Sleep Duration is Associated with Caudate Volume and Executive Function

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Research Article

Keywords: Caudate Nucleus, Sleep Duration, Executive Functions, Structural Imaging

Posted Date: April 21st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1538850/v1

Abstract

The role of the caudate volume in sleep has been implicated. Previous literature showed that the caudate volume is associated with longer habitual sleep duration in older adults. However, the association between sleep duration and caudate volume remains unknown in the younger population. In this study, we examined the caudate volume in youth to older adults (10 to 85 years old) with a greater sample size (*N* = 463). The volumetric size of the caudate nucleus showed significantly positive association with habitual sleep duration. Sleep duration showed significant association with executive function performance. However, caudate volume did not significantly predict executive function. Our results suggested that sleep duration is associated with the caudate volume and executive function. It is also suggested that there are some external mechanisms that modulate executive function which prevent the caudate-sleep relation's effect on executive function.

Introduction

The caudate nuclei have been suggested to be a key region for sleep which may be accounted for by their role in reward/sensory processing and regulation of cortical excitability (Stoffers et al. 2014). Anatomically, caudate volume has been found to be associated with sleep duration. In older adult humans, larger caudate volume was related to both longer total sleep time and the shorter Stroop response times, i.e. enhanced executive functioning, induced by mild exercise (Won et al. 2019). In a PET study, the caudate showed significant increase in activity during REM and a notable decrease in activity from pre-sleep wakefulness to slow wave sleep (Braun, 1997). While the majority of neurons in the caudate have been found most active during REM and wakefulness, a small sector of caudate neurons demonstrated heightened activity during slow wave sleep, regulating the sleep-wakefulness cycle, along with involuntary movements (Oniani et al. 2009). These findings together suggest that sleep stages may be modulated by the caudate nucleus in some way.

Caudate disruption resulting in unsuccessful sleeping patterns has been repeatedly shown. EEG results after implementing destruction of the caudate via uni- and bilateral injections of kainic acid on rats induced a constant state of alertness and inability to sleep for two days (Vataev & Oganesyan, 2000). In humans, diminished caudate recruitment was found to be associated with sleep impairment and also with subjective report of hyper-arousal, a key element of insomnia. During an awake executive function task in fMRI, the caudate showed less activity in subjects with insomnia and control subjects assigned to experience slight sleep disruption (Stoffers et al. 2014). In addition, an association was found between increased subjective reports of hyper-arousal and the decreased caudate engagement in subjects with insomnia (Stoffers et al. 2014).

The caudate nuclei are also suggested to be involved in obstructive sleep apnea (OSA). Symptoms of depression and anxiety which can accompany OSA were found to show increased correlation to substandard resting-state functional connectivity (FC) of the caudate with other areas of the brain. The bilateral caudate showed smaller FC to the bilateral inferior frontal gyrus and right angular gyrus in OSA

patients who were additionally more prone to episodes of anxiety and depression, compared to healthy controls (Song et al. 2018). These results suggest the possibility that deprived sleep due to OSA may be a result of disrupted caudate functionality. Indeed, caudate functional disconnectivity was induced by sleep deprivation in male subjects with healthy sleeping patterns who were subjected to 36 hours of total sleep deprivation, resulting in defective functional connectivity of the left caudate with the postcentral gyrus and inferior temporal gyrus of the cortex (Wang et al. 2021). On the other hand, it has been demonstrated that stimulation of the caudate can show sedative effects. Stimulation of the caudate on cats during calm wakefulness resulted in notable behavioral changes, including drowsiness, from low frequency stimulation, and even sleep, from extended moderate stimulation (Gogichadze et al. 2017).

Sleep has been found to influence executive function. Sleep continuity has been shown to be associated with better executive function across age groups (Wilckens et al. 2014). In adolescents, sleepiness but not sleep duration has been found to be associated with executive function (Anderson et al. 2009). However, while caudate recruitment was smaller in those with sleep disturbance in an executive function task, sleep disturbance did not significantly affect performance in executive function (Stoffers et al. 2014).

Previous literature strongly suggests the possible role of the caudate on sleep duration. To our best knowledge, however, the association between the caudate volume and sleep duration in other age ranges have not been studied. In this study, we aimed to examine the association between caudate volume and sleep length, as well as executive functioning across a wide age range in adult human MRI data. We employed a large data set (67 subjects, 10–85 years old) to assess the association.

Methods

The MRI images and the demographic data of the enhanced Nathan Kline Institute-Rockland Sample (Nooner et al. 2012) were obtained from Collaborative Informatics and Neuroimaging Suite (Biswal et al. 2010). This data subset consisted of 467 individuals (42.10 ± 20.38 years old; 288 females and 179 males) without known neurological preconditions (such as stroke, tumor and traumatic brain damage) and MRI contraindications and with Delis-Kaplan executive function system (D-KEFS) Tower of London (Delis et al. 2001) scores as well as Pittsburgh Sleep Quality Assessment index (PSQI) scores, which measures sleep quality over the previous month through self- reporting (Buysse et al. 1989). High-resolution structural T1 volume was acquired as 176 sagittal slices of 1mm thickness (voxel size = 1x1x1mm, TR = 1900ms and TE = 2.52ms, FOV = 256). The caudate volume was estimated using *mri_segstats* in the Freesurfer image analysis suite (version 7.2.0; http://surfer.nmr.mgh.harvard.edu). A multiple linear regression was tested to predict the PSQI (sleep length) based on bilateral caudate volume, age and sex. In order to measure executive function, rule violations per item ratio in the Tower of London task was used (Stoffers et al. 2014). To examine the association between sleep duration and executive functions, a linear regression was tested to predict the rule violations based on the PSQI (sleep length). In order to examine the association between the caudate volume and executive functions, a multiple linear regression was tested to predict the rule violations based on bilateral caudate volume, age and sex.

