic Activity	Characteristic Wave Form	Time Spent (Young Adults)
REM	muscle atonia; rapid eye movements	low-voltage, mixed-frequency pattern; PGO spikes	20-25%
NREM Stage 1	Slow rolling of eyes	sinusoidal alpha wave activity (10Hz)	about 5%
Stage 2		sleep spindles (12-14 Hz)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

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

<u>Memory Processing:</u>

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

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

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

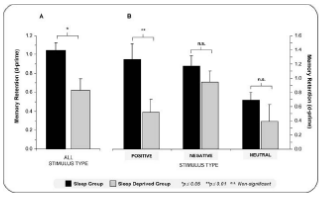
Sleep and Memory Processing

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

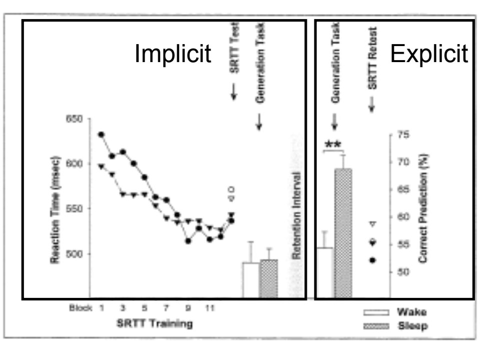
- **Consolidation** appears to be the stage most impacted by sleep
- **Consolidated** memory trace is fairly stable across time until recalled from memory for task practice and **reconsolidated** (which may also be sleep dependent)

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

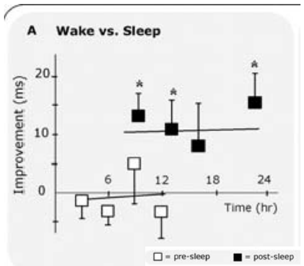
Sleep and Memory Consolidation

Procedural (implicit) memories are less well linked with sleep



(Fisher et al. 2006)

Motor skill improvement is related to sleep but not time

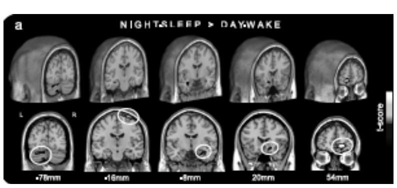


(Walker, 2006)

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 <u>next-day</u> 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

Type of Sleep	Characteristic Activity	Characteristic Waveform From Electroencephalograms	Time Spent (%) Young Adults	Older Adults	People With Stroke
↓ Rapid eye movement	Muscle atonia; rapid eye movements	Low-voltage, mixed-frequency pattern; ponto-geniculo-occipital spikes	17–23	13–20	17
Non-rapid eye movement					
↑ Stage 1	Slow rolling of eyes	Sinusoidal alpha wave activity (10 Hz)	3–7	7–12	13
↓ Stage 2		Sleep spindles (12–14 Hz) and K complexes	45–55	39–55	61
↓ Slow-wave sleep (stages 3 and 4)		High-amplitude slow delta waves (0.5–2 Hz)	19–25	5–16	5

(Siengsukon & Boyd, 2009)

Aging and stroke change the time spent in different phases of sleep

Type of Sleep	Characteristic Activity	Characteristic Waveform From Electroencephalograms	Time Spent (%) Young Adults	Older Adults	People With Stroke
Rapid eye movement	Muscle atonia; rapid eye movements	Low-voltage, mixed-frequency pattern; ponto-geniculo-occipital spikes	17–23	13–20	17
Non-rapid eye movement					
↓ Stage 1	Slow rolling of eyes	Sinusoidal alpha wave activity (10 Hz)	3–7	7–12	13
↑↑ Stage 2		Sleep spindles (12–14 Hz) and K complexes	45–55	39–55	61
Slow-wave sleep (stages 3 and 4)		High-amplitude slow delta waves (0.5–2 Hz)	19–25	5–16	5

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

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

Siengsukon, C. & Boyd, L.A. (2008) Sleep enhances implicit motor skill learning in individuals post-stroke. *Topics in Stroke Rehabilita*tion

Siengsukon, C.F., Boyd, L.A. (2009) Does Sleep Promote Motor Learning: Implications for Physical Rehabilitation. *Physical Therapy*.

Siengsukon, C.F., Boyd, L.A. (2009) Sleep enhances off-line spatial and temporal motor learning after stroke. *Neurorehabilitation and Neural Repair*.

Siengsukon, C.F., Boyd, L.A. (2009) Sleep to learn after stroke: Implicit and explicit off-line motor learning. *Neuroscience Letters*.

