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Original Article

ORIGINAL ARTICLE

Sleep deprivation and compensatory cognitive effort on a visual information processing task

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Abstract

Study Objectives: Total sleep deprivation (TSD) is often associated with worse performance on tasks of attention and working memory, but some studies show no performance changes. One possibility is that greater compensatory cognitive effort is put forth to achieve similar results after TSD. We aimed to better understand the relationship between TSD, cognitive engagement, and performance outcomes following TSD.

Methods: Twenty healthy adults completed cognitive testing following a night of normal sleep and again after ~55 hours of TSD. Participants detected target letters in low (3-item) and high (10-item) load visual letter displays on the span of apprehension task with concurrent pupillometry, a measure of cognitive effort.

Results: We found significantly poorer detection accuracy and marginally longer response times following TSD across both arrays. In both arrays, significantly greater preparatory pupillary responses were found just prior to array onset. There was also a significant session by array interaction for pupillary responses, such that significantly greater dilation was found for the 3-letter array after TSD, while a nonsignificant decline in dilation was found following the 10-letter array after TSD.

Conclusions: These results suggest a complex relationship between attentional control and cognitive resource allocation following TSD. Sleep-deprived individuals may allocate more compensatory cognitive effort to easier tasks but choose to disengage from more challenging cognitive tasks that have little perceived reward or probability of success to preserve diminishing cognitive resources. More work is needed to better delineate the underlying neurological systems involved in these processing load-dependent attentional control mechanisms after TSD.

Statement of Significance

This study shows sleep deprivation plays an important role in cognitive effort. These findings support prior frameworks, such as the adaptive gain theory, which suggests that tonic and phasic activation within the locus coeruleus-noradrenergic (LC-NA) system is associated with both pupillary responses and subsequent decisions to engage or disengage from a particular task. Findings add to the current body of literature suggesting that pupillometry can be used as a proxy for studying cognitive effort and is especially useful in total sleep deprivation (TSD) given decrements in performance on cognitive measures may not always be observed. Future work may pair pupillometry with functional neuroimaging to determine whether pupillary responses are correlated with changes in the neurological systems impacted by TSD.

Key words: compensation; cognitive effort; resource allocation; processing load; sleep deprivation

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Introduction

Sleep deprivation and short sleep duration (<7 hours) are an increasingly common problem, and approximately 35% of adults in the United States sleep less than 7 hours per night [1]. Sleep deprivation is associated with multiple health-related risk factors, such as higher rates of heart attack [2] and stroke [3], increased markers of inflammation [4], higher levels of circulating cortisol [5], and reduced immune response to injury [6, 7]. Cognitively, sleep deprivation is a predictor of worse performance on tasks of attention and working memory, cognitive vigilance, and decision-making [6], and has been linked with lower motivation [8] and ability to tolerate stress [9]. However, the impact of sleep deprivation on cognition varies across studies and there remains mixed evidence about the interaction between sleep deprivation and factors such as neurological systems recruited to complete tasks, cognitive effort, and motivation to complete tasks after total sleep deprivation (TSD) compared to normal sleep [8, 10, 11].

The neurological mechanisms underlying changes in cognitive performance following short or prolonged TSD are not entirely understood. Increased sleep pressure resulting in microsleeps [6] and instability in alertness and vigilance levels [12] have been cited as potential contributors to inconsistent cognitive performance. There is also substantial evidence to suggest that the locus coeruleus (LC) – noradrenergic (NA) system, which is important to cortical activation, attention, and sleep–wake cycles [13], is impacted by sleep deprivation such that sustained attention and other cognitive tasks become more effortful [14]. The prefrontal cortex (PFC)—which is necessary for attentional control and decision-making [15]—shares bilateral connections with the LC and is important to cortical activation in accordance with task demands [16, 17]. Multiple studies have found that the PFC is especially vulnerable to TSD, and frontally mediated functions, such as sustained attention, working memory, and executive control, are often more significantly impacted [18–20]. Conceivably, changes in activation patterns within these systems may impact cognitive performance following periods of short or prolonged sleep deprivation.

