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Naturally occurring circadian rhythm and sleep duration are related to executive functions in early adulthood

Running head: SLEEP AND EXECUTIVE FUNCTIONS IN EARLY ADULTHOOD

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Total number of words: 250+5000

Number of references: 40

The authors disclose no actual or potential conflicts of interest.

SUMMARY

Experimental sleep deprivation studies suggest that insufficient sleep and circadian misalignment associates with poorer executive function. It is not known whether this association translates to naturally occurring sleep patterns. 512 of full-term born members of the Arvo Ylppö Longitudinal Study (mean age=25.3, SD=0.65) (44.3% men) wore actigraphs to define sleep duration, its irregularity and circadian rhythm (sleep midpoint) over a one week period (mean 6.9 nights, SD=1.7). Performance-based executive function was assessed with the Trail Making Test, Conners' Continuous Performance Test, and Stroop. The self-rated Adult version of Behavior Rating Inventory of Executive Function was used to assess trait-like executive function.

We found that performance-based and self-reported trait-like executive function correlated only modestly (all correlations ≤0.17). Shorter sleep duration associated with more commission errors. Later circadian rhythm associated with poorer trait-like executive function as indicated by the BRIEF Metacognitive Index and the Behavior Regulation Index. Those belonging to the group with the most irregular sleep duration performed slower than others in the Trail making test Part A. All associations were adjusted for sex, age, socio-economic status, and body mass index.

In conclusion, naturally occurring insufficient sleep and later circadian rhythm showed modest associations with poorer executive function. Shorter habitual sleep duration was associated with lower scores performance-based tests of executive function, and later circadian rhythm was mostly associated with poorer trait-like executive function characteristics. Our findings additionally suggest that sleep duration and circadian rhythm associate with different domains of executive function, and there are no additive effects between the two.

Keywords: cognitive, attention, self-control, self-regulation, young adults, sleep timing

INTRODUCTION

Executive functions (EFs) are considered the central control systems for complex behaviour, such as attention, planning and goal setting, inhibitory abilities, and cognitive flexibility. EFs can be defined both as permanent characteristics of an individual (Friedman et al., 2016), and as fluctuating test performance affected by states such as stress (Shields et al., 2016), sleep deprivation (Rossa et al., 2014), alcohol consumption (Day et al., 2015), medication (Moeller et al., 2014), and mood (Cotrena et al., 2016).

As a rather stable characteristic of an individual, EFs can be evaluated with self-ratings, such as the Behavior Rating Inventory of Executive Function (BRIEF) (Roth et al., 2005). Regarding performance-based EFs, there are several objective tests targeting their different aspects such as attention (Conners, 2004), working memory (Reitan, 1958), and inhibitory control (Bohnen et al., 1992). A recent review concluded that there are two different constructs of EF: self-reports are mainly indices of goal pursuit, whereas performance-based EF tests estimate the efficiency of cognitive abilities, and the constructs correlate only modestly (.19) with each other (Toplak et al., 2013).

Several experimental sleep deprivation studies have reported domain-specific associations with performance-based EFs (Jackson et al., 2013, Lo et al., 2012, Banks and Dinges, 2007). Some studies have reported slower reaction times, but no weakening of inhibitory control in sleep deprived subjects (Cain et al., 2011, Dixit and Mittal, 2015, Bratzke et al., 2012) while others reported poorer performance in tasks requiring higher executive functions, such as risk-taking (Rossa et al., 2014) or divergent thinking (Vartanian et al., 2014), but with no effect on reaction times.

However, sleep deprivation occurs not only in experimental studies, but also under natural conditions, which provides greater ecological validity to study the consequences for cognitive functions. In particular, as young adults are more prone to have a later circadian rhythm (Duffy et al., 2015) and as there are several studies reporting a growing prevalence of both longer and shorter sleep (Bin et al., 2013), there is an increasing need to investigate the outcomes of naturally occurring sleep in this age group. Later circadian rhythm may result in shorter sleep duration, daytime sleepiness, and an increasing amount of weekend catch-up sleep (Juda et al., 2013). Circadian misalignment and both long and short sleep duration are all associated with several detrimental outcomes such as depression (Wittmann et al., 2006), higher risk for cardio-vascular diseases (Wong et al., 2015), and poorer overall well-being (Rutters et al., 2014, de Souza and Hidalgo, 2015); it is still unknown how these associations are manifested in everyday executive functioning.