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:

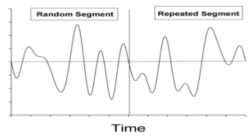
1. sleep/implicit,
2. sleep/explicit,
3. no-sleep/implicit,
4. no-sleep/explicit groups

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

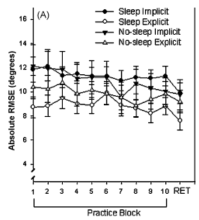
Group Characteristics

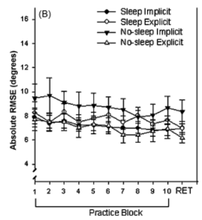
	Time post-stroke (month)	Fugl-Meyer	Orpington	Side of Lesion
Stroke Sleep	87.56 (60.9)	43 (16.1)	2.36 (.68)	3 Left; 6 Right
Stroke No-sleep	69.78 (43.5)	48.25* (15)	2.65 (.91)	3 Left; 6 Right

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)

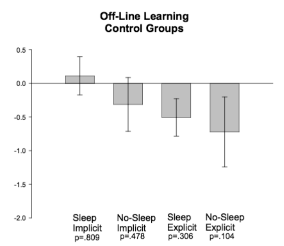
Sleep associated improvements in tracking error for the implicit and explicit stroke group



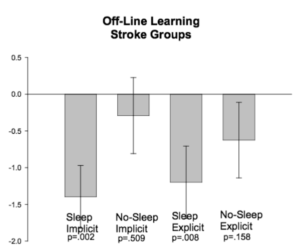


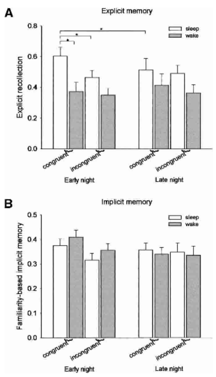
Stroke Controls

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

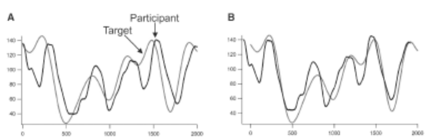




Recall…
In young healthy people, sleep aides the formation of explicit but not implicit memories

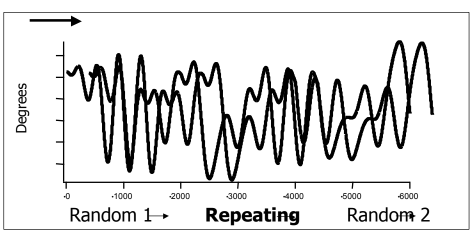
Drosopoulos et al, 2009

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

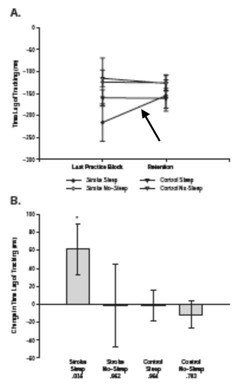


Wulf & Schmidt, 1997

Time Lag of Tracking

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

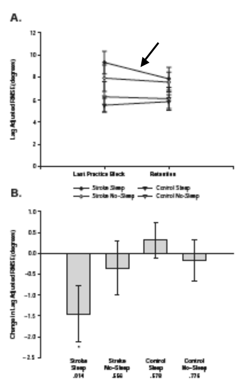
Time lag a Cerebellar function



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=.875)
- Stanford Sleepiness Scale at practice (p=.179) or retention (p=.252) (1=wide awake, 7=sleep soon)
- MMSE (p=.131)
- Pittsburgh sleep quality scale (p=.776)
- Geriatric Depression Scale (.270)
- average sleep (p=.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

Type of Sleep	Characteristic Activity	Characteristic Waveform From Electroencephalograms	Time Spent (%)		
			Young Adults	Older Adults	People With Stroke
Rapid eye movement	Muscle atonia; rapid eye movements	Low-voltage, mixed-frequency pattern; ponto-geniculo-occipital spikes	17–23	13–20	17
Non-rapid eye movement					
Stage 1	Slow rolling of eyes	Sinusoidal alpha wave activity (10 Hz)	3–7	7–12	13
Stage 2		Sleep spindles (12–14 Hz) and K complexes	45–55	39–55	61
Slow-wave sleep (stages 3 and 4)		High-amplitude slow delta waves (0.5–2 Hz)	19–25	5–16	5

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

(Siengsukon & Boyd, 2009)

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

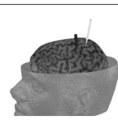
Final Thought

"It's practice, with sleep, that makes perfect"

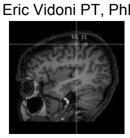
(Walker, 2006

Thanks to

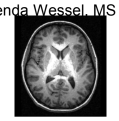
Catherine Siengsukon PT, PhD



Eric Vidoni PT, PhD



Brenda Wessel, MS PT



Bubblepreet Randhawa, MS, PT


UBC
Canada Foundation for Innovation
Fondation canadienne pour l'innovation
Canada Research Chairs
www.chairs-chaires.gc.ca
American Heart Association
Learn and Live®
BRITISH COLUMBIA
The Best Place on Earth
NORTH
GROWTH MANAGEMENT LTD.
Vancouver CoastalHealth
Research Institute
Healthier lives through discovery
KU
Michael Smith Foundation for
Health Research