In addition to its role in PFC activation, the LC also influences arousal within the autonomic nervous system and innervates structures that control pupillary responses to stimuli [21]. Pupil dilation, in particular, is associated with LC-NA-dependent activation, and inhibition of the LC contributes to pupil constriction and sedation [22]. Multiple studies have indicated that increased pupil size may be used as a marker of task-related cognitive effort, with pupil size increasing as a function of task demands (see review by van der Wel and van Steenbergen [23]). Task-evoked patterns in pupillary constriction and dilation in response to stimuli have also been examined to determine if these patterns were associated with differences in task performance [10, 24]. Differences in baseline, pre-stimulus (preparatory), and task-evoked pupil diameter have all been used as an approximation of task engagement. Further, Wang and colleagues [25] found an inverse relationship between pre-stimulus (preparatory) pupil dilation and reaction time, suggesting a link between pre-stimulus pupil responses, response loading, and response time.

While there are multiple factors that impact cognition following sleep deprivation [4, 9, 26], motivation and cognitive effort are crucial constructs to consider in sleep-deprived individuals. Massar and colleagues [8] proposed a "neuroeconomic framework of motivational decline under sleep deprivation," which suggests that individuals will make a values-based choice about the effort they are willing to exert in order to gain an expected reward. Following TSD, these authors pose that there is an overall devaluation in the cost-benefit ratio of completing a task such that sleep-deprived individual are more likely to withdraw effortful exertions to complete a task unless the rewards are sufficiently high [8]. A number of studies have shown that tasks that were not perceived as especially effortful following normal sleep are often perceived as being much more effortful after TSD [6, 27]. Thus, decisions to engage or disengage from a task must take factors related to TSD into account, such as the cognitive resources available to invest in different tasks. Functional neuroimaging studies support the notion that TSD is associated with changes in neural activation patterns that have been associated with decrements in task performance following TSD compared to normal sleep [28–32]. Thus, as task difficulty increases following sleep deprivation, the decision to engage with the task must take into consideration not only the probability of success, but also whether the amount of cognitive resources required to complete the task is worth the perceived reward.

To examine the relationship between sleep deprivation, cognitive effort, and performance metrics at varying levels of task difficulty, we administered a visual information processing task with low- and high-processing loads and recorded pupillary responses as an objective index of cognitive resource allocation during the task. We examined whether pupillary responses to stimuli significantly changed following a period of sleep deprivation and whether the impact of sleep deprivation on pupillary responses varied as a function of task difficulty. We hypothesized that sleep deprivation would be associated with slower reaction time and a greater number of errors, but that participants would allocate greater cognitive effort to compensate for sleep deprivation effects on neural efficiency, especially at lower loads when possibilities of success are arguably higher, in order to achieve the "reward" of optimal performance. We also examined preparatory effort by examining pre-stimulus changes in pupil diameter. Given that Wang et al. [25] found that greater pre-stimulus preparatory pupil dilation (effort) was associated with better target detection performance, we predicted that greater pupil dilation during the preparatory phase would be associated with better task performance after TSD.

Methods

Participants

Healthy participants were recruited from the University of California, San Diego UCSD campus and the general community. This study was approved by the UCSD Human Subjects Committee and each participant reviewed and signed an approved informed consent form prior to study enrollment. Data from this study were taken from a larger 5-day study analyzing the impact of extended operations (e.g. within military personnel) on neurological functioning and cognitive performance. Participants were excluded for: (1) any neurological, medical, or psychiatric disorder; (2) head injury with loss of consciousness >15 minutes; (3) eye injury or disease that might affect pupil motor function; (4) substance abuse or dependence other than caffeine; (5) self-reported average nightly total sleep time <7 or >9 hours; (6) caffeine consumption >300 mg/day; alcohol

consumption more than two standard drinks per day. For 1 week prior to the study, participants maintained a regular sleep–wake schedule, based on their habitual schedule, and this was monitored with daily sleep diaries and actigraphy (sleep measured objectively from a wrist-watch device). Participants were asked to stop all alcohol and caffeine consumption as of 3 days prior to the start of their laboratory stay, and this was enforced throughout the rest of the protocol. Each participant was compensated for participation in the larger sleep deprivation study.