There are few epidemiological studies linking young adults' naturally occurring sleep with EF, but the findings are consistent. In a study (Wilckens et al., 2014) of 112 adults, shorter objectively measured sleep duration associated with poorer task-switching performance in both younger (mean age 23 years (y)) and older (mean age 63y) age groups. In a study of 154 young adults, subjective complaint of poor sleep quality associated with a deficit in sustained attention (Gobin et al., 2015). Self-reported circadian misalignment, or preference towards eveningness, has been reported to associate with lower self-regulation abilities (Digdon and Howell, 2008, Tangney et al., 2004). Additionally, performance in several objective EF tests is associated with circadian rhythm and time of day, suggesting sleep timing may play a part in performance-based EF (Hahn et al., 2012). Similarly, irregular sleep as night-to-night variation in sleep, has been shown to associate with more frequent attention problems (Whiting and Murdock, 2016) and subjective well-being

(Lemola et al., 2013). Also, sleep variability may account for some of the sleep-related decline in cognitive performance, especially in emerging adults (Whiting and Murdock, 2016).

To our knowledge, no prior study has reported associations between naturally occurring, objectively measured sleep and both self-reported and performance-based EF in the same study. In addition, while most of the studies have targeted the effects of sleep duration, there is a lack of knowledge relating to circadian rhythm, sleep regularity and both self-reported and objectively measured EF. Accordingly, we set out to examine whether objectively measured and naturally occurring sleep patterns associated with both self-reported and performance-based measures of executive function in early adulthood. We hypothesized that sleep duration, as well as its variation, would be associated with both subjectively and objectively derived measurements of poor EF.

METHODS

Study design and participants

Participants of the current study came from the Arvo Ylppö Longitudinal Study (AYLS)(Heinonen et al., 2008, Wolke et al., 1998). Participants were recruited from 15,311 deliveries in seven maternity hospitals of Uusimaa province in 1985-86. The sample comprised 2193 infants (54% boys). Of them, 1913 subjects were invited to a follow-up study during 2009–2011, excluding those who were not traceable, lived abroad or other region. Of the invited, 991 subjects, (52% of the invited; 480 (48%) men), participated in a clinical study at Folkhälsan Research Center, Helsinki, Finland. Of them, 805 (47% men) were born full-term (gestation age≥37 weeks), which was the inclusion criteria for the current study, as we have previously shown that prematurity may associate with both sleep (Bjorkqvist et al., 2014) and EF (Pyhala et al., 2011). Of them, complete objectively measured sleep data were available from 512 participants (44% men). Of these, valid BRIEF data were available from

412 (42% men) and performance-based EF data from 491 participants (44% men) for Trail Making, from 490 for Stroop (44% men), and from 500 participants (44% men) for Conners' Continuous Performance Test (CPT II). Further cohort details are available (Riegel, 1995, Wolke et al., 1998, Heinonen et al., 2008).

The study was approved by the Coordinating Ethics Committee of Helsinki and Uusimaa Hospital District, and the original study protocol was approved by the ethics committees of participating hospitals. Written informed consent was obtained from participants.

Attrition

Those with valid sleep data differed from the rest of the term-born subjects (N=805) regarding three respects: they were more likely to be women (p=0.04) and, to have mothers with higher pre-pregnancy weight and BMI (both p=0.02) compared with other term-borns. They did not differ in respect to their age, socio-economic status (SES), or, BMI (all p-values>0.10).

Sleep

Sleep duration, regularity, and timing from 4393 nights were measured objectively using actigraphs (mean 6.9 nights, range 3-10) (Actiwatch AW7, Cambridge Neurotechnology Ltd., UK). Procedure and scoring were similar to those reported previously (Pesonen et al., 2014). A total of 814 nights with irregular events, such as night shift work, or, alcohol consumption were excluded, as well as nights with self-reported sleep-affecting medicine administration, resulting in a measurement of 3579 nights.

