Age-related changes in aspects of the sleep-activity cycle and their relationship to associative memory performance

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BACKGROUND

- Sleep-activity cycles are cued by circadian rhythms, which are endogenously generated patterns that control cyclical physiological processes.
- Circadian rhythms change throughout the lifespan and may account for changes older adults commonly experience in sleep behavior, such as increased morningness preference, greater sleep fragmentation, delayed sleep onset, and decreased total sleep time.[1]
- Among older adults, disruptions in circadian rhythms have been linked to increased risk for cognitive dysfunction[2] and neurodegenerative disorders.[3]
- **The aim of the current study is to investigate how sleep-activity cycles change with aging, and how sleep-activity measures are related to associative memory performance.**

METHODS

Participants

Total participants	• 56 YA 51 OA	healthy adults recruited from the greater Austin community
Participants with circadian rhythm data and scan completion	• 53 YA 41 OA	age = 21±3.69 years, range = 60-81 years age = 67±5.22 years, range = 18-30 years
Participants with > 55% accuracy on memory task	• 52 YA 38 OA	accuracy = 88.7 ± 13.5%, rt = 904 ± 189 ms accuracy = 80.6 ± 19.7%, rt = 1196 ± 268 ms

YA = Younger Adults, OA = Older Adults

Materials

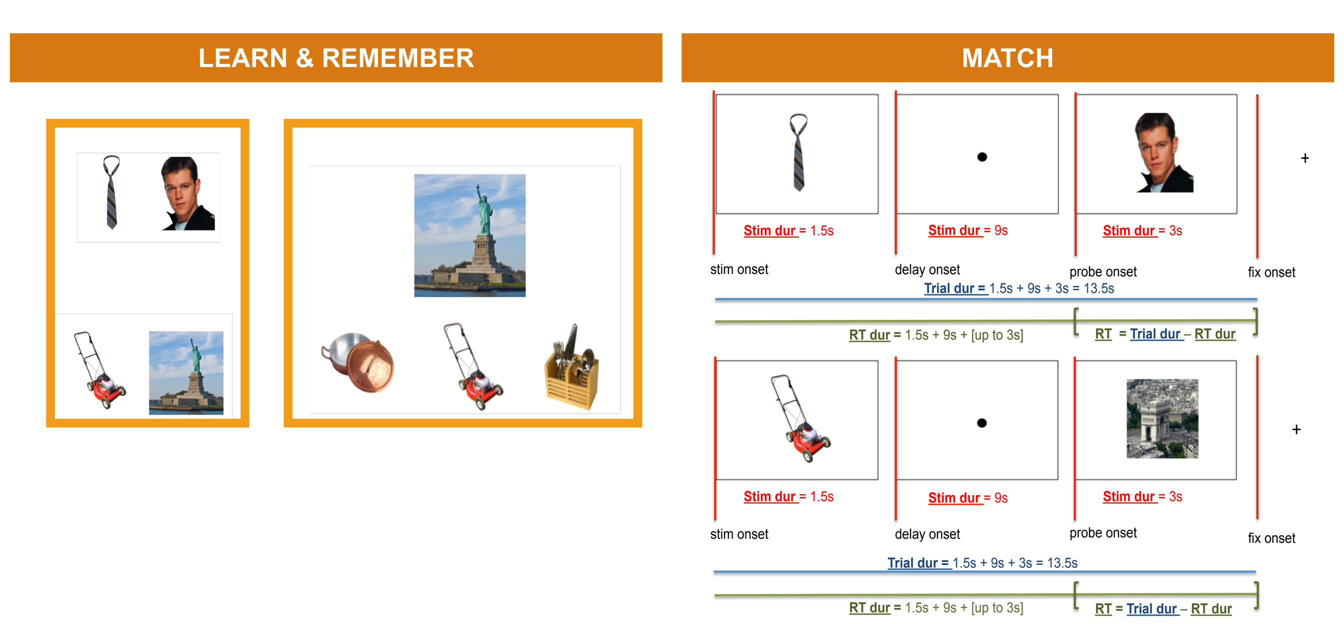
- Assessments: PSQI, CESD, GDS, Stroop Color-Word Test, Trail Making Test, FAS, WMS IV, WAIS-IV Vocabulary, CVLT-II
- Actiwatch 2, Actiware 6.0 (Philips Respironics, Bend, OR, USA)
- Daily sleep diary
- Siemens Skyra 3T scanner
  - fMRI
    - Associative memory task