A total of 32 participants initially enrolled in this study; however, one did not complete follow-up testing, one reported abnormal eye dryness which limited their ability to see the stimulus items following sleep deprivation, and ten participants had excessive artifacts in pupillometry data. These 12 participants were excluded from final analyses, leaving a total sample size of 20 participants. Data loss due to factors such as participants falling asleep during task administration and artifacts introduced from droopy eyelids in especially sleepy patients is commonly reported [33, 34]. However, to determine if results were biased as a result of attrition, we ran analyses comparing performance on the SOA task for participants that were dropped from the study to those that were retained. Participants excluded from final analyses did not differ significantly from participants included on any of the pupil or performance measures at baseline or any performance measures following TSD, except for significantly slower response time to the 10-letter condition following TSD in the group that was dropped (M = 1082.91, SD = 255.68) compared to the group that was retained (M = 900.3, SD = 197.69; $t(29) = 2.22$, $p = .035$). Participants were also given the Psychomotor Vigilance Test (PVT) [35] after TSD approximately 2–3 hours prior to the SOA task as part of the larger sleep deprivation study, and t-tests, bootstrapped due to unequal sample sizes, showed no significant differences between groups in terms of median reaction time or lapses (trials with reaction time >500 ms) data for this task (p = .250 and .140, respectively). Taken together, these findings suggest those excluded were not simply worse on SOA task performance and did not generally show greater levels of attention impairment following TSD. Demographic data for participants retained for final analyses are presented in Table 1.

Table 1. Demographics data for study participants (n = 20)

	M (SD)	Range
Age (years)	23.95 (4.9)	19–38
Education (years)	15.40 (1.3)	13–18
	n	%
Sex		
Male	7	35
Female	13	65
Race/ethnicity		
Caucasian	14	70
Black/African-American	1	5
Hispanic/Latino	2	10
Asian	3	15

Sleep deprivation

Each participant spent six nights and days in the UCSD General Clinical Research Center's Laboratory for Sleep and Chronobiology (GCRS-LSC). During the first night, each participant underwent a polysomnography (PSG) study to determine if there were any baseline sleep disorders, which served as exclusion criteria. On the second night, they were asked to sleep