Sleep duration refers to actual sleep duration and was determined by the actigraph's algorithm. In accordance to previously published recommendations, a coefficient of variation was calculated as the standard deviation of sleep duration across a minimum of 7 days of measurement

divided by the individual average of sleep duration×100 (Rowe et al., 2008). Thus, the amount of data available for variation in sleep was smaller than in other sleep measurements (N=322, 63% of entire sample).

Circadian rhythm was defined by sleep midpoint over both weekday and weekend nights, calculated as the time point when half of the assumed sleep duration had passed since sleep onset.

Executive function measures

Performance-based EF

To examine performance-based EF we used three validated neurocognitive tests.

The Trail Making Test (TMT) (Reitan, 1958) consists of part A and B, which require simple motor skills and attention. Part B additionally depends on executive control, mental flexibility, divided attention and, fluid intelligence (Salthouse, 2011). Lower scores indicate better performance. A proportional ratio score was calculated (B-A/A) in order to evaluate performance irrespective of motor skills. A smaller ratio score indicates a smaller difference between motoric performance and more complex processing.

The Stroop (Bohnen et al., 1992) test consists of Part 1 and Part 2. Performance in baseline requires speech motor function, whereas the second part additionally requires selective attention, processing speed, and cognitive flexibility. An interference score (Part 2-Part 1) was calculated as a further measure of EF, higher scores indicating poorer performance.

CPT (Conners, 2004) is a computerized test which measures sustained attention and inhibitory control in a simple task of responding to target letters, resulting in hit reaction time, commission errors (false responses), and a D prime score estimating attentiveness. Higher reaction

time indicates slower performance, a larger number of commission errors indicates impulsiveness, and a higher D prime score indicates better attentiveness. According to study protocol, sleep measurements began the same or following day as CPT testing.

Self-reported, trait-like EF

We used a validated 75-item adult version of the Behavior Rating Inventory of Executive Function (BRIEF-A) questionnaire (Roth et al., 2005). It results in a Global Executive Composite (GEC) score (Cronbach alpha = .92), which can be broken down into two indices: the Behavioral Regulation Index (BRI) (Cronbach alpha = .83) and the Metacognition Index (MI) (Cronbach alpha = .91). BRI evaluates the ability to control behaviour and emotional responses. MI evaluates the ability to solve problems via planning and organization, and it includes questions about initiating tasks and activities, working memory capacity, monitoring problem-solving, and organizing everyday environment. Higher scores in all scales indicate worse EF.

Covariates

We made adjustments for sex (male/ female), age (years), BMI (weight and height measured by the research nurse) and self-reported socio-economic status (SES) as highest completed or soon to be completed education (from I=lower secondary to IV=university education).

Statistical analyses

All statistical analyses were done using IBM SPSS Statistics version 23.0. We performed logarithmic transformations on several scores (all TMT indices, the CPT Commissions score, all BRIEF-A raw scores) to attain normality. To facilitate interpretation, all EF variables were transformed into standardized T-scores (mean=50, SD=10).

We used linear regressions to study the continuous associations, and to better illustrate the associations between sleep and EFs, we divided the sleep variables into tertiles by sex and used ANCOVA to compare the mean group differences. Those belonging to the shortest (sleep duration<6.5 hours in men, or<6.9 h in women) or the longest sleep duration (sleep duration>7.2 hours in men, 7.6 h in women) tertile were compared to the rest of the sample. Those belonging to the latest sleep midpoint tertile (midpoint>4.99 hours in men, 4.29 in women) were compared to the rest of the sample, and those belonging to the tertile with most irregular sleep (irregularity>6.76 in men, and >5.95 in women) were compared to the rest of the sample. Cohen's d was calculated as a measure of effect size.

Additionally, a combination of these groups were created as follows: a "late-short" belonging to both the latest midpoint tertile and the shortest sleep duration tertile (n=44), and a "late-long" group belonging to both the latest midpoint tertile and longest sleep duration tertile (n=79). In order to investigate the potential accumulating measures of poor sleep, these groups were compared against the rest of the sample. We report analyses with group mean differences and 95% confidence intervals (95% CI).

