The role of sleep in healthy brain ageing

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Overview

– Dementia background
– A few sleep fundamentals
– Evidence linking sleep and dementia
– Assessment of sleep disturbances in older people
– What treatments are available?
– Top ten tips for patients
What is dementia?

- Impairment of brain functions such as memory, language, executive functioning, personality, attention, processing speed
- Two key principals underlie the concept of dementia:
  1) Person has experienced decline from a previously higher level of functioning
  2) Significantly impaired ability to function at work or usual activities.
- Many different types of neurodegenerative dementia:
  - Alzheimer's disease (AD)
  - Vascular dementia (VaD)
  - Mixed dementia
  - Frontotemporal dementia (FTD)
  - Lewy Body dementia
  - Parkinson’s disease dementia
  - ............amongst others........
Rationale for Dementia Risk Reduction

Around 50% of the risk for Alzheimer’s disease is due to modifiable risk factors

Sperling et al., 2011; Dubois et al., 2007; Norton et al, 2014
Pathology in the brain leading to dementia occurs 10-20 years before symptoms emerge.

Sleep disturbance is a key feature of all the major dementias.
A few sleep fundamentals
The structure of nocturnal sleep

- Sleep is divided into 2 main types:
  - Non Rapid Eye Movement (NREM) divided into 4 stages
    - stage 1 (light sleep), 2, 3, 4
  - Rapid Eye Movement (REM)
- 90 min cycles
Sleep-wake activity is a balance between sleep pressure and circadian alerting signal.
How does the sleep-wake system change as we age?

- Shallow, fragmented
- Decreased slow wave sleep (deep sleep)
- Decreased Rapid eye movement (REM; dreaming) in second half
- Decreased sleep duration
- Daytime sleepiness
- Longer to recover from lack of sleep
- Circadian: decreased amplitude, advanced timing

The benefits of sleep

- Mood, alertness, wellbeing
- Regulation of immune responses and pro-inflammatory cytokines including IL-6, CRP, TNF-alpha
- Health effects (restriction = ↑ glucose sensitivity and ↑ insulin resistance, ↑ BP and heart rate)
- Synaptic density/strength/efficiency
What are the functions of sleep?

Hippocampal neurogenesis

Prolonged sleep loss/disruption may effect hippocampal neurogenesis

- Supports the production of new cells and their development into neurons
  - 1 day loss, little effect
  - Prolonged disruption leads to major decreases in hippocampal cell proliferation
- REM - cell proliferation
- NREM + REM - the number of cells that subsequently develop into adult neurons

Human studies:
- Sleep restriction and poor sleep quality are associated with smaller hippocampi
What are the functions of sleep?

Sleep Dependent Memory

Sleep spindles

Impaired memory processing
What about circadian rhythms?

- Co-regulates timing, structure and consolidation of sleep
- Generated by the suprachiasmatic nucleus (SCN) of the hypothalamus (‘Master clock’)
  - Regulated by environmental signals
  - Exerts circadian influence via many signals particularly melatonin, a hormone produced by the pineal gland
- Multiple age related changes
Sleep-wake problems in older adults

- 50% of older adults have chronic sleep complaints
  - Prevalence range 9-69%
- Insomnia: Most frequent complaint in later-life (rates 30-60% or 12-25% using more stringent criteria)
- Older adults twice as likely to be prescribed a sedative or hypnotic than younger adults
Obstructive sleep apnoea (OSA) is an emerging risk factor for dementia, increasing the risk of MCI and dementia at an earlier age.

How is sleep disturbance linked to cognitive decline?

- **Role of overnight sleep**
  - Glymphatic system – clearance of toxins, waste and b-amyloid
  - Immune/inflammatory regulation
  - Neurogenesis
  - Synaptic plasticity

- **Impaired sleep quality**
  - Sleep duration, insomnia
  - Night-time awakenings
  - Epigenetic mechanisms

- **Obstructive sleep apnoea**
  - Fragmented sleep
  - Hypoxemia
  - Oxidative stress/cardiovascular mechanisms

Obstructive sleep apnoea (OSA) is an emerging risk factor for dementia, increasing the risk of MCI and dementia at an earlier age.
Evidence linking sleep and dementia
Why are we concerned about sleep and brain degeneration?

- Alzheimer’s Disease:
  - Predictive of more rapid decline and shorter survival
  - Prospective studies: Poor self-reported sleep & PSG sleep quality increases risk

- Parkinson’s Disease
  - Prodromal feature
  - Linked to poor quality of life and depression

- Dementia with Lewy Bodies
  - REM Sleep Behaviour Disorder

Naismith, Rogers & Lewis 2011; Weldemichael & Gorssman, 2010; see Wu & Swaab, 2007
Is self-reported sleep quality a predictor of dementia?

- 18 longitudinal studies (n= 246,786) subjects at baseline and n=25,847 dementia cases after an average 9.49 y of follow-up.
- Subjects who reported sleep disturbances had a higher risk of incident all-cause dementia, AD, and vascular dementia, RR = 1.19.
Is sleep duration a predictor of dementia?

6 studies examined risk of MMSE cognitive decline (n = 46,068 subjects)

Pooled RR per 1 h increases in sleep duration was 0.99 (95% CI 0.97–1.01)

“The U” shaped curve with lowest point located at 7 h was detected

4 studies examined risk for MCI/dementia (n = 24305, 2718 cases)

The “J” shaped dose–response association between sleep duration and the risk of MCI/dementia was found (combined RR for per 1 h increases in sleep duration = 0.98, 95% CI 0.97–1.00)

Non-linear associations between sleep duration and the risks of mild cognitive impairment/dementia and cognitive decline: a dose–response meta-analysis of observational studies

Ying Liang¹ · Ling-Bo Qu² · Hao Liu¹

Aging Clinical and Experimental Research
https://doi.org/10.1007/s40529-018-1005-y

REVIEW
What is the nature of the sleep-wake changes in Alzheimer’s?

- 40-50% - sleep disturbance
- Daytime agitation, nocturnal insomnia, restlessness - ‘Sundowning’
- Hypersomnia
- Up to 40% of nocturnal time awake
- Daytime napping
- Predictive of more severe cognitive decline
- In early AD, linked to working memory, verbal fluency, memory change and executive functioning
- Linked to carer burden and institutional care

Bonanni et al, 2005; Cooke et al, 2006
AD: sleep architecture and circadian change

- Amplification of usual ageing changes
- More stage 1 sleep, fragmented sleep
- Predictive of more pronounced cognitive decline
- Sleep apnoea 35-63%
  - 33-70% have sleep disordered breathing
  - 70-80% of patients with dementia with AHI > 5
  - 48% with AHI > 20
- Reduced and poorly formed sleep spindles:
  - Related to memory consolidation
- Prominent circadian change
- Degeneration in SCN ⇒ decreased melatonin
- Neuropathological studies – decreased melatonin in pineal gland

Weldemichael & Gorssman, 2010; see Wu & Swaab, 2007
Sleep problems are common in people living with dementia and affect individuals and families. They include:

- Difficulty falling asleep
- Night-time awakenings
- Waking too early
- Excessive daytime sleepiness
- They may cause people with dementia to move to care homes
- So sleep problems may be more common in people with dementia living in care homes
- There are no systematic reviews or meta-analyses on this topic.

