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Age-Related Differences in Brain Functional Connectivity and Associations with Sleep-Activity Cycles

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Introduction

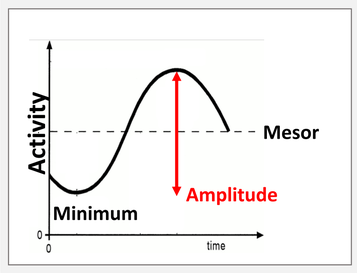
- While acute sleep effects on functional connectivity have been studied in young adults, little is known about how daily sleep-activity patterns play a role in brain network functional connectivity in aging.
- We used resting state fMRI and actigraphy to investigate age-related differences in functional connectivity and corresponding differences in the relationship to sleep-activity measures.

Methods

Participants

- Healthy, cognitively normal volunteers
- Older adults (60-90)
  - N = 37
- Young adults (18-30)
  - N = 40

Actigraphy



Functional Connectivity

- rsfMRI collected with Siemens Skyra 3T
- Schaefer 400 node parcellation
- Regression analysis with Network Brain Statistics

Graph Metrics

- Participation coefficient
- Modularity
- Clustering coefficient
- Global efficiency

Actigraphy data were collected using Actigraph 2.0 watches (Philips Respironics, Bend, OR, USA) in zero-crossings mode using 30-second epochs. Watches were worn on the left wrist for a minimum of 10 consecutive days. Sleep-activity measures were computed using an extended cosinor model described by Marler et al. (2006). **Resting state data** were collected using a Siemens Skyra 3T scanner (Siemens AG, Healthcare Sector, Erlangen, Germany, 32 channel head coil, TR/TE:1500/30ms, 66 axial slices, voxel=2x2x2mm, 240 time points). Preprocessing was completed using fMRIprep (Esteban et al., 2018) and xcpEngine (Ciric et al., 2018). We used confound regression with 6 motion parameters, CSF, and white matter. TRs with framewise displacement > 0.25 mm were regressed out. A FFT filter was applied from 0.008 Hz to 0.1 Hz. xcpEngine was also used to extract time series from 400 nodes defined by the Schaefer parcellation (Schaefer et al., 2017) to create full correlation functional connectivity matrices. Regression analysis was conducted with Network Brain Statistics (Zalesky et al., 2010). Significant networks were visualized using BrainNet Viewer (Xia et al., 2010). **Functional connectivity graph metrics** were computed using Brain Connectivity Toolbox (Rubinov & Sporns, 2010). Proportional thresholds ranging from 5% to 25% in 5% increments were applied to connectivity matrices. Graph metrics were calculated for each threshold and averaged across thresholds for t-test age group comparisons.

Results

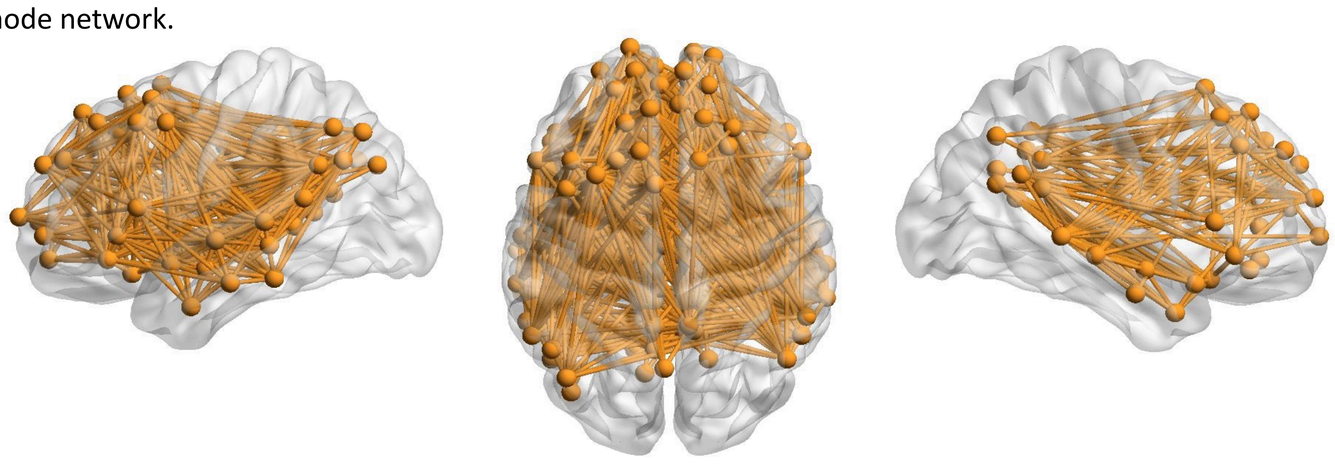
How does functional connectivity differ between healthy older adults and young adults?

Whole Brain Analyses

- Older adults showed widespread decreased functional connectivity at a whole brain level (NBS: t=3.5, p<0.001, k = 10000, intensity, 2722 edges, 359 nodes).