RESULTS

 [Table 1]

Participant characteristics are presented in Table 1. There were several differences between men and women: men had higher BMIs, women had longer sleep duration, earlier sleep midpoint and less irregularity in sleep than men (all p-values <.001). Men were faster in TMT Part A, and had higher ratio scores (p-values ≤.004). In Stroop, women were faster in Parts 1 and 2 (p-values ≤0.02); in CPT men were faster (p<.001). Regarding the subjective EF measures, women reported higher scores on the BRI (p≤.005).

In both men and women, sleep duration and midpoint (men: r=0.13, p=0.05, women: r=0.21, p<0.001), sleep duration and duration irregularity (men: r=-0.17, p=0.036; women: r=-0.15, p=0.049), as well as midpoint and duration irregularity (men: r=0.29, p<0.001; women: r=0.16 p=0.039) all correlated significantly.

Associations of covariates with outcomes

Several correlations between covariates and EF outcomes were significant: higher BMI correlated with higher BRIEF scores in MI, BRI, GEC (r=0.15, p=0.002; r=0.12, p=0.018; r=0.15, p=0.003, respectively) and worse performance in Stroop Part 1 and Part 2 (r=0.12, p=0.009; r=0.12, p=0.006, respectively), and poorer D Prime (r=-0.09, p=0.04).

Higher SES correlated with better EF scores: MI (r=-0.15, p<0.001), BRI (r=-0.25, p<0.001), GEC (r=-0.20, p<0.001), Stroop Part 1 (r=-0.13, p=0.003), Stroop Part 2(r=-0.18, p<0.001), Stroop interference (r=-0.13, p=0.004), Commissions (r=-0.16, p<0.001), D Prime (r=0.15, p=0.001), TMT Part A (-0.13, p=0.005), and TMT Part B (r=-0.23, p<0.001).

Associations between the performance-based and self-report EF measures

To examine the associations of self-reported and performance-based EF, we ran Pearson correlations. Out of 27 correlations, five were significant, indicating that worse outcome in BRIEF associated modestly with poorer performance in performance-based EF. GEC score correlated with Part A from TMT and Part 1 from Stroop (r=0.13, p=0.011; r=0.13, p=0.008, respectively), BRI score correlated with Parts A and B from the TMT(r=0.17, p=0.001; r=0.10, p=0.04, respectively). MI score correlated with Part 1 from Stroop (r=0.14, p=0.004).

Sleep duration and EF

Supplemental Table 2 shows the associations as continuous and Figure 1, panel A, presents the mean differences in the EF scores between the shortest sleep duration tertile vs. other tertiles. The continuous and binary analyses shows similar pattern of significant associations. Those belonging to the shortest sleep duration tertile made more commission errors (p=0.038, Cohen's d=0.24) and had lower attentiveness as indicated by lower D prime score (p=0.047, Cohen's d=0.23) in the CPT.

Panel B presents the mean differences in the EF scores between the longest sleep duration tertile vs. other tertiles. Those belonging to the longest sleep duration tertile had better EF performance as indicated by fewer commission errors (p=0.035, Cohen's d=0.23) in the CPT.

[Figure 1]

Sleep irregularity and circadian rhythm and EF

Supplemental Table 2 shows the associations as continuous and Figure 1, Panel C presents the mean differences in the EF scores between the most irregular sleep tertile vs. other tertiles. Irregular sleep was associated with a slower performance in TMT Part A (p=0.04, Cohen's d=0.30), and lower ratio score (p=0.029, Cohen's d=0.25).

Panel D presents the mean differences in the EF scores between the latest sleep midpoint tertile vs. other tertiles. A late sleep midpoint was associated with poorer self-reported EF as indicated by higher MI, BRI, and GEC scores in the BRIEF (p<0.001; p=0.042, and p<0.001 respectively, Cohen's d=0.47; 0.26; 0.41, respectively), and faster performance in TMT Part B (p=0.030).

Accumulation of short sleep and late circadian rhythm

Those with both late circadian rhythm and short sleep duration ("late-short", n=44) had poorer trait-like EF compared to the rest of the sample in all three BRIEF measures: they had higher MI scores [mean difference (95% CI)=4.46 (0.80, 8.11); p=0.017], higher BRI scores [3.53 (0.18, 6.88); p=

0.035], and higher GEC scores [4.34 (0.80, 7.87);p=0.017]. Those with late circadian rhythm and longest sleep duration ("late-long", n=79) differed from the rest of the sample in three respects: they made less commission errors [-2.71 (-5.21, -0.22); p=0.033], had higher MI scores [4.04 (1.15, 6.93); p=0.006], and higher GEC scores [3.59 (0.73, 6.44); p=0.014]. There were no other significant associations.