Method

We searched electronic databases to November 2017.

- Included: studies reporting prevalence or associates of sleep problems on validated questionnaires or actigraphy in people with dementia living in care homes
- Excluded: studies reporting sleep apnoea, restless legs syndrome, or circadian rhythms
- Two researchers independently decided if studies fulfilled inclusion criteria
- Two raters independently rated study quality according to criteria and reached consensus

Studies

- 52/172 papers included
- 45 on prevalence & 19 on associates
- We emailed authors for further papers and data
- Additional data received from 16 studies
- Most studies from Europe (35)
- Others from Australia (4), China (3), Japan (3), South Korea (2), USA (1), and Brazil (1)
- We meta-analysed pooled estimates of prevalence
- Synthesised reports of associated factors
- We divided sleep problems into:
  a. Clinically significant cases on validated questionnaires
  b. Any symptoms on validated questionnaires
  c. Night-time sleep problems measured on actigraphy

How prevalent are sleep problems?

- Measured on questionnaires
  - Clinically significant sleep problems: 17 studies; n=6860
  - Any symptoms of sleep problems: 27 studies; n=14,184
- Measured on actigraphy
  - Sleep efficiency <85%: 5 studies; n=240

What is associated with sleep problems?

- Longer time living in a care home
- Medication use (antidepressants, anxiolytics, AChEI, sedatives)
- Lower quality of life
- More neuropsychiatric symptoms (agitation, challenging behaviour, depression)
- Higher staff distress
- More agitation
- Higher anxiety
- More pain

Conclusions

- 20% of people with dementia living in care homes have clinically significant sleep problems
- Actigraphy (sleep efficiency <85%) may overestimate how many people have sleep problems as measuring movement
- However staff may not realise that residents are awake at night
- Both agitation and increasing dementia severity are associated with sleep problems on questionnaires and actigraphy
Are sleep-wake changes evident in Mild Cognitive Impairment (MCI)?

PSQI sleep disturbance: 63% of MCI and 44% of controls

<table>
<thead>
<tr>
<th></th>
<th>Unique R², %</th>
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<tbody>
<tr>
<td>Antidepressant use</td>
<td>ns</td>
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<tr>
<td>Time spent exercising</td>
<td>ns</td>
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<tr>
<td>Disability rating</td>
<td>ns</td>
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<tr>
<td>Age</td>
<td>0.9</td>
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<td>Depression</td>
<td>14.6</td>
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<tr>
<td>Alcohol</td>
<td>4.3</td>
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<tr>
<td>Education</td>
<td>3.4</td>
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<tr>
<td>MMSE</td>
<td>1.9</td>
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<tr>
<td>Shared predictor variance</td>
<td>10.4</td>
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</tbody>
</table>

Full model: R² = 35.5, n = 158 MCI

Method: 1) Forced entry, age; 2) Stepwise entry, all significant univariate predictors.
Non-significant univariate predictors include: Vascular risk factors (heart disease, diabetes, cholesterol, smoking history, hypertension), Body Mass Index, Medical burden, Anxiety

McKinnon et al 2014
Is sleep macroarchitecture altered in MCI?

Unpublished data, meta-analysis: 14 studies
- REM Latency (+31 mins)
- Total sleep time (-27 mins)
- Sleep efficiency -5%
- WASO (+18 mins)
- Latency (+6 mins)
- ODI (+10.8)
- Not SWS or AHI

### REM latency (standardised mean difference)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD Total</th>
<th>Weight</th>
<th>Weight Mean</th>
<th>Weight Mean Diff</th>
<th>W, F, 95% CI</th>
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<td>MCI vs Control</td>
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### Sleep efficiency (standardised mean difference)

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<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
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### Wake after sleep onset (standardised mean difference)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Weight Mean</th>
<th>Weight Mean Diff</th>
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How do sleep changes relate to brain integrity in Mild Cognitive Impairment?

Self-report and actigraphic sleep relates to decreased connectivity between temporal and parietal networks.

Self-report sleep relates to PET and CSF amyloid levels in healthy and MCI.

Increases in the wake promoting hormone orexin.

# Delving deeper: sleep microarchitecture in MCI

## Polysomnography

<table>
<thead>
<tr>
<th></th>
<th>Controls N=40</th>
<th>MCI N=60</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time, mins</td>
<td>363.4 (68.4)</td>
<td>352.7 (100.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Sleep efficiency/100</td>
<td>76.1 (10.6)</td>
<td>73.8 (14.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Lowest O2 desaturation, %</td>
<td>87.1 (5.1)</td>
<td>85.9 (5.2)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Sigma power (C3-M2), 12-15Hz</strong></td>
<td>0.73 (.2)</td>
<td>0.64 (.2)</td>
<td>* d=0.46</td>
</tr>
<tr>
<td>Slow spindle range</td>
<td>0.72 (.19)</td>
<td>0.64 (0.21)</td>
<td>**</td>
</tr>
<tr>
<td>Fast spindle range</td>
<td>0.49 (.19)</td>
<td>0.42 (.21)</td>
<td>ns</td>
</tr>
<tr>
<td>Delta, 1-4.5Hz</td>
<td>2.6 (.2)</td>
<td>2.5 (0.2)</td>
<td>*</td>
</tr>
<tr>
<td>Alpha, 8-12Hz</td>
<td>1.27 (.2)</td>
<td>1.16 (.2)</td>
<td>*</td>
</tr>
</tbody>
</table>

Naismith et al [isubmitted](#)
Mechanisms by which sleep may promote brain integrity: The Glymphatic system

- The interstitial/extracellular concentration of b-amyloid has circadian oscillation - higher in the wake (even in states of darkness) state than the sleep state.
- Xie et al in Science (2013) showed that sleep clears B-amyloid via the glymphatic system, particularly in slow wave sleep.
- Sleep deprivation accelerates amyloid plaque deposition, whilst promoting sleep with orexin antagonists inhibits plaque formation.
Are circadian rhythms linked to cognitive decline?