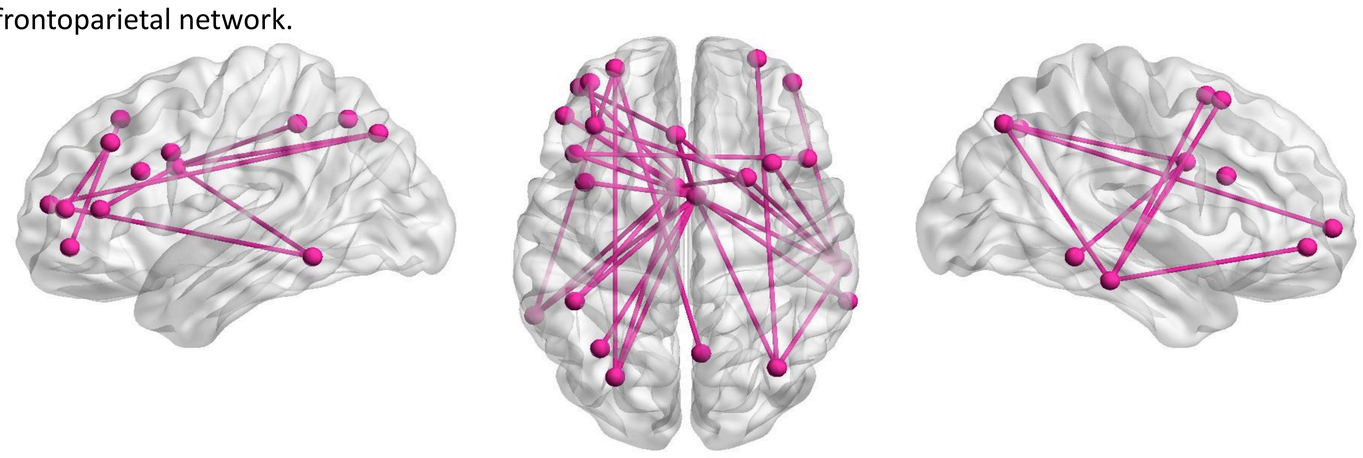
Within-Network Analyses

- **Default Mode Network:** Older adults showed significantly decreased functional connectivity within the default mode network.



Young Adults > Older Adults
NBS: t=2.5, p<0.001, k=10000, intensity
617 edges, 89 nodes

- **Frontoparietal Network:** Older adults showed significantly decreased functional connectivity within the frontoparietal network.



Young Adults > Older Adults
NBS: t=2.5, p=0.042, k=10000, intensity
31 edges, 23 nodes

Age Differences in Functional Connectivity Metrics

- At the whole brain level, older adults had significantly lower global efficiency (t=2.86, p=0.006) compared to young adults.
- Older adults had significantly greater efficiency in frontoparietal areas compared to young adults (t=-2.064, p=0.048).

How are sleep-activity cycles related to brain integration in older adults compared to young adults?

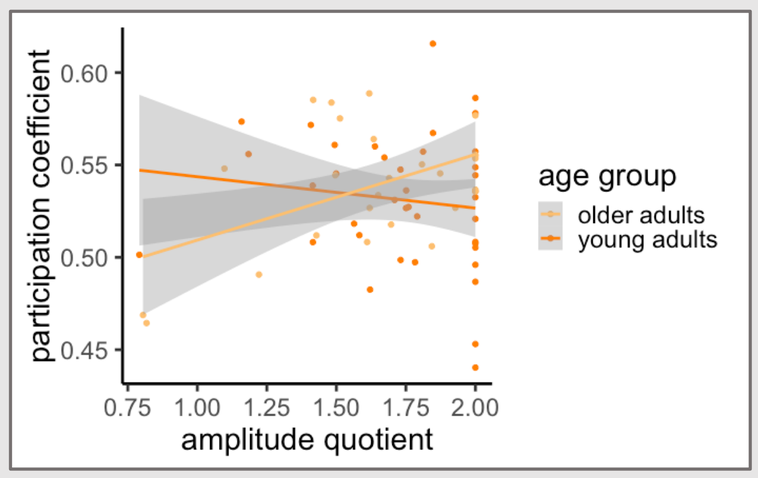
Sleep-Activity Measures

amplitude quotient – higher quotient describes a more robust circadian rhythm, and accounts for variation in activity levels across individuals

minimum – lower circadian minimum indicates more restful sleep

Sleep-Activity Patterns and Resting State Network Integration

- Older adults with greater sleep-activity stability from day to day (higher amplitude quotient) had greater network integration (mean participation coefficient) at a whole brain level (p=0.025) and within the default mode network (p=0.006).
- More restful sleep (lower circadian minimum) was also associated with greater mean participation coefficient at a whole-brain level (p=0.043) and within the default mode network (p=0.005) in older adults.



- Young adults with greater mean sleep time had greater network integration (lower clustering coefficient, p=0.026) at the whole brain level. Sleep time effects were not significant in older adults.

Conclusions

- Older adults had widespread decreased functional connectivity at a whole brain level, and decreased functional connectivity within default mode and frontoparietal networks.
- Older adults had lower global efficiency at a whole brain level compared to young adults. Within the frontoparietal network, older adults had greater efficiency.
- Greater day-to-day stability in sleep-activity patterns (higher amplitude quotient) was associated with greater brain integration (higher mean participation coefficient) in older adults, whereas total sleep time was important for brain integration (lower clustering coefficient) in young adults.

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