Title

Does objectively-assessed sleep moderate the association between history of major depressive disorder and task-switching?

Authors

Wilckens, Kristine
Kline, Christopher
Bowman, Marissa
et al.

Publication Date

2020-03-15

DOI

10.1016/j.jad.2020.01.003

Peer reviewed

HHS Public Access

Author manuscript

J Affect Disord. Author manuscript; available in PMC 2024 October 06.

Published in final edited form as:

J Affect Disord. 2020 March 15; 265: 216–223. doi:10.1016/j.jad.2020.01.003.

Does objectively-assessed sleep moderate the association between history of major depressive disorder and task-switching?

Kristine A. Wilckens[a,*], **Christopher E. Kline**[b], **Marissa A. Bowman**[c], **Ryan C. Brindle**[d], **Matthew R. Cribbet**[e], **Julian F. Thayer**[f], **Martica H. Hall**[a]

[a]Department of Psychiatry, University of Pittsburgh School of Medicine, 3801 O'Hara Street E-1124, Pittsburgh 15213, PA, United States

[b]Department of Health and Physical Activity, University of Pittsburgh, Pittsburgh, PA, United States

[c]Department of Psychology, University of Pittsburgh, Pittsburgh, PA, United States

[d]Department of Cognitive and Behavioral Science & Neuroscience Program, Washington and Lee University, Lexington, VA, United States

[e]Department of Psychology, University of Alabama, Tuscaloosa, AL, United States

[f]Department of Psychological Science, University of California at Irvine, Irvine, CA, United States

Abstract

Background: Executive function and psychomotor speed are consistently impaired in patients with major depressive disorder (MDD). Persistent cognitive impairments after depression remission are thought to reflect "scarring" from the neurotoxic effects of hypothalamic-pituitary-adrenal axis activity during a depressive episode. As sleep also deteriorates with depression and restores daytime executive functions, we examined whether adequate sleep could be protective against task-switching and psychomotor impairments associated with a history of MDD.

Methods: This cross-sectional study tested task-switching associations with MDD history, sleep, and their interaction to determine whether sleep continuity and sleep duration moderate the relationship between MDD history and task-switching performance.

Results: After adjusting for age, sex, education, current depressive symptoms, and use of anti-depressants, a history of MDD, particularly recurrent MDD, was associated with slower response speed and disproportionately lower accuracy on repetition trials compared to switch trials, reflecting impaired adoption of a task-set. Regardless of MDD history, higher wake after sleep

[*]Corresponding author. krw37@pitt.edu (K.A. Wilckens).

CRediT authorship contribution statement

Kristine A. Wilckens: Conceptualization, Formal analysis, Writing - original draft. **Christopher E. Kline:** Conceptualization, Writing - review & editing. **Marissa A. Bowman:** Conceptualization, Writing - review & editing. **Ryan C. Brindle:** Conceptualization, Writing - review & editing. **Matthew R. Cribbet:** Conceptualization, Writing - review & editing. **Julian F. Thayer:** Conceptualization, Writing - review & editing. **Martica H. Hall:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

None.

onset and shorter total sleep time were associated with slower response times, but neither sleep measure moderated the association between depression history and task-switching performance.

Limitations: This cross-sectional study cannot assess the causal direction of associations. One night of sleep in the laboratory was used to assess sleep and a single task-switching paradigm was used to assess executive function.

Conclusions: These results suggest that longer, more continuous sleep is associated with greater psychomotor speed across healthy controls and those with a history of MDD, but MDD-task-switching associations are not mitigated by longer or more continuous sleep.

Keywords

Major depressive disorder; Depression history; sleep; Cognitive function; Executive function

1. Introduction

Cognitive function is commonly impaired in patients with major depressive disorder (MDD) with the most common deficits in sustained attention, short-term memory, psychomotor slowing (Gorwood et al., 2014; Paelecke-Habermann et al., 2005), and executive functions, such as task-switching or set-shifting (Austin et al., 2001; Snyder, 2013; Vanderhasselt and De Raedt, 2009). Beyond impairments concurrent with depression, a major depressive episode is thought to have lasting neurotoxic effects, or “scarring” (Santesso et al., 2008), within brain regions responsible for regulating the hypothalamic-pituitary-adrenal (HPA) axis through executive control, including the frontal cortex, anterior cingulate, basal ganglia, and hippocampus (Jacobson and Sapolsky, 1991; Schmaal et al., 2015; Sheline et al., 1999).

Prolonged HPA axis activity during a depressive episode leads to changes in cortical and hippocampal serotonin receptors and loss of trophic support from brain derived neurotrophic factor (BDNF) protein (Willner, 2017), leading to shrinkage of dendritic spines, loss of granule cells, and suppression of hippocampal neurogenesis (Willner, 2017), as well as reduced density and length of apical dendrites of the anterior cingulate cortex (Radley et al., 2004). Such cortical reorganization may contribute to cognitive impairments following a depressive episode. Accordingly, many studies have shown that patients with remitted depression continue to show impairments in executive function and psychomotor speed (Hasselbalch et al., 2011), and more numerous depressive episodes may be associated with greater impairments (Vanderhasselt and De Raedt, 2009). As MDD is the leading cause of disease burden world-wide (Moussavi et al., 2007), identification of factors that moderate the cognitive effects of MDD history may be promising in mitigating functional impairments, as well as minimizing risk for subsequent MDD episodes (Vanderhasselt and De Raedt, 2009), by suppressing the response of the HPA axis to stress (Radley et al., 2004).

As sleep disturbances are often co-morbid with depression (Bei et al., 2018; Franzen and Buysse, 2008; Sadler et al., 2018) and adequate sleep supports cognitive functions including executive function and attention (Anderson and Horne, 2003; Basner et al., 2013; Couyoumdjian et al., 2010; Killgore, 2010; Muzur et al., 2002; Pace-Schott and Spencer, 2011; Wilckens et al., 2018, 2016, 2014b), better sleep could be protective against executive

function and psychomotor impairments arising from a history of MDD (Mander et al., 2016). We tested this hypothesis in 28 adults with no history of MDD and 25 remitted adults with a history of MDD. Measures included polysomnographic (PSG) sleep assessments of wake after sleep onset (WASO) and total sleep time (TST), clinician-based assessments of depression history and current depressive symptoms, and an objective task-switching paradigm. This paradigm assessed overall accuracy and response speed to assess overall performance and psychomotor speed, and effects of switching on accuracy and response speed as measures of executive function.