Brain effects of circadian misalignment:

Altered timing of melatonin onset in MCI: associations with memory performance

Naismith et al, 2014
Sleep-Wake Disturbances in Parkinson’s Disease

- Sleep fragmentation
  - Insomnia (early, mid & late)
  - Discomfort (Wearing Off, Dystonia, Nocturia)
- Daytime somnolence
- Rapid Eye Movement sleep behaviour disorder (RBD)
- Restless legs syndrome (RLS)
- Sleep-disordered breathing
Look out for REM Sleep Behaviour Disorder

- Prodromal feature of Parkinson’s disease and Dementia with Lewy Bodies (80% of RSBD cases progress to DLB)
- Loss of normal muscle atonia during REM sleep
- Dream enactment behaviour
- Congruent motor activity
  - Punching or shouting
- Injury
  - Self & bed partner 33%

People with RSBD 120 more likely to develop these neurodegenerative diseases up to 20 years later
Diagnostic Criteria

- **International Classification of Sleep Disorders (ICSD) – 2**
  - REM without atonia during a sleep study
  - Abnormal REM behaviour on a sleep study
  - History of sleep related injury
  - Absence of REM related epileptiform activity
  - Absence of other potential etiology such as drug related, OSA

Limitations

- Scoring of REM sleep difficult in PD
  - Multiple arousals
- Subjective interpretation of RWA
  - Can be highly variable
- Limited access to PSG
  - Actigraphy
  - Questionnaires
Melatonin secretion in PD

- Early stage but treated PD & Controls
- Plasma melatonin (every 30 mins)
- No phase differences (advance or delay)
- Lower Area UC

Videnovic et al JAMA Neurol 2014

Does dopaminergic treatment influence circadian disturbance?

- 27 healthy controls
- Patient groups (matched)
  - 13 unmedicated patients
  - 16 medicated patients
How is sleep disordered breathing linked?

Sleep disordered breathing is associated with:

- Cognitive impairment on fronto-subcortical tasks (Naismith et al 2014)
- MCI + dementia 5 years later (Yaffe et al 2011)
- Neuropsychological dysfunction in MCI (Terpening et al 2014)
- Increased dementia risk at 15-year follow-up n=1081, part. Severe OSA (AHI>30) OR = 2.35 (Lutsey et al 2017)
- Meta-analysis, n>4million, SDB 26% more likely to develop cognitive impairment (Leng et al 2017)
How is sleep disordered breathing linked?

Is Obstructive Sleep Apnoea Related to Neuropsychological Function in Healthy Older Adults? A Systematic Review and Meta-Analysis

Nathan Cross, Amit Lappé, Jonathon Pe, Ronald R. Grahn, Nathaniel Marshall, S. L. N. N.

Participants: Healthy participants with a mean age > 50 years.

Diagnosis: Only objectively defined OSA as measured by a validated sleep apnoea diagnostic device.

Comparisons: Matched controls with AHI < 5.

Outcome measures: Scores on standardised neuropsychological tests.

Study design: Cross-sectional or case-control data. Correlations between cognitive outcomes and measure of OSA severity (i.e. AHI) were included.

13 studies

Forest plot of individual mean and weighted effect sizes across all cognitive domains. Effect size estimates are based on a random-effects model.

Subgroup analyses of moderators of the association between neuropsychological performance and OSA. Q-test was performed for between-group heterogeneity, using a mixed effects model.
Oxygen desaturation particularly problematic

Linked with reduced cortical thickness in temporal lobes bilaterally, which in turn is associated with poorer memory

N = 83 ‘at risk’ of dementia

<table>
<thead>
<tr>
<th>Variables included in analysis</th>
<th>Component 1: ‘Oxygen desaturation’</th>
<th>Component 2: ‘Sleep disturbance’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnoea-Hypopnea Index</td>
<td>0.774</td>
<td>0.489</td>
</tr>
<tr>
<td>Oxygen Desaturation Index</td>
<td>0.856</td>
<td>0.311</td>
</tr>
<tr>
<td>%TST Saturation O\textsubscript{2} below 90%</td>
<td>0.842</td>
<td>0.154</td>
</tr>
<tr>
<td>Lowest saturation O\textsubscript{2} (inverted)</td>
<td>0.855</td>
<td>-0.115</td>
</tr>
<tr>
<td>Sleep Efficiency (inverted)</td>
<td>0.001</td>
<td>0.768</td>
</tr>
<tr>
<td>Awakening Index (n/hr)</td>
<td>0.115</td>
<td>0.780</td>
</tr>
<tr>
<td>Arousal Index (n/hr)</td>
<td>0.454</td>
<td>0.734</td>
</tr>
<tr>
<td>Variance explained</td>
<td>42.8%</td>
<td>30.1%</td>
</tr>
</tbody>
</table>


Shaded cells represent the variables contributing to each component (loading > 0.5)

Cross et al, Eur R Journal, 2018
Functional significance

- 19 MCI (50–79; mean 67.8 years)
- 23 Controls (51–78; mean 63.3 years)
- Neuropsychological, medical assessment
- Sleep lab at Brain and Mind Centre
- No difference in demographic or sleep architecture
- AusEd\textsuperscript{TM} driving simulator

In MCI, driving crashes, steering and speed deviations relate to having oxygen desaturation during sleep.
Assessment of sleep disturbances in older people
Ways to assess sleep

1. Questionnaires and clinical interview

The Pittsburgh Sleep Quality Index (PSQI)

Instructions: The Pittsburgh Sleep Quality Index (PSQI) assesses sleep quality and patterns over the past month. This scale should indicate the most accurate way for the majority of days and nights in the past month. Please answer all questions. The score ranges from 0 to 21.

- 1.5 How often do you wake up at night? (0 never, 1 = once a week, 2 = 2-3 times a week, 3 = 4-5 times a week, 4 = 6-7 times a week)
- 2.5 How satisfied are you with your sleep? (0 = very dissatisfied, 1 = dissatisfied, 2 = neutral, 3 = satisfied, 4 = very satisfied)
- 3.5 How disrupted is your sleep by nighttime awakenings? (0 = not at all, 1 = a little, 2 = moderately, 3 = a lot)
- 4.5 How often do you take daytime naps? (0 = never, 1 = once a week, 2 = 2-3 times a week, 3 = 4-5 times a week, 4 = 6-7 times a week)
- 5.5 How many minutes of sleep did you lose due to nighttime awakenings? (0 = none, 1 = 1-2 minutes, 2 = 3-5 minutes, 3 = 6-10 minutes, 4 = 11-20 minutes, 5 = 21-30 minutes)
- 6.5 How often do you use alcohol or drugs to help you fall asleep or stay asleep? (0 = never, 1 = once a week, 2 = 2-3 times a week, 3 = 4-5 times a week, 4 = 6-7 times a week)
- 7.5 How many hours of sleep do you need to feel rested? (0 = 1-2 hours, 1 = 3-4 hours, 2 = 5-6 hours, 3 = 7-8 hours, 4 = 9-10 hours, 5 = 11-12 hours)
- 8.5 How many hours of sleep did you get last night? (0 = 1-2 hours, 1 = 3-4 hours, 2 = 5-6 hours, 3 = 7-8 hours, 4 = 9-10 hours, 5 = 11-12 hours)
- 9.5 How satisfied are you with your sleep? (0 = very dissatisfied, 1 = dissatisfied, 2 = neutral, 3 = satisfied, 4 = very satisfied)