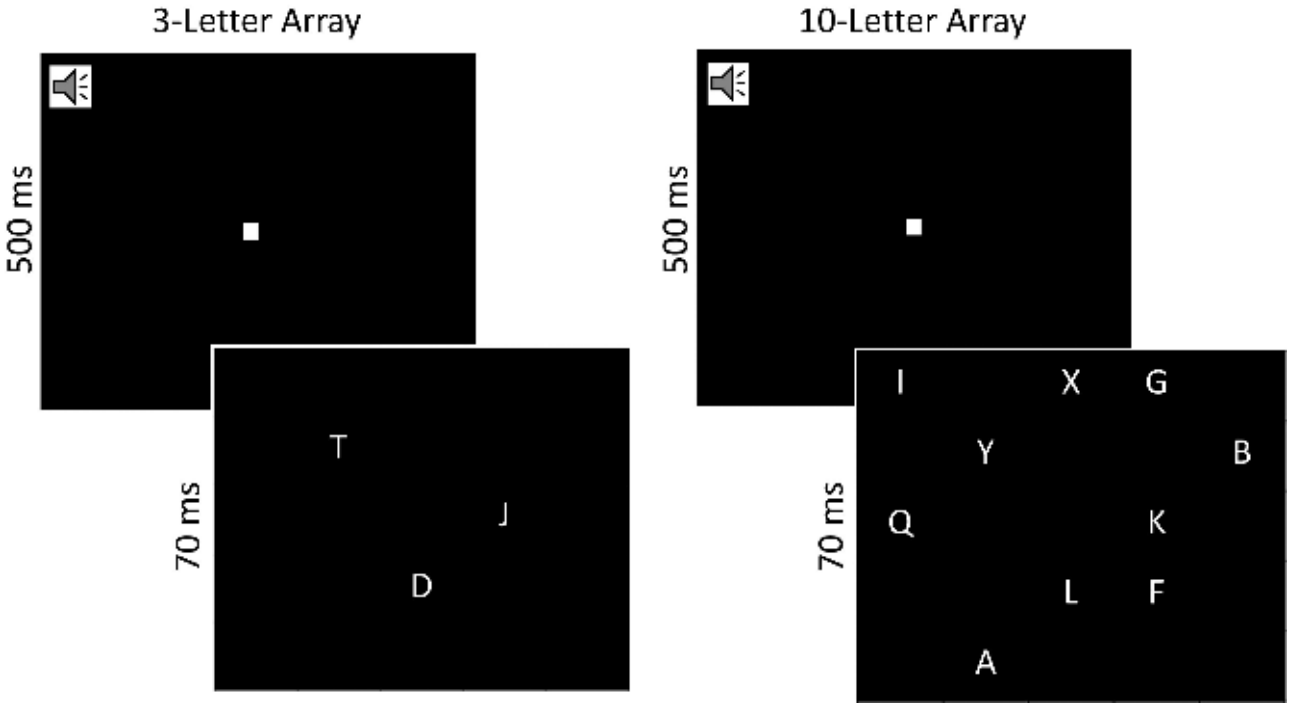

Figure 1. This is the span of apprehension (SOA) task, with the 3-letter trial on the left and the 10-letter trial on the right. During the testing trials, there is an initial tone and screen with white fixation square on a black background. This was followed by either the 3- or 10-letter array. Participants were then asked whether they saw a T or an F on the screen presented.

according to the same habitual sleep–wake schedule maintained at home for the prior week and underwent a second PSG. PSG sleep disorder screens were only included during the first night. Baseline testing (normally sleeping condition) was performed at 13:00–15:00 on day 2 of the study. Participants were sequestered in the sleep lab from the first night to the end of the study and were asked to remain awake for two nights (nights 2 and 3) beginning the morning after night 2 (~66 hours). This extended sleep deprivation timeframe was used to determine the impact of TSD beyond the typical 24- to 36-hour models typically used. Testing for the sleep deprivation condition occurred on day 4 between 13:00 and 15:00, following ~55 hours of TSD. Testing was completed in the early afternoon to reduce the potential additional impact of circadian rhythms that are often seen in the early morning or late afternoon. On the remaining two nights, participants again slept according to their habitual sleep schedule, though no further pupillometry testing occurred after day 4.

Cognitive performance: span of apprehension task

The span of apprehension (SOA) task was originally created by Estes and Taylor to determine an individual's ability to apprehend multiple objects at one time [36], and performance on this task is often used to test processing speed efficiency [37, 38]. This task was chosen for the present study given its sensitivity to detecting processing load effects (i.e. 3-letter and 10-letter arrays) [38–40]. On the SOA task, participants were asked to identify one of two target letters, either a "T" or an "F," presented on the computer screen for 70 ms within a group of other distracting letters. Participants were instructed that only one of the two target letters would be presented on the computer screen on each trial. The target was embedded in arrays containing either 2 (3-letter condition) or 9 distracting letters (10-letter condition), which were randomly selected from the remaining letters of the English alphabet (Figure 1). Participants were asked to press either the left button on a button box (indicating a "T" was present) or the right button (indicating an "F" was present). Both detection accuracy and speed were stressed in instructions ("try to be as accurate as you can, but also press as fast as you can"). Participants were also asked to refrain from blinking during the trials, but during the inter-trial interval they were encouraged to blink their eyes.

Participants were given 10 practice trials (5 consecutive 3-letter trials; 5 consecutive 10-letter trials) to ensure they understood the instructions. Each participant received accuracy feedback on their performance during the practice trials, but no feedback was given on test trials. A total of 64 trials were administered in blocks of 8 per condition in the following sequence, which controls for fatigue/habituation effects: 3-letter, 3-letter, 10-letter, 10-letter, 10-letter, 10-letter, 3-letter, 3-letter, for a total of 32 test trials per array condition. At the start of each trial, a tone sounded and a white fixation square appeared on the center of the computer monitor with a black screen background, which remained on the screen for 500 ms before the letter arrays were displayed for 70 ms as white letters on a black screen background (Figure 1). A 5-second inter-trial interval was maintained. The target and distracting letters were randomly assigned to locations in a 5 × 5 matrix with an equal number of T and F targets presented in each condition. The visual angle subtended by the 5 × 5 matrix was 33.4° × 28.3° (height × width) and by each array element was 5.2° × 5.4°. The number of correct target identifications (max 32) and the median response time per condition were calculated.

Cognitive effort: pupillometry

Participants sat in a height adjustable chair with their head stabilized in a chin rest with forehead bar in room with controlled ambient lighting (85 lux). Pupil size was recorded from the left eye using a Micromeasurements System 1200 corneal-reflection-pupil-center infrared pupillometer. A video camera sensitive to infrared light and an infrared light source were positioned 24 cm from the participant below the field of view, while the participant stared at a fixation square on a computer monitor placed 77 cm directly in front of the field of view. Analog pupil area was digitized at a 60-Hz sampling rate and saved for later analysis offline. The resolution of the pupillometer was .05 mm diameter, but with signal averaging, differences on the order of .01–.02 mm can be reliably detected.