2. Methods

2.1. Study overview

This report reflects a secondary analysis from a study of major depression history and cardiovascular disease risk (HL104607) that was a follow-up to four larger cohort studies as described previously (Brindle et al., 2018). We briefly describe these procedures below. At the time of the follow-up study, participants completed a clinician-based psychiatric interview including the Hamilton Depression Rating Scale (HDRS), a computer-based task-switching experiment, and two nights of overnight polysomnographic (PSG) sleep assessments in the laboratory.

2.2. Participants

Participants were originally recruited for four cohort studies at the University of Pittsburgh between 1982 and 1999. One study was focused on sleep in adults without personal or first-degree family history of psychiatric disorders (MH024652) (Ehlers et al., 1998). The other three studies were focused on sleep in individuals with MDD (MH029618, MH049115, MH041884) (Carrier et al., 2001; Ehlers et al., 1998; Frank et al., 2008; Thase et al., 1997). Three hundred and thirty-nine participants were re-contacted between 2010 and 2014 to participate in a study of sleep, depression, and cardiovascular disease risk. Of the 177 that consented to the follow-up study, 70 participated in a task-switching experiment that was added to the protocol in 2012.

For the purposes of the present analyses which focused on MDD history in middle and older age, we excluded participants with current MDD ($n = 7$), participants with a history of psychosis or bipolar disorder ($n = 7$), and participants younger than 40 years of age ($n = 3$). Three participants opted not to complete the PSG assessment, but otherwise had both task-switching and MDD history data; these participants were included in all possible analyses to optimize statistical power for main effects of MDD history. The remaining 50 participants included in the present analyses ranged from 48 to 79 years of age.

Participants were grouped based on MDD history in two ways: lifetime MDD history and recurrent MDD history. Participants who had at least one major depressive episode in their lifetime were categorized into the lifetime MDD history group ($n = 25$). Participants included in the no lifetime MDD history group reported no history of major depression in their lifetime ($n = 28$). One control participant was diagnosed with depression not otherwise specified at the time of the PSG study and one participant with an MDD

history was diagnosed with post-traumatic stress disorder at the time of the PSG study. Sensitivity analyses on significant results excluding these two participants did not lead to any changes (data not shown). Participants were also grouped based on recurrent MDD history. Participants who had more than one major depressive episode were categorized into the recurrent MDD history group (n = 17). Participants who had one or less major depressive episode were categorized in the no recurrent MDD history group (n = 36). This study was approved by the University of Pittsburgh Institutional Review Board. All participants provided written informed consent and were compensated for their participation.

2.3. Assessments

2.3.1. Clinical interview—Participants completed a mental health assessment upon entering the follow-up study. This assessed lifetime psychiatric history through a Structural Clinical Interview for DSM-IV Axis I Disorders (Spitzer et al., 2002) with a trained clinician. Clinicians also completed the 17-item HDRS to assess current depressive symptoms.

2.3.2. Task-switching paradigm—The task-switching paradigm has been described elsewhere (Wilckens et al., 2017, 2014b) (Fig. 1). Briefly, participants were asked to view a single-digit number on the screen and perform one of two tasks on a trial-by-trial basis. In one task they judged whether the single digit number was greater than or less than 5 (the probe number was never 5); in the other task, they judged whether the number was odd or even. For each trial, the number was inside a circle or a square. The circle cued the participant to perform the greater than/less than task, and the square cued the participant to perform the odd/even task. Participants had a practice block to familiarize themselves with the experiment and the task cues. They subsequently completed a single task block of each of the two tasks, and then completed a switching block where the shape task cue varied trial-by-trial. The cue was either the same as the previous trial (repeat) or was different from the previous trial (switch). Time to prepare on each trial was manipulated by varying the interval between the shape cue and the probe number (0 ms, 750 ms, or 1500 ms).

2.3.3. Polysomnography (PSG)—Participants completed a two-night PSG sleep assessment. The first night served as an adaptation night and apnea screen. The second night was used in the current analyses to avoid first-night effects (Agnew et al., 1966). Wake after sleep onset (WASO) was calculated as the number of minutes spent awake after sleep onset. Total sleep time (TST) was calculated as the number of minutes spent sleeping across the night. WASO and TST were chosen as sleep variables of interest because these two measures are most consistently associated with executive function in middle age and older populations (Scullin and Bliwise, 2015; Wilckens et al., 2014a,b).

2.4. Statistical analyses

Multivariate analyses of variance (MANOVA) and chi square tests were used to characterize the sample in terms of demographic, clinical, and sleep variables as a function of lifetime MDD history and recurrent MDD status (Table 1). Continuous demographic and clinical variables (age, education, and HDRS) were included as dependent variables in one MANOVA testing MDD history group differences. Categorical demographic and clinical

variables (sex and antidepressant usage) were tested as a function of MDD history with chi square tests. A second MANOVA to characterize the MDD history groups in terms of sleep dependent variables (WASO, TST, and AHI) included all demographic and clinical variables as covariates (age, sex, education, HDRS, and antidepressant usage).

The main analyses consisted of two sets of repeated measures ANOVAs to assess main effects and interactions between depression history, sleep measures, and task-switching performance as a function of overall accuracy and response time and interactions with block type (single task block or switching block). A second set of repeated measures ANOVAs tested interactions with switch condition (repeat or switch trial). Interactions with block type allowed us to assess global switch costs which reflect the costs associated with managing two tasks within the switching block compared with the single task block (Kray and Lindenberger, 2000). Interactions with switch condition allowed us to assess local switch costs within the switching block which reflect the costs associated with adopting and maintaining a task-set on repeat trials, and disengaging from a task-set on switch trials (Kray and Lindenberger, 2000). Overall response speed across single and switching blocks was considered a proxy for condition-independent psychomotor slowing (White et al., 1997). Although the task-switching paradigm also varied in preparation time, we chose to simply account for preparation time but not test for preparation time interactions for the current analyses as this would involve three-way interactions with a three-level factor that would be difficult to interpret and may be spurious with the current sample size. Preparation condition was accounted for by including it as a repeated measure in the ANOVAs testing effects of switch condition in the switching block, without assessing preparation condition interactions. Post-hoc simple slope analyses were tested for significant associations involving sleep variables.