DISCUSSION

This study aimed to increase understanding on the relations of naturally occurring sleep patterns and executive functions in young adulthood, a period of great irregularity in sleep and other environmental and biological changes. We found significant associations with sleep and both self-reported and performance-based EF measures. In accordance with previous reports, we found only modest correlations between self-reported and performance-based measures of EF, indicating that they reflect distinct constructs of EF.

Our approach aimed to detect poor habitual sleep patterns over an extensive period of time, allowing us to estimate the associations of EF and sleep duration, irregularity, and late timing. These measures reflect different aspects of sleep behaviour, and even though they were correlated in our sample, their associations with different EF measures were heterogeneous, suggesting separate vulnerabilities.

Our study suggests that short sleep even in everyday lives impairs performance in EF tests, reflected as a more error-prone and inattentive response style in the CPT. With respect to long sleep duration, only one significant association was observed in terms of fewer errors in the CPT performance. These observations were in line with the experimental evidence from sleep deprivations studies (Jackson et al., 2013, Lo et al., 2012), one prior observational study (Wilckens

et al., 2014), and indicate that even under naturally occurring circumstances, shorter habitual sleep duration is associated with weaker EF.

High variation in sleep duration was associated with performance-based measures of EF, namely TMT: more irregular sleep was associated with poorer performance in Part A, but better EF performance as indicated by a smaller ratio score. This suggests that sleep irregularity is associated specifically with poorer motoric performance but not with poorer complex processing.

Later circadian rhythm was associated with poorer self-reported EF traits, as shown by worse scores in Global Executive Composite, the Behavior Regulation Index, and the Metacognitive Index subcomponents. This study is the first to report how EF relates to objectively measured sleep midpoint. It is in line with previous studies suggesting subjective preference for evening chronotype is associated with poorer self-control (Digdon and Howell, 2008). Problems in sleep timing and self-regulation are likely to be a double burden reflecting negatively on academic achievements and future career paths.

Later circadian rhythm was associated with longer rather than shorter sleep duration, and we found no detrimental associations between performance-based EF and accumulating measures of poor sleep (i.e. late midpoint combined with long/ short sleep). Sleep timing and duration are likely to reflect different aspects of sleep behaviour; later circadian rhythm was associated with subjective experience of poor EF, hence, it is possible that longer sleep duration reflects lack of self-control.

As strengths we measured naturally occurring sleep objectively in a relatively large sample of young adults, and include both self-reported trait-like EF as well as performance-based state-like EF into the same study.

As limitations, the cross-sectional design of this study does not allow for any causal inferences. It is also not known whether a 7-day actigraphy period truly corresponds to the habitual

sleep patterns over a longer time span. Also, it is likely that there are common underlying factors between trait-like EF and later circadian rhythm, such as personality traits.

Finally, the associations between sleep duration and different performance-based EF yielded a rather heterogeneous pattern of results, with all associations pointing to hypothesized directions, but only few reaching statistical significance. However, when comparing our findings with experimental sleep deprivation studies, dose-response relationship corresponds well: the difference between shortest and longest sleep duration tertiles in our study corresponds to that of 42 minutes, while sleep deprivation studies have induced even a whole nights' sleep loss. Modest effect sizes were thus predictable.

We contribute to the literature by showing that within a young adult population born at term, naturally occurring short sleep duration and later circadian rhythm associate with poorer executive function. Our findings suggest that proneness to eveningness is related to worse trait-like behavioural regulation characteristics, which is likely to have a negative influence on a wide spectrum of actions in daily life. We found only few associations between irregular sleep patterns and later sleep rhythm and performance-based EF. Together these results indicate that both naturally occurring sleep timing and other aspects of sleep behaviour influence executive functions, but in different domains: a later sleep rhythm is related to trait-like EF characteristics, whereas shorter sleep duration worsens the immediate performance.

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