Pupillary responses to cognitive tasks with visual displays that increase in luminance are typically bimodal waveforms, with an initial light reflex constriction followed by a peak dilation response. In response to the SOA task in this study, two constriction responses were observed (Figure 2). An initial small light reflex to the increased luminance of the fixation square (white pixels on dark screen) was observed prior to array exposure and was followed by a larger light reflex to the brighter stimulus arrays and subsequent dilation evoked by array processing (Figure 2). The constriction response to the array was expected to be impacted by the number of letters on the dark background, with larger responses in the 10-letter than in the 3-letter condition. We accounted for this array light reflex by calculating the dilation-constriction difference (computing dilation

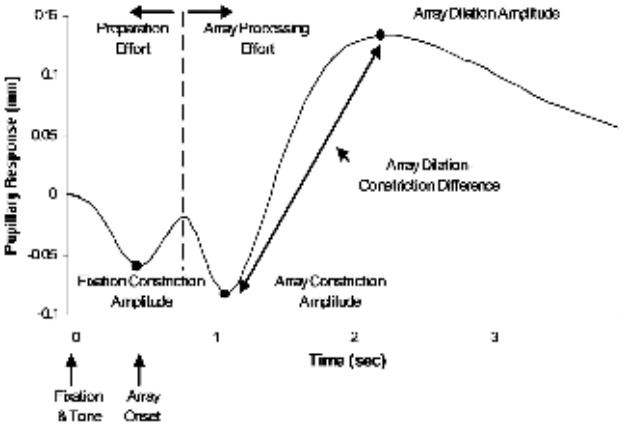

Figure 2. Pupillary response waveform (change in pupil diameter relative to baseline) evoked by the span of apprehension task, and pupillary response variables derived from the waveform. At the start of each trial, a dark screen was replaced by a white fixation square in the center of the monitor and a tone was sounded. An initial small light reflex constriction response to the increased luminance of the fixation square was observed prior to array exposure (preparation effort). Three- or 10-letter arrays were displayed 500 ms after trial onset as white letters on a black screen for 70 ms. The arrays evoked a larger light reflex and a subsequent dilation response (array processing effort). Pupil constriction to increased light exposure from the stimulus presentation was accounted for with the array dilation-constriction difference.

responses relative to peak array constriction). The fixation constriction response is an earlier constriction response that preceded the array onset. Pupillary light reflexes are reduced (i.e. less constriction or greater pupil diameter) under cognitive load [41]; and pupillary responses during the interval between fixation and stimulus onset on other visual information processing tasks have been interpreted as preparatory cognitive effort (e.g. Wang et al. [25]), so pupillary constriction responses to the fixation stimulus were interpreted as preparatory cognitive effort. Thus, seven pupillary response variables were derived from this waveform: (1) baseline pupil diameter—average of five samples recorded immediately prior to fixation on each trial; (2) fixation constriction amplitude (preparatory effort)—difference between baseline and the smallest diameter between 0 and 800 ms; (3) array constriction peak amplitude—difference between baseline and the smallest diameter between 800 and 1500 ms; (4) array dilation peak amplitude (array processing effort)—difference between baseline and the largest pupil diameter occurring between 1000 and 4000 ms; (5) array dilation-constriction amplitude difference (array processing effort controlling for array luminance)—the primary pupillary response measure; (6) latency to array constriction peak amplitude; and (7) latency to array dilation peak amplitude (see Figure 2).

Statistical analyses

Data cleaning methods for the pupillometry data were previously described (Granholm et al. [42]). Briefly, a computer algorithm was used to remove blinks and artifacts (identified as large changes in dilation outside the possible rate of change in pupil area) from digitized trail waveforms (4 seconds) and replaced discarded data using linear interpolation. Trials were discarded if over 50% of the waveform was comprised of blinks. A two-pass five-point digital smoothing filter (3.7 Hz) was then applied to the data, and valid trials were averaged for each condition. Participants who did not have at least five valid trials in each array size condition were excluded because visual inspection of the waveforms indicated instability with fewer than five trials averaged. For the final sample of 20 participants with valid pupil data, cleaning procedures resulted in valid pupil trials with a mean (*SD*) of 24.30 (5.57) for baseline 3-letter trials, 23.00 (6.78) for the baseline 10-letter trials, 11.65 (6.73) for the sleep deprivation 3-letter trials, and 12.15 (7.41) for the sleep deprivation 10-letter trials.