Analyses were run with age, sex, and education as covariates, as these factors are commonly associated with task-switching performance and the sleep measures examined here. For significant associations involving depression history, sensitivity analyses additionally adjusted for current depressive symptoms with the HDRS excluding sleep questions and current antidepressant use. Significant associations involving sleep variables additionally adjusted for apnea hypopnea index (AHI) to minimize the likelihood that sleep-cognition associations were driven by cognitive impairments arising from sleep-disordered breathing. Results are reported before and after Holm-Sidak multiple comparisons correction to account for the four factors (lifetime and recurrent MDD history and WASO and TST) assessed. Data from analyses reported here will be made available upon request.

3. Results

3.1. Demographic, clinical, and sleep characteristics

Table 1 displays the demographic, clinical, and sleep characteristics for study participants. Compared to control participants, those with a history of MDD had higher current depressive symptoms and they were more likely to be taking antidepressants at the time of the study. Similar differences were found between those with and without recurrent depression. In addition, those with recurrent depression were more likely to be female.

3.2. MDD history

Main effects of MDD history on performance and interactions with block (single-task versus switching) and switch condition (repeat versus switch) are displayed in Table 2 for accuracy and Table 3 for response time. Both lifetime MDD history and recurrent MDD history showed significant associations with conditions of task-switching performance after adjusting for age, sex, and education. Overall accuracy and response time were significantly poorer in the recurrent MDD history group (Fig. 2a). Both lifetime MDD history and recurrent MDD history showed a significant interaction with switch condition, whereby those with an MDD history had significantly poorer accuracy particularly in the repeat condition (Fig. 2b), which measures successful adoption of a task-set (Morcom and Rugg, 2002; Wilckens et al., 2011). These relationships persisted after accounting for HDRS-assessed current symptoms of depression and current use of antidepressants, with the exception of a marginally significant lifetime MDD history × switch interaction after adjusting for antidepressant use ($p < 0.1$ [Table 2]). Effects of MDD history on accuracy persisted after correcting for multiple comparisons.

3.3. Sleep and interactions with MDD history

Both higher WASO and shorter TST were linearly associated with slower response times across task blocks (single-task and switching blocks) (Table 3, Fig. 3a), and this relationship was moderated by block for WASO (Table 3). The relationship with WASO was stronger for switching block response time (Fig. 3b) ($\beta = 0.336$, $t = 2.98$, $p = 0.005$ for the switching block, and $\beta = 0.203$, $t = 1.681$, $p = 0.10$ for the single task blocks). Significance was unchanged after adjusting for AHI. Only the association between WASO and response time survived Holm-Sidak multiple comparisons correction. Although WASO had one outlier > 3 standard deviations above the mean, the block × WASO interaction on response time was marginally significant in the same direction after removing this outlier ($F(1,42) = 3.47$, $p = 0.07$). Both WASO and TST relationships with response time were not moderated by switch condition (switch versus repeat) (Table 3) and there were no significant linear relationships between PSG-assessed sleep and accuracy (Table 2).

Contrary to our hypotheses, there were no significant interactions between WASO or TST with MDD history for accuracy or response time (Tables 2 and 3), irrespective of whether analyses did or did not adjust for *current* depression symptoms. The simple slopes for the relationship between sleep and response time across blocks and within the switching block separated by recurrent MDD history status are presented in Fig. 3.

3.4. Summary of results

A history of MDD, particularly recurrent MDD, was associated with slower response speed and disproportionately lower repeat condition accuracy. Across patient types, higher WASO and shorter TST were each associated with slower response times regardless of MDD history. MDD history and PSG-assessed sleep did not interact in their association with task-switching accuracy or response speed.

4. Discussion

4.1. Effects of MDD

A history of major depression may have persistent neurotoxic effects that impair executive functions and lead to cognitive slowing even after patients are remitted. Here we found that individuals with a history of MDD, particularly recurrent MDD, showed significantly poorer performance in terms of overall accuracy and response speed, as well as impaired task-set adoption when switching between tasks (lower accuracy boost on repeat trials). These associations persisted after adjusting for current depressive symptoms. Specifically, recurrent MDD history was associated with overall slowing, unmoderated by block (single task or switching), and poorer overall performance across task blocks. Moreover, lifetime MDD history and recurrent MDD history were also associated with impaired task-set adoption, as evidenced by the absence of a boost in performance on repeat trials compared to switch trials, as is expected in the current paradigm (Kray and Lindenberger, 2000; Monsell, 2003; Wilckens et al., 2014a). These findings are consistent with other studies showing lasting effects of depression on set-shifting (Austin et al., 2001; Snyder, 2013; Vanderhasselt and De Raedt, 2009) and psychomotor speed (Hasselbalch et al., 2011) in remitted patients. Our findings extend these data by showing that these effects are most consistent in individuals with a recurrent MDD history and are not driven by current depression symptoms, as participants with current MDD were excluded and analyses adjusted for current symptoms of depression. Overall, the main effects of MDD history suggest a deficit in both psychomotor speed as well as executive function characterized by impaired task-set adoption when task-switching for individuals with a history of MDD.

It is worth noting that in this sample we did not find significant effects of MDD history on the sleep variables tested. This finding is consistent with a meta-analysis which demonstrated that despite significant disturbances in sleep efficiency and duration (Mayers and Baldwin, 2006) during a depressive episode, after remission only sleep architecture variables (slow-wave sleep and rapid eye movement sleep) show persistent effects (Pillai et al., 2011).

In line with the view that a history of MDD is associated with longlasting executive and psychomotor impairments, one study found impairments on a Stroop inhibition task both during a depressive episode and after significant depressive symptom improvements six months later (Hammar et al., 2010). Moreover, a meta-analysis of depression history and brain volume showed that recurrent MDD, but not singleepisode MDD, was associated with smaller hippocampal volume (Schmaal et al., 2015). These studies, combined with our current findings, may suggest a dose-response relationship whereby more frequent depressive episodes lead to longer lasting neurocognitive deficits, even after remission. Alternatively, executive function and psychomotor impairments may interfere with top-down regulation of the HPAaxis, contributing to relapses in depression, in line with the view that attention-based cognitive therapies are promising for avoiding relapse (Davidson, 2016; Teasdale et al., 1995).