2. Diary and Actigraphy

Sleep Diary

3. PSG

Schematic representation of the PSG

4. Melatonin

Graph showing melatonin levels over time
How to assess for sleep disturbance in community dwelling older people

**Polysomnography**

- Sleep efficiency, duration, oxygen desaturation, apnoea-hypopnoea index in REM and Non-REM sleep
- **Pros:** detects sleep disorders undetected by other means
- **Cons:** costly, waiting lists, artificial environment

**Actigraphy, with sleep diary**

- Sleep latency (from diary), Sleep efficiency (from software), Nighttime behavior (visual), Sleep duration (from software), Circadian rhythmicity (wake time from software and visual inspection), Sleep behaviours (from diary)
- **Pros:** Ecological validity, gives markers of circadian rhythmicity
- **Cons:** Some specialized knowledge/training to score

**Self-report**

- Pittsburgh Sleep Quality Index (>5)
- Insomnia Severity Index (>7)
- Multivariate Apnoea Index
- Berlin Questionnaire
- Epworth Sleepiness Scale
- **Pros:** Quick, easy to administer, clinical cutoffs
- **Cons:** Sometimes poor correlation with polysomnography, may be hindered by poor recall in those with cognitive impairment, may be linked to depressive symptoms
# Pittsburgh Sleep Quality Index (cognitively intact, ?MCI)

**Sleep Quality Assessment (PSQI)**

**What is PSQI, and what is it measuring?**

The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month.

**INSTRUCTIONS:**

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

## During the past month,

1. When have you usually gone to bed?
2. How long (in minutes) have you taken you to fall asleep each night?
3. What time have you usually gotten up in the morning?
4. A. How many hours of actual sleep did you get at night?
   B. How early/late were you in bed?

### Scoring

<table>
<thead>
<tr>
<th>Component</th>
<th>Score</th>
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<tbody>
<tr>
<td>Component 1</td>
<td>KS Score</td>
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<tr>
<td>Component 2</td>
<td>KS Score + (50-100)</td>
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<tr>
<td>Component 3</td>
<td>HS Score + (10-20)</td>
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<tr>
<td>Component 4</td>
<td>Total of 4 items x 100 + (50-100)</td>
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<tr>
<td>Component 5</td>
<td>Total of 4 items x 100</td>
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<tr>
<td>Component 6</td>
<td>MS Score</td>
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<tr>
<td>Component 7</td>
<td>PS Score</td>
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</tbody>
</table>

Add the seven component scores together __________________  Global PSQI  _______________

A total score of “5” or greater is indicative of poor sleep quality.

If you scored “5” or more it is suggested that you discuss your sleep habits with a healthcare provider.

---

Add items: Score of ≥5 – sleep disturbance
Epworth Sleepiness Scale

Add items:
Score of ≥8 → refer for PSG
Screening for Sleep Apnoea

Berlin Questionnaire

1. Complete the following:
   Height: ___________ Weight: ___________
   Age: ___________ Gender: ___________

2. Do you snore?
   ____ Yes
   ____ No
   ____ Don’t know

If you snore:

3. Your snoring is...
   ____ Slightly louder than breathing
   ____ As loud as talking
   ____ Louder than talking
   ____ Very loud, can be heard in adjacent rooms

4. How often do you snore?
   ____ Nearly every day
   ____ 3-4 times a week
   ____ 1-2 times a week
   ____ 1-2 times a month
   ____ never or nearly never

5. Has your snoring ever bothered other people?
   ____ Yes
   ____ No

6. Has anyone noticed that you quit breathing during your sleep?
   ____ Nearly every day.
   ____ 3-4 times a week
   ____ 1-2 times a week
   ____ 1-2 times a month
   ____ never or nearly never

7. How often do you feel tired or fatigued after your sleep?
   ____ Nearly every day
   ____ 3-4 times a week
   ____ 1-2 times a week
   ____ 1-2 times a month
   ____ never or nearly never

8. During your wake time, do you feel tired, fatigued, or not up to par?
   ____ Nearly every day
   ____ 3-4 times a week
   ____ 1-2 times a week
   ____ 1-2 times a month
   ____ never or nearly never

9. Have you ever nodded off or fallen asleep while driving a vehicle?
   ____ Yes
   ____ No
   ____ If yes, how often does it occur?
   ____ Nearly every day.
   ____ 3-4 times a week
   ____ 1-2 times a week
   ____ 1-2 times a month
   ____ never or nearly never

10. Do you have high blood pressure?
    ____ Yes
    ____ No
    ____ Don’t know

BMI (Body mass index) = ___________

(see next page for scoring instructions)

Scoring the Berlin Questionnaire
The questionnaire consists of 3 categories related to the risk of having sleep apnoea. Patients can be classified into High Risk or Low Risk based on their responses to the individual items and their overall scores in the symptom categories.

Categories and Scoring:

- **Category 1:** items 2, 3, 4, 5, and 6;
  - Item 2: if ‘Yes’, assign 1 point
  - Item 3: if either of the last two options is the response, assign 1 point
  - Item 4: if either of the first two options is the response, assign 1 point
  - Item 5: if ‘Yes’ is the response, assign 1 point

- **Category 2:** items 7, 8, and 9;
  - Item 8: if either of the first two options is the response, assign 1 point
  - Item 9: if ‘Yes’ is the response, assign 1 point

Add points. Category 1 is positive if the total score is 2 or more points.

- **Category 3** is positive if the answer to item 10 is ‘Yes’ or if the BMI of the patient is greater than 30kg/m². (BMI is defined as weight (kg) divided by height (m) squared, i.e., kg/m²).

High Risk: if there are 2 or more categories where the score is positive.

Low Risk: if there is only 1 or no categories where the score is positive.

Additional Question: item 9 should be noted separately.