Results

Between sleep duration and caudate volume, a significant regression equation was found ($F(3, 460) = 6.67$, $p < 0.001$, Fig. 1) with an adjusted R^2 of 0.035. The predicted sleep length (hours) was equal to 5.83 + 0.00016 (caudate volume) − 0.0088 (age) + 0.2 (sex). Caudate volume and age significantly predicted sleep length.

Sleep length predicted rule violations. A significant regression equation was found ($F(1, 462) = 4.491$, $p < 0.001$) with an adjusted R^2 of 0.015. The predicted rule violations were 10.083−0.16 (sleep length).

Although age significantly predicted rule violations, the caudate volume did not predict rule violations. A significant regression was found ($F(1, 463) = 7.05$, $p < 0.001$) with an adjusted R^2 of 0.037, where he predicted rule violations were 9.29 + 0.000015 (caudate volume: p = 079) + 0.013 (age: p < 0.001) + 0.062 (sex: p = 0.61).

Discussion

This study examined the associations among caudate volume, sleep duration, and executive functions. (1) The caudate volume showed significant positive association with sleep duration. (2) The sleep duration predicts executive function performance. However, (3) the caudate volume did not predict executive function performance. There was a significant association

Although previous literature is limited for the association between caudate volume and sleep duration, a positive association between the caudate and sleep length are consistent with previous studies. Previously, a significant relationship between longer habitual total sleep time and greater caudate volume was found in older adults (Won et al. 2019). Our results replicated this relation in a wider age range, supporting the link between greater caudate volume and longer sleep duration. Additionally, insomnia and induced sleep disruption, i.e smaller total sleep duration, results in lower caudate activity (Stoffers et al. 2014). Induced shorter sleep leads to reduced caudate activity. This may potentially account for the link between caudate volume and sleep duration, through which greater caudate activity by greater mass is associated with longer sleep.

Previous findings showed that longer sleep duration was associated with exercise induced improvements in executive function, but no significant relationship was found between caudate volume and executive functioning responses in general (Won et al. 2019). Our study found a subtle but significant association between longer sleep and executive function, while previous literature did not detect significant influence of sleep deprivation to executive function- specifically the same measure rule violations per item ratio in the Tower of London task (Stoffers et al. 2014). This may suggest that habitual sleep length influences executive function performance but not pathological and induced sleep deprivation.

No significant direct association was found between caudate volume and executive function, while the sample size in our study is not small ($N = 467$). Subjects with insomnia and controls subjected to acute

sleep disruption showed less functional activity of the caudate during executive functioning (Stoffers et al. 2014). This may suggest that an external mechanism such as the orbitofrontal cortex regulates executive function independent of the association between sleep duration and executive functions (Stoffers et al. 2014). Caudate-executive function relationship may be more involved in acute sleep deprivation, rather than habitual sleep length.

It has to be addressed that this study is not able to determine the causal relationship between the caudate volume and sleep. Greater caudate volume results in longer habitual sleep or longer habitual sleep results in greater caudal volume. In addition, this study did not examine activities of the caudate but instead tested the size of the anatomical apparatus. Examining the caudate activity and sleep duration as well as executive function may elucidate mechanisms behind these associations.

This study demonstrated that the caudate volume is associated with sleep length but not with executive function performance, while sleep length is associated with executive functions. It is suggested that the caudate influences or is influenced by habitual sleep durations.

Declarations

Disclosure: No conflict of interest to disclose

Acknowledgements

Principal support for the enhanced NKI-RS project is provided by the NIMH BRAINS R01MH094639-01 (PI Milham). Funding for key personnel also provided in part by the New York State Office of Mental Health and Research Foundation for Mental Hygiene. Funding for the decompression and augmentation of administrative and phenotypic protocols provided by a grant from the Child Mind Institute (1FDN2012-1). Additional personnel support provided by the Center for the Developing Brain at the Child Mind Institute, as well as NIMH R01MH081218, R01MH083246, and R21MH084126. Project support also provided by the NKI Center for Advanced Brain Imaging (CABI), the Brain Research Foundation, and the Stavros Niarchos Foundation. Image preprocessing was performed using the supercomputer cluster at the Mississippi Center for Supercomputing Research partly funded by the National Science Foundation (EPS-0903787).

Funding: None

Conflicts of interest/Competing interests: None of the authors have a conflict of interest to declare.

Ethics approval: This study is not considered to be a human subject study.

Consent to participate: N/A (No direct participation to this study)

Consent for publication: Both authors consent for publication

Availability of data and material: The original data is available at the NKI-RS website

Code availability: The tractography code will be available at https://olemiss.edu/projects/dnl/ upon publication.

Authors' contributions: NJF and TI both designed the study, analyzed the data and drafted the manuscript.

Compliance with Ethical Standards

Dr. Ikuta has received speaker's honoraria from Eli Lilly and Daiichi Sankyo and is a consultant for Dainippon Sumitomo Pharma. The authors declare that they have no conflict of interest. This article does not contain any studies in which the authors performed on human participants or animals.

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Figures

Figure 1

Association between sleep duration (hours) and bilateral caudal volume (mm^3).

Supplementary Files

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