4.2. Associations with sleep

Across MDD history groups, higher WASO and shorter TST were associated with slower response speed, with WASO showing stronger relationships with response speed in the switching block. This finding suggests that WASO is associated with greater global switch costs. These costs reflect the effort to coordinate and manage two tasks in a switching block, compared to managing one task in a single task block (Kray and Lindenberger, 2000). Associations among impaired sleep continuity and shorter sleep durations and response speed in the present study are consistent with our and others' prior studies showing a specific association between WASO and task-switching (Bratzke et al., 2009; Couyoumdjian et al., 2010; Wilckens et al., 2017, 2014b), and specifically the task-coordination process captured by global switch costs (Wilckens et al., 2014b), as well as our prior findings of a relationship between shorter TST and slower response time (Wilckens et al., 2014b). Moreover, the fact that associations with response time were stronger than associations with accuracy is consistent with our prior study of actigraphy-assessed sleep and task-switching (Wilckens et al., 2014b).

Contrary to our hypotheses, the association between MDD history and task-switching was not moderated by WASO or TST across any of the cognitive conditions assessed. These results fail to support our hypothesis that adequate sleep may be protective against executive and psychomotor impairments associated with recurrent depression. Instead, our results suggest that a history of recurrent MDD is associated with cognitive impairments despite remission, and that cognitive impairments relative to controls are not tempered with more adequate sleep. Nonetheless, the significant main associations with WASO and TST suggest that participants with and without a history of MDD benefit similarly in psychomotor speed and task coordination from lower WASO and longer TST.

Two prior studies of sleep-cognition relationships suggest differences in the sleep-cognition association depending on *current* depression symptoms. One study (Mellor et al., 2018) found significant moderating effects of current depression on the association between shorter TST and slower working memory speed and higher WASO and slower executive function speed (response inhibition), whereby sleepresponse time associations were stronger in participants with current MDD. These findings are broadly consistent with our linear associations with WASO and TST across MDD history status. Another study (Sutter et al., 2012) found that individuals with greater symptoms of subclinical depression showed a stronger relationship between subjective sleep quality and several domains of cognition, including set-shifting, reasoning, and fluency. These prior studies, though testing effects of current depression, converge with the present results to suggest that higher WASO and shorter TST are associated with executive function and psychomotor speed in individuals with depression as well as those with remitted depression.

4.3. Limitations and future directions

The current study has several limitations with respect to assessing the protective role of sleep in the "scarring" effects of MDD. Although our findings show more robust and consistent effects with a recurrent depression history, and although we adjusted for current depressive symptoms, we cannot confirm the directionality of MDD-cognition associations

due to the study's cross-sectional design. Alternatively, given that executive function deficits common in MDD are critical for emotion regulation, associations with MDD history may precede a depressive episode (i.e., individuals with executive function deficits have poorer emotion regulation leading to a depressive episode (Snyder, 2013)). Moreover, participants with a depression history were more likely to be taking antidepressants at the time of the study, which can affect sleep (Wichniak et al., 2017) and exhibit some benefits to cognitive function (Papakostas, 2015). Studies assessing executive function over the course of the onset and remission of depressive could address some of these issues.

Higher WASO and shorter TST were linearly associated with slower response speed across MDD history groups, but these sleep measures did not moderate the association between MDD history and any of the assessed task-switching measures. Although these null findings may be a function of low statistical power due to the size of the sample, the interactions did not approach significance (e.g., all p-values > 0.27, and many p-values > 0.90) despite robust main associations with MDD history and sleep. Nonetheless, the question of whether sleep may moderate effects of depression on cognition is worth pursuing in other experimental designs. For instance, in the current study, sleep was measured while participants were euthymic. Whether high sleep continuity and adequate sleep time *during* a depressive episode is protective against cognitive impairments and neurotoxicity remains an open question. Moreover, even though the single night of PSG-assessed sleep measured here was adequate to detect sleep-performance associations, a single night may be inadequate to assess the moderating role of sleep in MDD. Future work measuring sleep over longer periods of time during and after a depressive episode with polysomnography or actigraphy may be beneficial in addressing the proposed questions.

The current study had a relatively wide age range (48–79 years), which likely enhanced variability in relation to age-related cognitive impairments and underlying cortical atrophy, independent of depression history. Studies examining cognitive impairments and cortical atrophy in middle age and older adults separately may help to clarify the mechanisms of cognitive deficits arising from a history of depression and provide more experimental control to assess the potential role of sleep.

Finally, although the current task-switching paradigm used multiple task conditions to assess task-set adoption and psychomotor speed, it did not include a wide battery of cognitive testing, nor did it assess cognitive change over time. Thus, it remains a possibility that other aspects of cognition not measured here could be associated with MDD, sleep, and the interaction between the two.

5. Conclusions

In a sample of middle age and older adults, MDD history, particularly a history of recurrent MDD, is associated with poorer psychomotor speed and executive function assessed with adoption of a task-set. Higher WASO and shorter TST are associated with slower response speed, particularly when switching tasks, but these sleep measures do not mitigate the task-switching impairments with an MDD history.

Acknowledgments

The authors thank Brian Allison, Bonnee Wettlaufer, Laura Samuelsson, Briana Taylor, Jean Miewald, and Annette Wood for assistance with the conduct and management of this study. This work was supported by grants from the National Institutes of Health: Primary T2 study was R01 HL104607 (M. Hall). T1 studies were R01 MH024652 and R01 MH029618 (D. Kupfer), R01 MH049115 (E. Frank), and R01 MH041884 (M. Thase). Investigator effort was supported by KOI AG049879 (Wilckens), K23 HL118318 (Kline), T32 HL082610 (Cribbet), and T32 HL07560 (Bowman). Infrastructure support was provided by UL1 TR000005 and UL1 RR024153.