If ‘high risk’ refer for sleep study

Others: MAP, STOP, STOP_BANG

Note: not validated for older people with cognitive impairment
Sleep Disorders Inventory

- Frequency, severity and caregiver burden of sleep disturbances 2-weeks prior
- Prevalences of sleep symptoms 3 (waking up during the night thinking its daytime) to 82% (getting up during the night)
- 7 items
- Score = average of frequency ratings x average of severity ratings (range – 12).
1. Look at sleep-wake patterns across 7-14 days
2. Look at activity levels during waking and sleep periods
3. Can detect delayed timing, advanced timing, irregular timing of sleep
4. Sleep onset, wake times, light, daytime naps, getting up at night
## Sleep diary

<table>
<thead>
<tr>
<th>DATE</th>
<th>LAST NIGHT I WENT TO BED AT</th>
<th>THIS MORNING I WOKE UP AT</th>
<th>LAST NIGHT I FELL ASLEEP IN</th>
<th>WHEN I WOKE I FELT</th>
<th>MY SLEEP WAS DISTURBED BY</th>
<th>DID YOU HAVE A NAP YESTERDAY?</th>
<th>IN THE 3 HOURS BEFORE BED, I HAD</th>
<th>DID YOU EXERCISE YESTERDAY?</th>
<th>DURATION</th>
<th>INTENSITY (1 - 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAY 1</td>
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<td>DAY 7</td>
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</tbody>
</table>
REM sleep Behaviour Disorder

- Vivid dreams?
- Dreams have an action-packed content?
- Dream contents match behaviour?
- Limbs move while sleeping?
- Hurt/almost hurt bed partner?
- Speaking/shouting/swearing
- Kicking/waving/saluting?
- Things fall down?
- Awoken by own movements?
- Remember dream contents well?
- Disturbed sleep?

Score >5 suggestive of RBD?

- Mostly widely used screening questionnaire
- Validated against the current diagnostic guideline
  - 84% sensitivity, 96% specificity
Have you ever been told, or suspected yourself that you seem to ‘act out your dreams’ while asleep for example, punching, flailing your arms in the air, making running movements?

Compared to current guideline
- 94% sensitivity
- 87% specificity
Polysomnography

Summary

Sleep Architecture

- Total sleep period (min) = 443.0
- Total sleep time (min) = 423.5
- Wake after sleep onset (min) = 25.0
- Sleep efficiency (%) = 92.6
- Sleep latency (min) = 4.5
- REM latency (min) = 86.0
- NREM sleep (min) = 326.0
- REM sleep (min) = 97.5

Respiratory*, Movement and arousal events

- Total AH1 (events/hr) = 0.7
- RERA index = 0.0
- RDI in REM (events/hr) = 2.5
- Minimum SpO2 during sleep (%) = 93
- ODI (desat/hr) = 0.7
- Total RDI (events/hr) = 0.7
- RDI in NREM (events/hr) = 0.2
- PLM Index (PLM/hr) = 0.3
- Limb Movement (Movement/hr) = 6.5
- Total arousal index (arousals/hr) = 6.1

(*Respiratory events = see page 4 for definition of apneas, hypopneas and RERA)
What treatments are available?
Things to considering when assessing and considering treatment options for sleep

- Depression
- Sleep disordered breathing
- Sleep expectations
- Medical conditions
- Medications
- Body mass index
- Sleep apnoea
- Exercise (not enough, wrong times)
- Raised core body temperature
- Lighting
- Nocturia, pain, discomfort
- Alcohol use
- Thyroid, menopause
- Circadian misalignment
- PLMS, Restless legs
Non-drug treatments for sleep in dementia

Studies: 2015-2017

Table 1. Results of trials testing nonpharmacological treatments

<table>
<thead>
<tr>
<th>Study</th>
<th>Strategy</th>
<th>Control group</th>
<th>Participants</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gibson et al. [17]</td>
<td>Mixed (light therapy, exercise, sleep education)</td>
<td>None</td>
<td>Fifteen community-dwelling dyads of carers and people with dementia</td>
<td>40% Dropout; Six participants improved</td>
</tr>
<tr>
<td>Tewary et al. [18]</td>
<td>Sleep education program for caregivers</td>
<td>None</td>
<td>Fourteen people with dementia (and carers)</td>
<td>50% Dropout; Improved sleep problems</td>
</tr>
<tr>
<td>Sekiguchi et al. [19]</td>
<td>Bright light therapy 1 h daily for 2 weeks</td>
<td>None</td>
<td>Seventeen people with dementia (people with Alzheimer’s disease, 8; people with vascular dementia, 4; DLB, 5)</td>
<td>Improved sleep disturbance in 4/17 mild-to-moderate patients with Alzheimer’s disease</td>
</tr>
<tr>
<td>Lai et al. [20]</td>
<td>Music with movement</td>
<td>Not applicable</td>
<td>Results not available</td>
<td>Not known</td>
</tr>
<tr>
<td>Krolak-Salmon et al. [21]</td>
<td>Multidisciplinary team intervention</td>
<td>None</td>
<td>424 people with dementia</td>
<td>Overall neuropsychiatric symptoms reduced in 329 people with data</td>
</tr>
<tr>
<td>Lazarou et al. [22]</td>
<td>Smart home/assistive technology</td>
<td>None</td>
<td>Four people with dementia</td>
<td>Improved sleep</td>
</tr>
<tr>
<td>Kodama et al. [23]</td>
<td>Physical activity reference values for a good sleep–wake pattern</td>
<td>None</td>
<td>117 older community-dwelling participants; 52 with dementia</td>
<td>51–55 min activity per day needed</td>
</tr>
</tbody>
</table>

DLB, people with dementia with Lewy bodies.
Brief behavioural therapy for cognitively intact older adults

- 4 sessions of (brief behavior therapy for insomnia) BBTi vs. self-monitoring control
- Improvements in sleep onset latency, wake after sleep onset, sleep efficiency, sleep quality, post-treatment and at 3-months follow-up
- Mood improvements in both groups
- No cognitive improvements on neuropsychological measures

McCrae et al, 2018
Cognitive Behaviour Therapy for MCI: “Sleep-well, think well” CBTi

- 8-week (4 session) pilot group intervention for MCI
  - 16 active treatment, 12 received information only
- Large effect size improvements:
  - Self-reported sleep quality, daytime sleepiness
  - Small to moderate (but non-significant) improvements in actigraphy (WASO, efficiency) and executive functioning.

![Graph showing ESS and PSG improvements over baseline and follow-up times.]
eCBTi in older men with depression - SOMNAGlozier et al in press, ANZJP

- RCT, n = 87 males, MDD

Relative ES at 12/52 = 0.35

Mean difference PHQ-9 4.3 (95% CI -1.2 to 9.8)
Sleep interventions for carers

6 session DREAMS-START (Dementia RELAted Manual for Sleep; STraTEgies for ReLaTives)

**Development Process of the DREAMS START Manual**

**Stage 1**
Background literature

Search for evidence regarding sleep disturbances in dementia and interventions to improve it.