Procedure

1. Screening
2. 10-day continuous activity measurements
   1. Actiwatch worn on left wrist
   2. Zero-crossings mode
3. MRI scanning
   1. Associative memory task
      - Minimum 55% accuracy
      - Reaction time < 3 sec

MEMORY TASK

- **Associative memory**, or the ability to learn and remember relationships between items, has been shown to be particularly susceptible to the effects of aging.[4]
- Memory was assessed using an associative memory task in which participants were tested on learned associations between either face-object or scene-object image pairs.[5]



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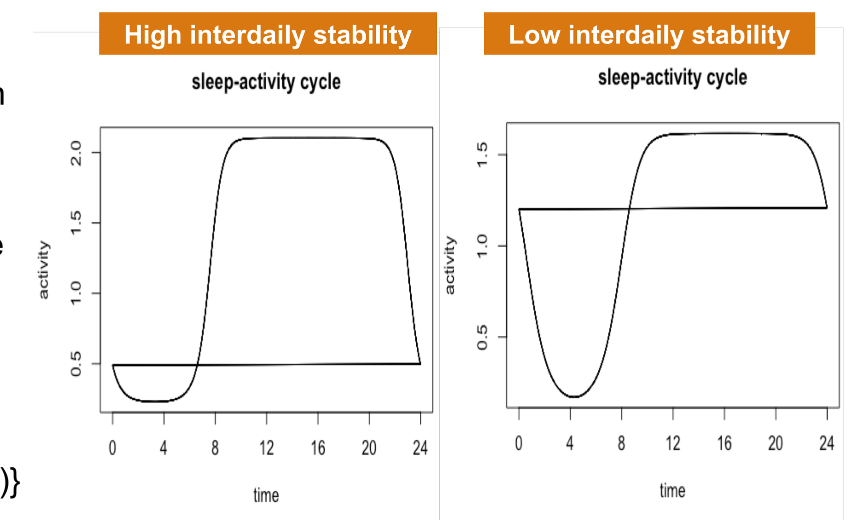
CIRCADIAN RHYTHM ANALYSIS

Sleep-activity measures, such as interdaily stability (IS), intradaily variability (IV), mesor (mean activity level), acrophase (time of peak activity), etc., were computed using both parametric and non-parametric methods.

- **Anti-logistic transformed cosine curve.** Cosine curves fit certain types of circadian data well, however they fail to capture the square-like shape of sleep-activity cycles. By using a sigmoidally transformed cosine curve, we are able to obtain a better representation of this data.[6,7]

$$r(t) = min * amp\,(l(c(t))$$

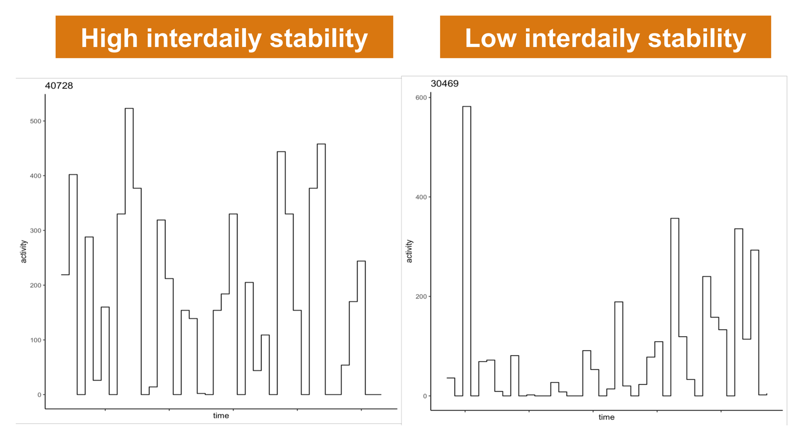
where $l(x) = \exp(\beta[x-\alpha]/\{1+\exp(\beta[x-\alpha])\}$ and $c(t) = \cos([t-\phi]2\pi/24)$



- **Non-parametric actigraphy.** Rather than using cosinor transforms, some researchers prefer non-parametric methods of computing circadian measures.[8] For example, interdaily stability is given by the formula:

$$IS = \frac{n\sum_{h=1}^{p}(\overline{X}_h - \overline{X})^2}{p\sum_{i=1}^{n}(\overline{X}_i - \overline{X})^2}$$