References

Agnew H Jr., Webb WB, Williams RL, 1966. The first night effect: an EEG studyof sleep. Psychophysiology 2, 263–266. [PubMed: 5903579]

Anderson C, Horne JA, 2003. Prefrontal cortex: links between low frequency delta EEG in sleep and neuropsychological performance in healthy, older people. Psychophysiology 40, 349–357. [PubMed: 12946109]

Austin M-P, Mitchell P, Goodwin GM, 2001. Cognitive deficits in depression: possible implications for functional neuropathology. Br. J. Psychiatry 178, 200–206. [PubMed: 11230029]

Basner M, Rao H, Goel N, Dinges DF, 2013. Sleep deprivation and neurobehavioral dynamics. Curr. Opin. Neurobiol 23, 854–863. [PubMed: 23523374]

Bei B, Asarnow LD, Krystal A, Edinger JD, Buysse DJ, Manber R, 2018. Treating insomnia in depression: insomnia related factors predict long-term depression trajectories. J. Consult. Clin. Psychol 86, 282. [PubMed: 29504795]

Bratzke D, Rolke B, Steinborn MB, Ulrich R, 2009. The effect of 40 h constant wakefulness on task-switching efficiency. J. Sleep Res 18, 167–172. [PubMed: 19645962]

Brindle RC, Duggan KA, Cribbet MR, Kline CE, Krafty RT, Thayer JF, Mulukutla SR, Hall MH, 2018. Cardiovascular stress reactivity and carotid intimamedia thickness: the buffering role of slow-wave sleep. Psychosom. Med 80, 301–306. [PubMed: 29381658]

Carrier J, Land S, Buysse DJ, Kupfer DJ, Monk TH, 2001. The effects of age and gender on sleep EEG power spectral density in the middle years of life (ages 20–60 years old). Psychophysiology 38, 232–242. [PubMed: 11347869]

Couyoumdjian A, Sdoia S, Tempesta D, Curcio G, Rastellini E, De Gennaro L, Ferrara M, 2010. The effects of sleep and sleep deprivation on task-switching performance. J. Sleep Res 19, 64–70. [PubMed: 19878450]

Davidson RJ, 2016. Mindfulness-based cognitive therapy and the prevention of depressive relapse: measures, mechanisms, and mediators. JAMA Psychiatry 73, 547–548. [PubMed: 27119526]

Ehlers CL, Kupfer DJ, Buysse DJ, Cluss PA, Miewald JM, Bisson EF, Grochocinski VJ, 1998. The Pittsburgh study of normal sleep in young adults: focus on the relationship between waking and sleeping EEG spectral patterns. Electroencephalogr. Clin. Neurophysiol 106, 199–205. [PubMed: 9743277]

Frank E, Kupfer DJ, Buysse DJ, Swartz HA, Pilkonis PA, Houck PR, Rucci P, Novick DM, Grochocinski VJ, Stapf DM, 2008. Randomized trial of weekly, twice-monthly, and monthly interpersonal psychotherapy as maintenance treatment for women with recurrent depression. Focus 6, 120–127.

Franzen PL, Buysse DJ, 2008. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. Dialogues Clin. Neurosci 10, 473. [PubMed: 19170404]

Gorwood P, Richard-Devantoy S, Baylé F, Cléry-Melun ML, 2014. Psychomotor retardation is a scar of past depressive episodes, revealed by simple cognitive tests. Eur. Neuropsychopharmacol 24, 1630–1640. [PubMed: 25129432]

Hammar Å, SØRensen L, Årdal G, Oedegaard KJ, Kroken R, Roness A, Lund A, 2010. Enduring cognitive dysfunction in unipolar major depression: a test–retest study using the Stroop paradigm. Scand. J. Psychol 51, 304–308. [PubMed: 20042028]

Hasselbalch BJ, Knorr U, Kessing LV, 2011. Cognitive impairment in the remitted state of unipolar depressive disorder: a systematic review. J. Affect. Disord 134, 20–31. [PubMed: 21163534]

Jacobson L, Sapolsky R, 1991. The role of the hippocampus in feedback regulation of the hypothalamic-pituitary-adrenocortical axis*. Endocr. Rev 12, 118–134. [PubMed: 2070776]

Killgore WD, 2010. Effects of Sleep Deprivation on Cognition, Progress in Brain Research. Elsevier, pp. 105–129.

Kray J, Lindenberger U, 2000. Adult age differences in task switching. Psychol. Aging 15, 126. [PubMed: 10755295]

Mander BA, Winer JR, Jagust WJ, Walker MP, 2016. Sleep: a novel mechanistic pathway, biomarker, and treatment target in the pathology of Alzheimer's disease? Trends Neurosci. 39, 552–566. [PubMed: 27325209]

Mayers AG, Baldwin DS, 2006. The relationship between sleep disturbance and depression. Int. J. Psychiatry Clin. Pract 10, 2–16. [PubMed: 24926763]

Mellor A, Bucks RS, Maul J, Sanders KA, McGowan H, Waters F, 2018. Sleep and cognition in older adults: does depression matter? An actigraphy and polysomnography study. Arch. Psychol 2.

Monsell S., 2003. Task switching. Trends Cognit. Sci 7, 134–140. [PubMed: 12639695]

Morcom AM, Rugg MD, 2002. Getting ready to remember: the neural correlates of task set during recognition memory. Neuroreport 13, 149–152. [PubMed: 11924877]

Moussavi S, Chatterji S, Verdes E, Tandon A, Patel V, Ustun B, 2007. Depression, chronic diseases, and decrements in health: results from the World Health Surveys. Lancet 370, 851–858. [PubMed: 17826170]

Muzur A, Pace-Schott EF, Hobson JA, 2002. The prefrontal cortex in sleep. Trends Cognit. Sci 6, 475–481. [PubMed: 12457899]

Pace-Schott EF, Spencer RM, 2011. Age-Related Changes in the Cognitive Function of Sleep, Progress in Brain Research. Elsevier, pp. 75–89.