**Stage 2**
First draft

Use the teams expertise in clinical interventions in dementia and sleep to develop the first draft of the manual.

**Stage 3a**
Focus group

Participants (Pts): 2 current & 2 former carers from the ASRN* Aim: initial thoughts on the first draft of the manual.

**Stage 3b**
Virtual reference group

Pts: The 4 carers from focus group + 3 more ASRN* members. Aim: Feedback on the manual via email, in parallel with 3a.

**Stage 4**
Facilitator versions made

Another version of the manual developed, with added prompts for the therapists.

**Stage 5**
Ongoing refinement

Ongoing refining by rehearsal through practising and getting feedback.

**Stage 6**
Therapists’ sign off

Therapists were required to demonstrate competency and accuracy in delivering the manual by role play.

**Stage 7**
Modified for clarity

Amendments made to the content and layout to form final versions of manuals for the trial.

**Stage 8**
Manual used in trial

Final versions of carer and facilitator manuals used for the trial.

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* ASRN = Alzheimer’s Society Research Network

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**ABSTRACT**

Background: 40% of people with dementia have disturbed sleep but there are currently no known effective treatments. Studies of sleep hygiene and light therapy have not been proven to include feasibility and acceptability and have shown 63-80% cessation. We had the feasibility and acceptability of a six-session manualized evidence-based non-pharmacological therapy Dementia RELAted Manual for Sleep; STraTEgies for ReLaTives (DREAMS-START) for sleep disturbances in people with dementia.

**Methods:** We conducted a parallel, two-armed, single-blind randomized trial and randomized 2:1 to intervention: Treatment as Usual. Eligible participants had dementia and sleep disturbances (score 5 or more Sleep Disorders Inventory) and a family carer and were recruited from two London memory clinics and the Dementia Research. Participants were an automatic for two weeks pre-randomization. Trained, clinically supervised psychology graduates delivered DREAMS-START in care setting in a intervention covering Understanding sleep and dementia: Making a plan (incorporating actigraphy information, light exposure using a light box), Dreaming and mindfulness: Difficult: night-time behaviors: Taking care of your own (inner) sleep and What worked Strategies for the future. Carers kept their manual, light box, and actigraphy records prior to intervention. Dementia assessment was masked to allocation. The co-primary outcomes were feasibility (76%) and eligible people consenting to the study) and acceptability (75% of intervention group attending 6 intervention sessions).

**Results:** In total, 46% of 69 (66%), 95% CI 56-76% eligible referrals consented between 01/08/2015 and 24/03/2017, 62 (65%), 95% CI 55-73% were randomized and 37 out of 42 (88%), 95% CI 75-96% adhered to the intervention.

**Conclusions:** DREAMS-START for sleep disorders in dementia is feasible and acceptable.
## Sleep disturbing psychototropic medications

<table>
<thead>
<tr>
<th>Drug Interventions</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cholinesterase Inhibitors</strong></td>
<td>Benefits to REM sleep, some studies, Donepezil – more Stage 2 and less Stage 1 sleep</td>
</tr>
<tr>
<td>(e.g. Aricept)</td>
<td>Can cause insomnia, disturbing dreams, REM Sleep Behaviour Dis.</td>
</tr>
<tr>
<td></td>
<td>No studies examine effects on memory, but beneficial effects in healthy or young samples</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td>May suppress REM, insomnia</td>
</tr>
<tr>
<td>(e.g. Zoloft)</td>
<td></td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td>May exacerbate sleep-wake disturbance in AD</td>
</tr>
<tr>
<td>(e.g. Seroquel)</td>
<td></td>
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<tr>
<td><strong>Sedative hypnotics</strong></td>
<td>Less disruption to sleep architecture</td>
</tr>
<tr>
<td>(e.g. Stillnox)</td>
<td>No known data on cognitive effects</td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Decrease SWS &amp; REM, reduce latency &amp; awakenings</td>
</tr>
<tr>
<td>(e.g. Valium)</td>
<td>Associated with EDS, falls, cognitive side-effects, confusion, Short-term use only</td>
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<tr>
<td></td>
<td>Clonazepam often effective for REM Sleep Behaviour Disorder</td>
</tr>
</tbody>
</table>

Naismith, Rogers, Lewis 2010; Cooke et al, 2006
## Other sleep disturbing medications

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Example of use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Blood pressure, glaucoma</td>
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<tr>
<td>Anticholinergics</td>
<td>COPD</td>
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<tr>
<td>Antihypertensives</td>
<td>High blood pressure</td>
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<tr>
<td>Corticosteroids (Prednisone)</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>H2 blockers (Zantac, Tagamet)</td>
<td>Gastroesophageal reflux or peptic ulcers</td>
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<tr>
<td>Levodopa, dopamine agonists</td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Adrenergic drugs</td>
<td>For life threatening events – e.g. asthma, cardiac arrest</td>
</tr>
</tbody>
</table>
Benzos do not seem to help sleep in AD.

REVIEW

Use of Benzodiazepines in Alzheimer’s Disease: A Systematic Review of Literature

Michaela DeFrancesco, MD, PhD, MSc; Josef Marksteiner, MD; W. Wolfgang Fleischhacker, MD; Imrich Blasko, MD, MSc

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Correspondence: Michaela DeFrancesco, MD, PhD, MSc, Department of Psychiatry and Psychotherapy, Division of General and Social Psychiatry, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria (Michaela.DeFrancesco@i-med.ac.at).

Abstract

Background: Benzodiazepines are frequently prescribed in patients with Alzheimer’s disease. Unfortunately, studies evaluating their benefits and risks in these patients are limited.

Methods: Clinical trials focusing on the effect of benzodiazepines on cognitive functions, disease progression, behavioral symptoms, sleep disturbances, and the general frequency of benzodiazepine use were included in this review. Published articles from January 1983 to January 2015 were identified using specific search terms in MEDLINE and PubMed Library according to the recommendations of The Strengthening the Reporting of Observational Studies in Epidemiology Initiative.

Results: Of the 557 articles found, 18 articles met predefined selection criteria and were included in this review (8 on frequency, 5 on cognitive functions, 5 on behavioral and sleep disturbances). The frequency of benzodiazepine use ranged from 8.5% to 20%. Five studies reported accelerated cognitive deterioration in association with benzodiazepine use. Two studies reported clinical efficacy for lorazepam and alprazolam to reduce agitation in Alzheimer’s disease patients. No evidence was found for an improvement of sleep quality using benzodiazepines.