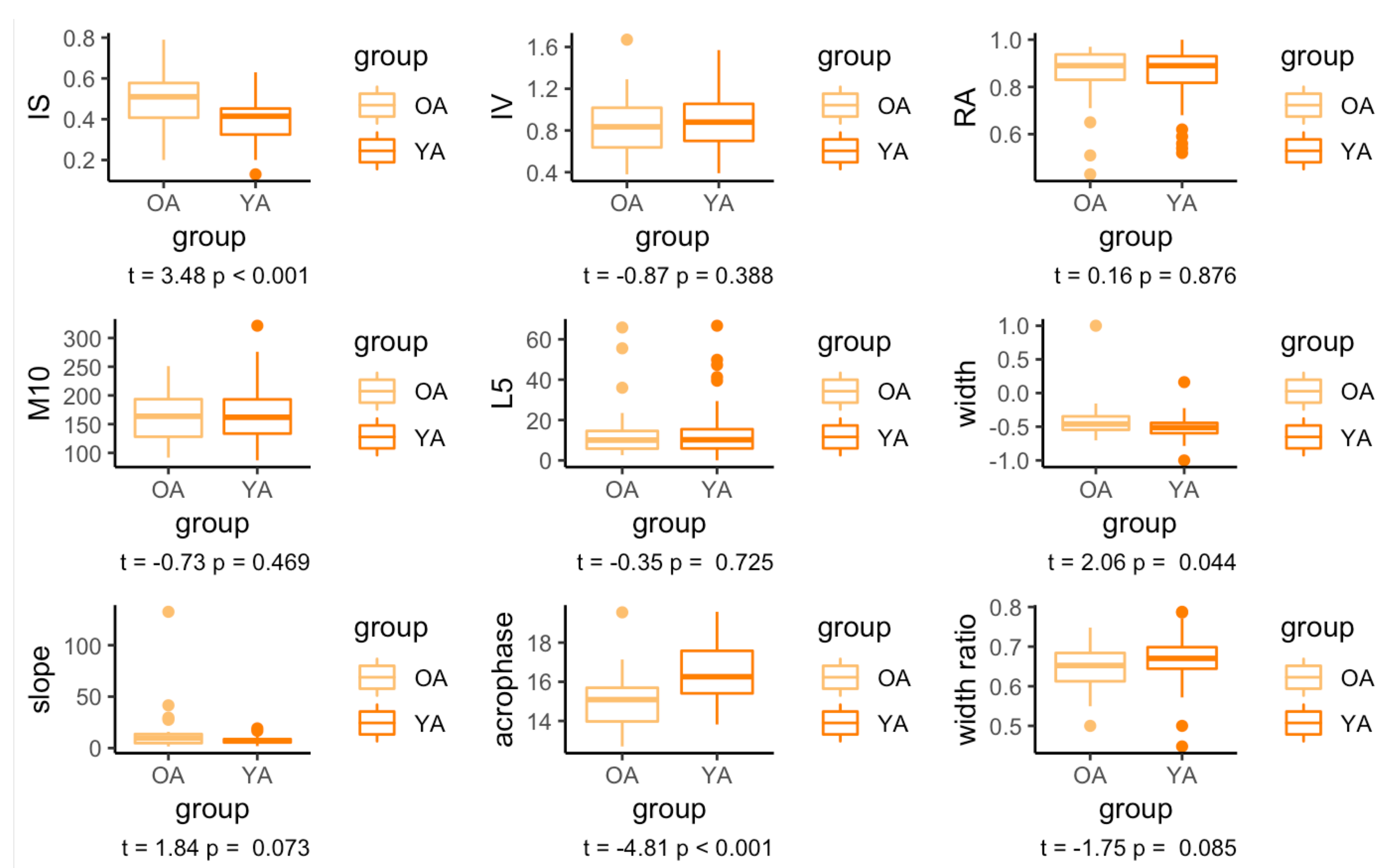
where $\overline{X}_i$ is the activity value from each sampling point, $\overline{X}_h$ is the hourly mean, and $\overline{X}$ is the grand mean of all data.



CIRCADIAN RHYTHMS AND AGING

Question: How do sleep-activity cycles differ in aging?