Paelecke-Habermann Y, Pohl J, Leplow B, 2005. Attention and executive functions in remitted major depression patients. J. Affect. Disord 89, 125–135. [PubMed: 16324752]

Papakostas GI, 2015. Antidepressants and their effect on cognition in major depressive disorder. J. Clin. Psychiatry 76, e1046. [PubMed: 26335095]

Pillai V, Kalmbach DA, Ciesla JA, 2011. A meta-analysis of electroencephalographic sleep in depression: evidence for genetic biomarkers. Biol. Psychiatry 70, 912–919. [PubMed: 21937023]

Radley JJ, Sisti HM, Hao J, Rocher AB, McCall T, Hof PR, McEwen BS, Morrison JH, 2004. Chronic behavioral stress induces apical dendritic reorganization in pyramidal neurons of the medial prefrontal cortex. Neuroscience 125, 1–6. [PubMed: 15051139]

Sadler P, McLaren S, Klein B, Jenkins M, 2018. Advancing cognitive behaviour therapy for older adults with comorbid insomnia and depression. Cognit. Behav. Ther 47, 139–154. [PubMed: 28784037]

Santesso DL, Steele KT, Bogdan R, Holmes AJ, Deveney CM, Meites TM, Pizzagalli DA, 2008. Enhanced negative feedback responses in remitted depression. Neuroreport 19, 1045–1048. [PubMed: 18580576]

Schmaal L, Veltman DJ, van Erp TGM, Samann PG, Frodl T, Jahanshad N, Loehrer E, Tiemeier H, Hofman A, Niessen WJ, Vernooij MW, Ikram MA, Wittfeld K, Grabe HJ, Block A, Hegenscheid K, Volzke H, Hoehn D, Czisch M, Lagopoulos J, Hatton SN, Hickie IB, Goya-Maldonado R, Krämer B, Gruber O, Couvy-Duchesne B, Renteria ME, Strike LT, Mills NT, de Zubicaray GI, McMahon KL, Medland SE, Martin NG, Gillespie NA, Wright MJ, Hall GB, MacQueen GM, Frey EM, Carballedo A, van Velzen LS, van Tol MJ, van der Wee NJ, Veer IM, Walter H, Schnell K, Schramm E, Normann C, Schoepf D, Konrad C, Zurowski B, Nickson T, McIntosh AM, Papmeyer M, Whalley HC, Sussmann JE, Godlewska BR, Cowen PJ, Fischer FH, Rose M, Penninx BWJH, Thompson PM, Hibar DP, 2015. Subcortical brain alterations in major depressive disorder: findings from the enigma major depressive disorder working group. Mol. Psychiatry 21, 806. [PubMed: 26122586]

Scullin MK, Bliwise DL, 2015. Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. Perspect. Psychol. Sci 10, 97–137. [PubMed: 25620997]

Sheline YI, Sanghavi M, Mintun MA, Gado MH, 1999. Depression duration but not age predicts hippocampal volume loss in medically healthy women with recurrent major depression. J. Neurosci 19, 5034–5043. [PubMed: 10366636]

Snyder HR, 2013. Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: a meta-analysis and review. Psychol. Bull 139, 81–132. [PubMed: 22642228]

Spitzer M, Robert L, Gibbon M, Williams J, 2002. Structured Clinical Interview For DSM-IV-TR Axis I disorders, Research Version. Biometrics Research. New York State Psychiatric Institute, New York Non-Patient Edition (SCID-I/NP).

Sutter C, Zöllig J, Allemand M, Martin M, 2012. Sleep quality and cognitive function in healthy old age: the moderating role of subclinical depression. Neuropsychology 26, 768. [PubMed: 22984799]

Teasdale JD, Segal Z, Williams JMG, 1995. How does cognitive therapy prevent depressive relapse and why should attentional control (mindfulness) training help? Behav. Res. Ther 33, 25–39. [PubMed: 7872934]

Thase ME, Kupfer DJ, Fasiczka AJ, Buysse DJ, Simons AD, Frank E, 1997. Identifying an abnormal electroencephalographic sleep profile to characterize major depressive disorder. Biol. Psychiatry 41, 964–973. [PubMed: 9110102]

Vanderhasselt MA, De Raedt R, 2009. Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: an event related potentials study. Biol. Psychol 81, 169–176. [PubMed: 19482234]

White DA, Myerson J, Hale S, 1997. How cognitive is psychomotor slowing in depression? Evidence from a meta-analysis. Aging Neuropsychol. Cognit 4, 166–174.

Wichniak A, Wierzbicka A, Walęcka M, Jernajczyk W, 2017. Effects of anti-depressants on sleep. Curr. Psychiatry Rep 19, 63. [PubMed: 28791566]

Wilckens KA, Ferrarelli F, Walker MP, Buysse DJ, 2018. Slow-Wave activity enhancement to improve cognition. Trends Neurosci.

Wilckens KA, Hall MH, Erickson KI, Germain A, Nimgaonkar VL, Monk TH, Buysse DJ, 2017. Task switching in older adults with and without insomnia. Sleep Med. 30, 113–120. [PubMed: 28215233]

Wilckens KA, Hall MH, Nebes RD, Monk TH, Buysse DJ, 2016. Changes in cognitive performance are associated with changes in sleep in older adults with insomnia. Behav. Sleep Med 14, 295–310. [PubMed: 26322904]

Wilckens KA, Tremel JJ, Wolk DA, Wheeler ME, 2011. Effects of task-set adoption on ERP correlates of controlled and automatic recognition memory. Neuroimage 55, 1384–1392. [PubMed: 21211568]

Wilckens KA, Woo SG, Erickson KI, Wheeler ME, 2014a. Sleep continuity and total sleep time are associated with task-switching and preparation in young and older adults. J. Sleep Res 23, 508–516. [PubMed: 24697907]

Wilckens KA, Woo SG, Kirk AR, Erickson KI, Wheeler ME, 2014b. Role of sleep continuity and total sleep time in executive function across the adult lifespan. Psychol. Aging 29, 658. [PubMed: 25244484]

Willner P., 2017. The chronic mild stress (CMS) model of depression: history, evaluation and usage. Neurobiol. Stress 6, 78–93. [PubMed: 28229111]