Conclusion: This systematic review shows a relatively high prevalence of benzodiazepine use but limited evidence for clinical efficacy in Alzheimer’s disease patients. However, there is a paucity of methodologically high quality controlled clinical trials. Our results underscore a need for randomized controlled trials in this area.

International Journal of Neuropsychopharmacology, 2015
Drug treatments for dementia

“A Cochrane review on pharmacotherapies: No definitive randomised controlled trial (RCT) evidence of improvements in actigraphy measures for melatonin, trazodone or ramelteon. Trazodone 50mg at night showed some potential for increased nocturnal sleep time and sleep efficiency in Alzheimer’s disease, but confirmation awaits a larger trial. Notably, no RCTs were found of medications such as hypnotics that are widely prescribed for sleep problems in dementia”

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Control group</th>
<th>Participants</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong et al. [28]</td>
<td>Melatonin</td>
<td>Placebo-controlled randomised trials (meta-analysis)</td>
<td>453 with dementia (305 with Alzheimer’s disease, 287 with primary outcome)</td>
<td>Negative primary outcome sleep efficiency (N= 287), but improved nocturnal sleep time (N = 305)</td>
</tr>
<tr>
<td>Macias Saint-Gerons et al. [29]</td>
<td>Trazodone</td>
<td>Naturalistic study of Spanish population</td>
<td>11766 individuals aged over 65 years</td>
<td>Increased use of trazodone for dementia and sleep problems</td>
</tr>
<tr>
<td>Labin et al. [30]</td>
<td>Dispersing of drugs with sedative properties (benzodiazepines, trazodone, quetiapine)</td>
<td>Naturalistic study of Canadian population</td>
<td>1181 469–1 603 809 individuals Aged over 66 years with drug benefit 2002–2013</td>
<td>Increased use of trazodone and decreased use of benzodiazepines over time, especially in those with dementia</td>
</tr>
<tr>
<td>Scorzalick et al. [31]</td>
<td>Mirtazapine, 15 mg</td>
<td>Placebo-controlled randomised trial</td>
<td>24 with Alzheimer’s disease</td>
<td>Increased daytime sleepiness Did not increase sleep efficiency or nocturnal sleep time</td>
</tr>
<tr>
<td>Leonpacher et al. [32*]</td>
<td>Citalopram, 30 mg (secondary analysis)</td>
<td>Placebo-controlled randomised trial</td>
<td>186 with Alzheimer’s disease</td>
<td>Increase in the severity of sleep disturbances in those with these present at week 9</td>
</tr>
<tr>
<td>Altnyazar et al. [33]</td>
<td>Agomelatine, 25 mg</td>
<td>No control, case study</td>
<td>A 91-year-old woman with Alzheimer’s disease</td>
<td>Improved both insomnia and depression</td>
</tr>
<tr>
<td>Kazui et al. [34]</td>
<td>Donepezil, 5 mg</td>
<td>24 healthy controls</td>
<td>16 DLB (8 with sleep disturbances at baseline)</td>
<td>Inconclusive but tendency towards decreased sleep disturbances in DLB at 14 weeks</td>
</tr>
<tr>
<td>Ishikawa et al. [35]</td>
<td>Memantine, 20 mg</td>
<td>None</td>
<td>12 with Alzheimer’s disease</td>
<td>Improved sleep and was well tolerated</td>
</tr>
</tbody>
</table>

DLB: people with dementia with Lewy bodies

The management of sleep disorders in dementia: an update.
Kinnunen, Kirsi; Vikhanova, Anastasia; Livingston, Gill
DOI: 10.1097/YCO.0000000000000370
Light therapy

• General principles:
  • Evening exposure delays sleep
  • Morning exposure advances sleep
  • Magnitude of circadian shifts depends on intensity and duration - brighter and longer duration produces larger shifts
  • Short wavelength light (blue light) has greatest effects

• Efficacy:
  • Reduction in nighttime awakenings in dementia
  • Benefits best for morning light and if sleep complaints (latency, efficiency, awakenings, total sleep time)
  • May have broader effects on cognition and mood in AD
  • Combination of light and melatonin may have superior effects
Studies of light therapy

- Healthy older people:
  - Munch et al: 2011: $n = 10$ older individuals
  - 2-hours of blue-enriched polychromatic light per day over 13 days delayed circadian timing by nearly 2-hours

- Nursing home residents:
  - Alessi: RCT, $n = 118$ nursing home residents
    - >30minutes exposure to sunlight (10,000lx)
    - Decreased daytime sleep and less nocturnal awakenings, increase in social activities

- People with dementia:
  - Riemersma RCT: $n = 189$ residents, most of whom had dementia
    - 4-weeks bright light (1000lx) all day (09:00-18:00) vs. dim (300lx) light. 19% reduction in depressive symptoms, 53% improvement in functioning and 5% improvements in cognition similar to found with cholinesterase inhibitors.

See review by Hanford and Figueiro, 2013
Melatonin

- Chronobiotic
- A powerful antioxidant & free radical scavenger
- Helps to clear harmful reactive oxygen species and reduce oxidative stress levels in brain tissue, as well as beta-amyloid in animal studies

- 6 melatonin administration studies in MCI
  - 5 double-blind, 1 open-label retrospective (n=651)
  - Doses: 1-9mg administered evening or bedtime
  - Duration 10 days to 3.5 years
  - Improvements in sleep quality and cognition, including psychomotor speed, set-shifting, memory

Cardinali et al, 2010; Dowling et al, 2008; Riemersma et al, 2007
Meta-analysis of melatonin trials in AD

- 7 studies (n = 462), duration 10 days to 24 weeks.
- AD subjects receiving melatonin treatment showed prolonged total sleep time at night (n = 305; SMD: 0.26).
- No improvements in cognition (MMSE or ADAS-Cog).
- The discontinuation rate was similar between the melatonin and placebo groups.
Treatment for REM Sleep Behaviour Disorder in PD

Melatonin 3-12mg at bedtime
- REM sleep most strongly regulated or modulated by the circadian timing system
- 31/38 patients reported improvements: 1 case report, 2 open-label prospective case series (iRBD), 2 retrospective case series
- Successfully treated patients include DLB, PD and MSA, Memory problems, sleep-disordered breathing
- Side effects - headache, sleepiness (AM), delusions/hallucinations
- Follow-up: effective and safe 2y

Clonazepam 0.25mg to 2mg, 30 minutes at bedtime
- Long acting benzodiazepine
  - Elimination half-life of 30-40 hours
- Partial or full response >80 %
- Adverse events: daytime sleepiness, confusion, cognitive
- Relative contraindications: sleep apnoea, dementia, falls history

Managing Sleep Fragmentation in Parkinson’s Disease

- Nocturia
  - Voiding ≥2 times per night
  - >60% of patients
- Depression
- Avoid alerting events
  - Computer, i-pad, phone (blue light)
- Non-pharmacological
- PD medications
  - Selegiline, Amantadine, Anticholinergic therapy
- Non-PD medications
  - Alpha-blockers (Reduced REM sleep)
  - Beta-blockers (Inhibit Melatonin secretion)
  - Corticosteroids (Cortisol stimulation)
- Uncontrolled motor symptoms, pain, wearing off
Sound waves to improve sleep

Increase slow waves

Sleep quality not quantity

The future...