- Older adults showed significantly greater interdaily stability (t=3.48, p<0.001) and earlier up-mesor (t=-3.35, p=0.001), down-mesor (t=-5.39, p<0.001), and acrophase (t=-4.821 p<0.001) relative to younger adults. Older adults also experience shorter durations of high activity (width (α), t=2.05, p=0.044).
- Results suggest older adults may have faster transitions from low to high activity (slope (β), t=1.96, p=0.057), however these findings were not statistically significant at α=0.05.
- There was no significant difference observed in intradaily variability (t=-1.13, p=0.261), relative amplitude (t=0.17, p=0.864), L5 (t=-0.35, p=0.725), or M10 (t=-0.73, p=0.469) between groups.



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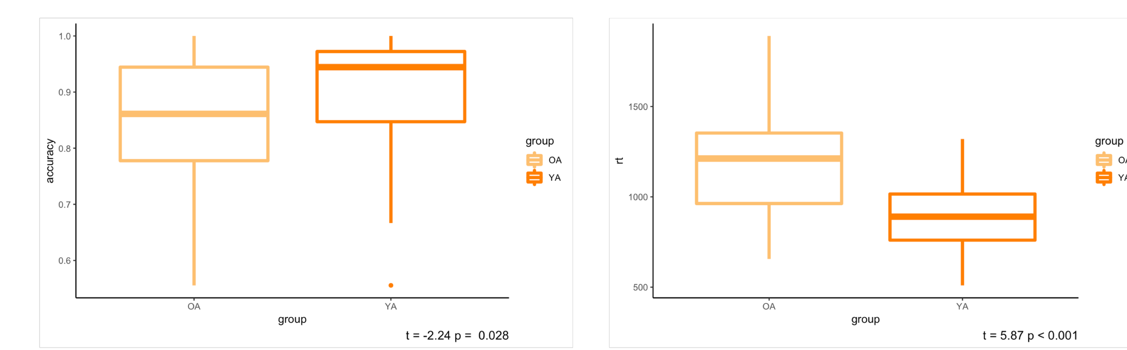
MEMORY PERFORMANCE

Question: How do sleep-activity measures relate to associative memory performance?

- Older adults exhibited significantly decreased accuracy (t=-2.24, p=0.028) and shorter reaction times (t=5.87, p<0.001) on the memory task.



Regression Analysis. Stepwise backward elimination was used to select significant predictors of associative memory task accuracy and reaction time.

- Results indicate that younger age, higher mean activity during the 10 hour most active period (M10), and shorter durations of high activity periods (width, α) predicted greater accuracy on the memory task, whereas greater relative amplitude of the rhythm (RA), greater activity during the night (min), and later transitions to higher activity periods (up-mesor) predicted lower accuracy.
- Age group was the only significant predictor for reaction time on the memory task. Younger adults were 291.9 ms faster on the memory task compared to older adults. Amplitude showed a trend toward significance with p=0.060.

accuracy = β0 + β1 age group + β2 RA + β3 M10 + β4 min+ β5 up-mesor + β5 width

Predictors	Estimate (β)	SE	p-value
Intercept	1.327	0.168	<0.001***
Age group YA	0.067	0.026	0.013*
Relative amplitude (RA)	-0.336	0.134	0.014*
M10	0.001	0.000	0.015*
Minimum (min)	-0.265	0.087	0.003**
Up-mesor	-0.024	0.008	0.005**
Width (α)	0.150	0.066	0.025*

$F(6,83)=3.916$, $p=0.002$, $R^2=0.221$, adjusted $R^2=0.164$

reaction time = β0 + β1 age group + β2 amp

Predictors	Estimate (β)	SE	p-value
Intercept	1409.19	119.83	<0.001***
Age group YA	-291.900	46.540	<0.001***
Amplitude (amp)	-139.82	73.41	0.060

$F(2,87)=21.93$, $p<0.001$, $R^2=0.335$, adjusted $R^2=0.320$

SUMMARY & CONCLUSIONS

- Circadian analysis suggests that older adults show greater interdaily stability, shorter durations of high activity, steeper rates of change between low activity and high activity periods, and earlier acrophases relative to younger adults.
- A significant regression model was found ($F(2,87)=21.93$, $p<0.001$, $R^2=0.335$, adjusted $R^2=0.320$) that accounted for 32% of the variance in reaction time. A significant regression model was also found ($F(6,83)=3.916$, $p=0.002$, $R^2=0.221$, adjusted $R^2=0.164$) that accounted for 16% of the variance in accuracy. Certain parametric circadian measures were important for predicting associative memory performance.
- Aspects of circadian rhythms corresponding to changes in associative memory may be important early predictors of cognitive changes associated with aging.

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