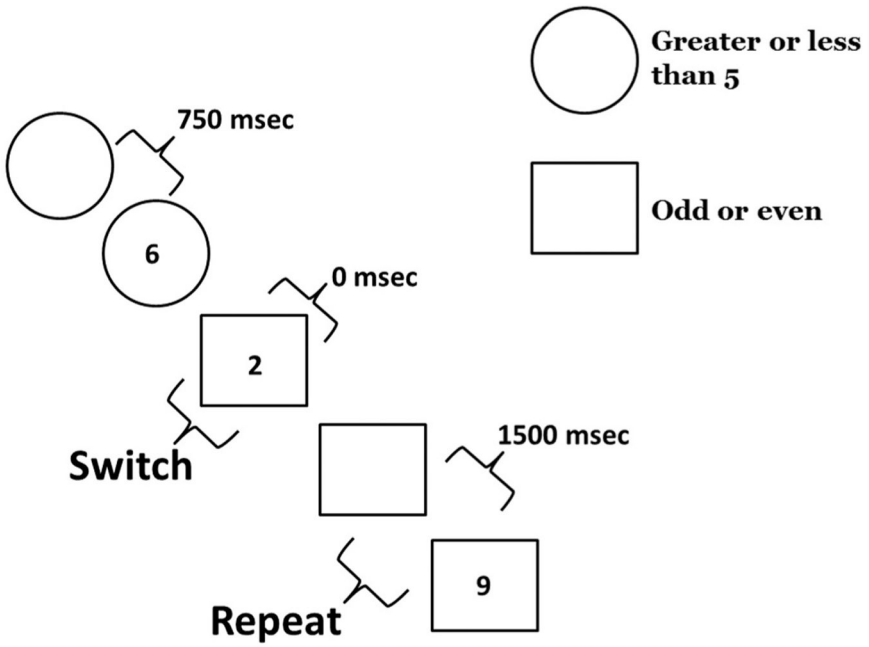

Fig. 1. Task-switching paradigm.

A sample sequence of trials from the switching block of the task-switching paradigm. A circle cues the participant to judge whether the subsequent number is greater than or less than 5. On the first trial, the number is 6, so the response is "greater than 5″. The next trial (a switch trial) cues the participant with a square to judge whether the number is odd or even, the number is 2, so the response is "even". The subsequent trial is a repeat, and the answer is "odd" for 9. The cue-target interval varied (0, 750, and 1500 ms). The cue-target interval was included as a covariate in the present analyses. Figure adapted from (Wilckens et al., 2017, 2014b).

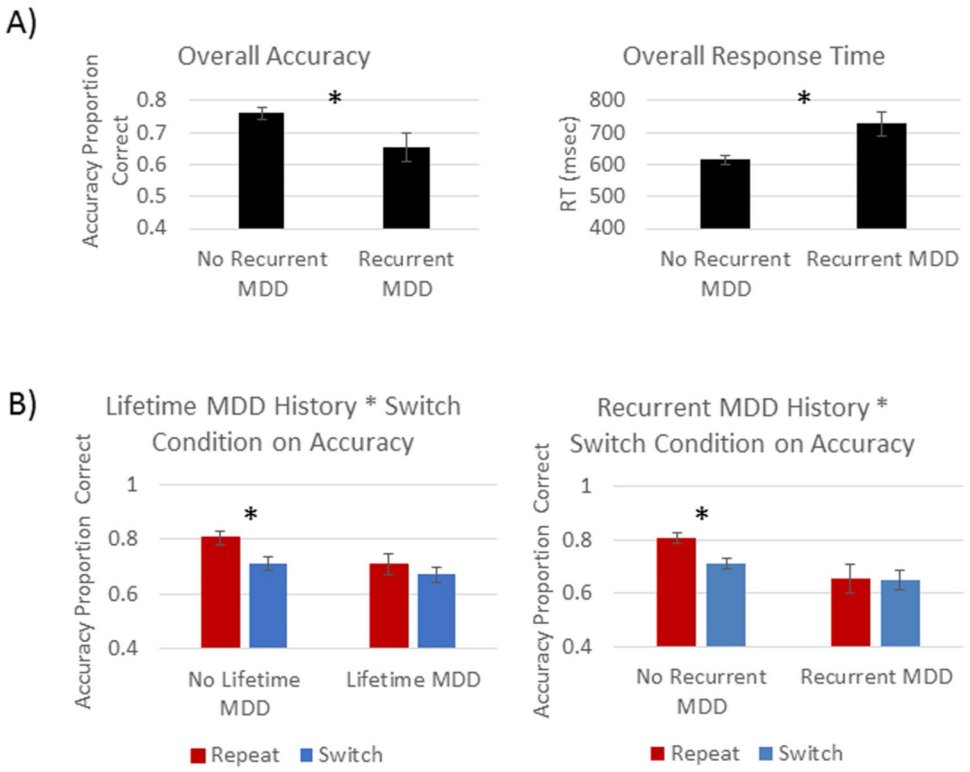

Fig. 2. Main effects and interactions with MDD history group.

A) Overall accuracy (left) and overall response time (right) were significantly poorer in the recurrent MDD group. B) Lifetime MDD history and recurrent MDD history significantly interacted with switch condition in accuracy. The expected performance boost associated with repeat trials was attenuated in participants with an MDD history.