Slide courtesy of A/Prof Chris Gordon, Sydney Nursing School
Top ten sleep tips for patients
1. Mind your mind: depression

Depression is one of the biggest predictors of poor sleep quality.

Need to deal with both sleep and mood problems not just one.

Depression may even be linked to the onset and recurrence of sleep disorders.
2. Mind your mind: stress and anxiety

- Some anxiety is useful
- Too much is unhelpful
- Have “worry time” before bed
  - Write down those worries on paper
  - Place them in a worry box (container)
  - Check them out in the morning
- Were they worth worrying about at night?

- Mindfulness and relaxation techniques (e.g. progressive muscle relaxation, yoga) can help
3. Keep physically active

- Increases deep sleep
- Reduces light sleep
- Improves circadian rhythms
- Reduces sleep fragmentation
- Optimal results if in morning or early afternoon
- Reduces time to fall asleep particularly with aerobic exercise
- Resistance training also beneficial
- Try not to do vigorous exercise too close to bedtime
4. Keep cognitively active

- There is a strong link between cognitive decline and sleep problems
- Emerging evidence that cognitive training can improve sleep
- Cognitive activity in the hours prior to sleep can also increase deep sleep stages
5. Keep your body clock ticking in time..

- **Behaviours**
  - Get up at the same time everyday
  - Avoid heavy meals prior to bedtime
  - Avoid raising body temperature at night
    - hot baths, heavy exercise

- **Light**
  - Light bright in morning and dim at night
  - Consider bright light therapy
    - Evening light = delayed sleep
    - Morning light = advances sleep
  - Blue light has greatest effects

- **Melatonin, prescribed by GP**
  - A powerful antioxidant & free radical scavenger
  - Helps sleep to occur within 2 hours
6. Use Naps wisely

› Prescribed ‘controlled napping’
  • Duration is important!
  • Nap less than 30 minutes
  • Nap earlier in day, not in evening
  • Counts in your total sleep count

› May improve alertness, cognition, mood

› Can be associated with sleep inertia (feeling ‘groggy’) if nap for too long

› Consider effects on night-time sleep
7. Beware substances and medications!

- Avoid caffeine
  - Decreases slow wave ‘deep’ sleep
  - Increases awakenings
  - Increases time to fall asleep
  - Can be helpful if wish to delay sleep
- Avoid alcohol
  - Sedative but disruptive
- Consider medications
  - Sleeping medications are only effective for short-term use (<2 weeks)
  - Increase risk of falls, dizziness, nausea, drowsiness, headaches
- Limit liquid before bed
- Eating 3-4 hours before bedtime
8. Consider assessment and treatment for sleep apnoea!

- San Diego CPAP study, n = 39-52
  - Less light sleep and awakenings, more deep sleep
  - Reductions in excessive daytime sleepiness
  - Improvements in memory

- Sustained effects of CPAP (MMSE 18-30)
  - Cooke et al, 2009: n = 10, 1-year follow-up (CPAP n = 5 vs. no CPAP)
  - Medium to large effect size improvements in executive functions, psychomotor speed, mood, daytime sleepiness

Ancoli-Israel et al., 2008; Chong et al, 2006; Cooke et al, 2009
9. Re-align sleep expectations

- Do not focus on the ‘perceived negative’ effects of poor sleep
- Set boundaries around thinking, worrying and planning
- It is normal to be alert when waking at the beginning or end of a dream
  - Drowsiness will soon follow
  - Usually takes 15-20 minutes

“Acceptance of good nights and bad nights – sleep problems will occur – it is what you do that matters”

Courtesy of Delwyn Bartlett, Woolcock
10. After you’ve tried everything....

- If you can’t sleep
  - Get up! Do not stay in bed awake for more than 20 minutes
  - Relax in a different environment
    - Dim lighting
    - Do not stimulate the mind
- Do not try to make up for lost sleep
- Consider formal CBT-I / sleep restriction therapy
- Use a sleep diary
- Talk to your doctor
Dealing with daytime sleepiness

› Limit the number of demanding activities you perform each day

› Schedule activities that are cognitively and physically demanding for periods when you feel most alert

› Take regular rest breaks or brief nap

› Ensure adequate light exposure

› Consider substance and medication review
Sleep–wake disturbance

- A prodromal and key feature of Alzheimer’s and synucleinopathies (PD, DLB)
- Long sleep duration, sleep-disordered breathing, circadian advance and changes to sleep architecture → problematic, as well as reports of poor sleep quality
- Bidirectional links, ? multiple mechanisms
- Non-pharmacological treatment methods (CBTi) current gold standard, but need more RCTs in MCI, AD, PD. Melatonin is likely to help MCI and AD.
- More screening is required and especially for sleep apnoea and REM Sleep Behaviour Disorder
- Now need to determine if treatment of sleep disturbance can slow disease
With thanks to:

- Prof Simon Lewis, Neurologist
- Prof Jim Lagopoulos, Neuroimaging
- Prof Ron Grunstein, Sleep physician
- Prof Ian Hickie, Psychiatrist
- Dr Shantel Duffy, NHMRC/ARC Fellow
- Dr Angela D’Rozario, NHMRC/ARC Fellow
- Dr Camilla Hoyos, NHMRC/ARC Fellow
- Dr Loren Mowzsowski, NHMRC/ARC Fellow
- Dr Haley LaMonica, Neuropsychologist
- Dr Dr Jerome Ip, Geriatrician/Neurologist
- Dr Catriona Ireland, Geriatrician
- Ms Stacey West, Clinical Trials coordinator
- Ms Carla Harounonian, PhD student
- Mr Nathan Cross, PhD student
- Mr Jonathon Pye, PhD student
- Mr Joe Michaelian, PhD student
- Mr Aaron Lam, PhD student

FUNDING

- NHMRC Dementia Leadership Fellowship
- NHMRC/ARC Dementia Fellowship Scheme
  - Heart Foundation Vanguard grants
    - Diabetes Australia
    - Dementia Australia

NHMRC Centre of Research Excellence to Optimise Sleep in Brain Ageing and Neurodegeneration (CogSleep)