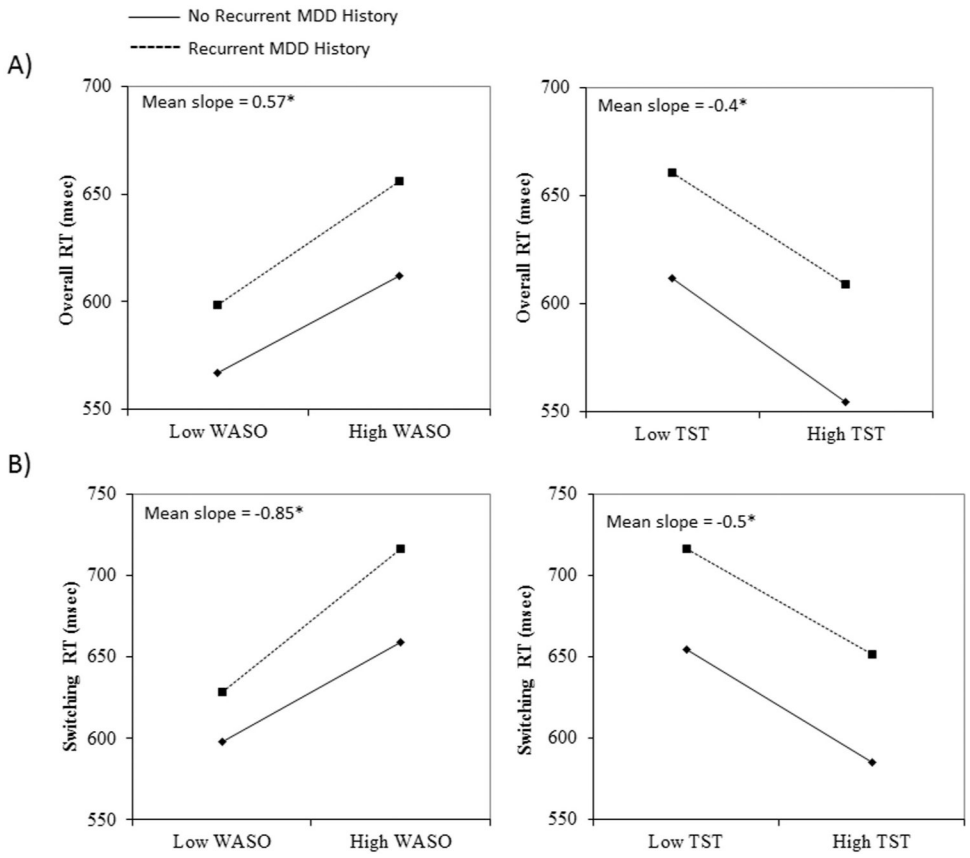

Fig. 3. Simple slopes for response time with WASO and TST stratified by MDD recurrence.

WASO (left) and TST (right) are associated with overall response time (RT) across both the single task and switching blocks (A) and limited to the switching block (B). The main effect of recurrent MDD history group and sleep did not significantly interact in their relationship with performance (response time shown here). Simple slopes are significant at the sample mean for WASO and TST, $*p < 0.05$.

Table 1

Demographic, clinical, and sleep characteristics as a function of lifetime depression status and recurrent depression status.

n	No lifetime MDD 28	Lifetime MDD 25	F/Chi square	*p*	No recurrent MDD 36	Recurrent MDD 17	F/Chi square	*p*
Age	59 (7.95)	63 (9.23)	2.79	0.10	59 (8.43)	64 (8.62)	3.87	0.06†
Sex% Female	50%	72%	2.67	0.10	50%	82.4%	**5.05**	**0.025**
Education	6.75 (1.21)	6.20 (1.73)	1.83	0.18	6.58 (1.20)	6.29 (1.99)	0.43	0.51
HDRS (no sleep)	**1.18 (1.61)**	**4.96 (3.34)**	**28.58**	< **0.001**	**2.06 (2.74)**	**4.88 (3.28)**	**10.85**	**0.002**
% Current Antidepressants	8**%**	**44%**	**8.96**	**0.011**	**8.3%**	**64.7%**	**20.52**	< **0.001**
PSG WASO	52.14 (50.24)	74.74 (40.74)	0.49	0.49	54.92 (46.82)	79.97 (43.01)	1.51	0.23
PSG TST	387.08 (64.78)	408.94 (66.65)	0.003	0.96	397.48 (12.06)	399.05 (17.26)	0.69	0.41
PSG AHI	7.31 (10.01)	9.44 (12.13)	0.33	0.57	7.26 (10.10)	10.54 (12.76)	2.70	0.11

Means with standard deviations in parentheses are presented unless otherwise noted. F and p values represent main effects of MDD history based on MANOVA or chi square. One MANOVA tested group differences in continuous covariates (age, education, and HDRS). Chi square was used to test group differences in dichotomous covariates (sex and current use of antidepressants). A second MANOVA controlled for all covariates while testing PSG variables. For PSG variables, $n = 25$ for no lifetime MDD, $n = 25$ for lifetime MDD, $n = 33$ for no recurrent MDD and $n = 17$ for recurrent MDD. Degrees of freedom (df) are 1,51 for covariates, and 1,44 for PSG variables. Bold font denotes significant between group differences, $p < 0.05$.

Table 2

Associations with accuracy adjusting for age, sex, and education.

	Overall accuracy		Interaction with block (Single vs Switching)		Interaction with switch condition (Switch vs Repeat Trial)	
	F	**p value**	**F**	**p value**	**F**	**p value**
Lifetime MDD	1.26	0.268	0.00	0.990	**6.30**	**0.015** **
Recurrent MDD	**7.28**	**0.010** *,**	0.05	0.833	**19.00**	< **0.001** *,**
PSG WASO	0.31	0.581	0.97	0.330	1.76	0.191
PSG TST	0.05	0.827	1.21	0.277	1.22	0.276
Lifetime MDD * PSG WASO	0.15	0.699	0.69	0.410	0.23	0.631
Recurrent MDD *PSG WASO	0.32	0.577	0.49	0.490	0.04	0.851
Lifetime MDD * PSG TST	0.01	0.919	0.01	0.932	0.05	0.827
Recurrent MDD *PSG TST	0.13	0.724	0.07	0.797	0.65	0.425

F and p values represent main effects and interactions involving task-switching accuracy based on repeated measures ANOVA. Bold font denotes significant associations, $p < 0.05$.

*Denotes significance after adjusting for antidepressants.

**Denotes significance after adjusting for current depression symptoms.

Table 3

Associations with Response Time (RT) controlling for age, sex, and education.

	Overall RT		**Interaction with block (Single vs. Switching)**		**Interaction with switch condition (Switch vs Repeat Trial)**	
	F	***p* value**			***F***	***p* value**
Lifetime MDD	1.12	0.295	0.28	0.599	0.13	0.718
Recurrent MDD	**5.17**	**0.028** [*,**]	2.01	0.163	0.13	0.718
PSG WASO	**6.79**	**0.012** [a]	**6.55**	**0.014** [a]	1.83	0.183
PSG TST	**5.73**	**0.021** [a]	1.65	0.205	0.61	0.441
Lifetime MDD * PSG WASO	0.03	0.862	0.06	0.809	0.63	0.432
Recurrent MDD *PSG WASO	0.06	0.804	0.54	0.465	0.84	0.366
Lifetime MDD * PSG TST	0.02	0.903	0.02	0.881	1.25	0.271
Recurrent MDD *PSG TST	0.02	0.896	0.002	0.968	0.70	0.408

F and p values represent main effects and interactions involving task-switching RT based on repeated measures ANOVA. Bold font denotes significant associations, $p < 0.05$.

[*] Denotes significance after adjusting for antidepressants.

[**] Denotes significance after adjusting for current depression symptoms.

[a] denotes significance after controlling for AHI in analyses with sleep variables.