All analyses were completed in SPSS version 25 [43]. Two by two repeated measures analyses of variance (ANOVA) were used to determine the main and interaction effects of session (baseline versus TSD) and array (3-letter versus 10-letter) on each of the seven pupillary response variables and SOA task performance (detection accuracy and response time). Significant interaction effects were followed with post hoc paired samples *t*-tests. Statistical significance was set at an α-value of 0.05 for all tests. To determine whether this sample size was adequately powered, we ran a post hoc sensitivity analysis in G*Power (3.1.9.7) [44]. Using a repeated measure ANOVA within factors design, with one group of 20 participants across two timepoints (baseline and TSD), alpha set to 0.05, power (1–β probability) of 0.80, expected correlation of 0.5, and nonsphericity correction of 1, we achieved a minimum Cohen's *f* of 0.33 or greater. This corresponds with a "medium" effect size [45] and suggests that we were adequately powered to detect medium to large effects, but may have been inadequately powered to detect small to medium effects.

Results

Table 2 displays the performance and pupillary response data for the subjects at baseline and following sleep deprivation, as well as repeated measures ANOVA results. Detection accuracy was significantly poorer in the 10-item condition compared to the 3-item array and in the normal sleep versus TSD across both array sizes, but the session by array interaction was not significant. Response time was significantly slower in the 10-item array than the 3-item

Table 2. Behavioral performance and pupillary response components for the span of apprehension task for each testing session

	Baseline		Sleep deprived		Session			Array			Session × array interaction		
Performance	3-letter	10-letter	3-letter	10-letter	*F*	*p*	(η^2)	*F*	*p*	(η^2)	*F*	*p*	(η^2)
Detection accuracy (#) (max: 32)	31.45 (0.83)	27.80 (2.38)	29.75 (2.79)	26.40 (3.79)	7.74	.012*	(.29)	53.51	.000*	(.74)	0.24	.629	(.01)
Response time (ms)	675.25 (114.92)	863.60 (174.05)	735.60 (119.14)	900.30 (197.69)	3.68	.070	(.16)	57.75	.000*	(.75)	0.60	.449	(.03)
Pupillary response													
Baseline pupil diameter (mm)	5.22 (.70)	5.21 (.77)	4.86 (.92)	5.00 (.84)	3.22	.089	(.15)	1.98	.176	(.09)	2.40	.138	(.11)
Fixation constriction amplitude (mm)	−.10 (.09)	−.11 (.09)	−.07 (.06)	−.06 (.05)	7.44	.013*	(.28)	0.00	.950	(.00)	1.59	.223	(.08)
Array constriction amplitude (mm)	.05 (.12)	−.03 (.15)	.07 (.14)	−.03 (.16)	0.40	.537	(.02)	27.45	.000*	(.59)	0.59	.451	(.03)
Array dilation amplitude (mm)	.27 (.12)	.30 (.14)	.40 (.24)	.28 (.20)	2.30	.146	(.11)	1.86	.189	(.09)	4.56	.046*	(.19)
Array dilation—constriction difference (mm)	.22 (.08)	.33 (.13)	.31 (.16)	.32 (.16)	1.92	.182	(.09)	5.27	.033*	(.22)	4.39	.050*	(.19)
Latency to array constriction (ms)	.92 (.04)	.88 (.07)	.91 (.07)	.85 (.08)	3.80	.066	(.17)	24.36	.000*	(.56)	0.81	.379	(.04)
Latency to array dilation (ms)	1.93 (.30)	2.21 (.47)	2.05 (.46)	2.23 (.72)	0.55	.467	(.03)	4.86	.040*	(.20)	0.30	.590	(.02)

All variables are *M* (*SD*). For all *F*-tests, df = 1,19.

array, and was marginally increased (p = .07) by sleep deprivation, but the session by array interaction was not significant.

With regard to the dilation-constriction difference score, which is an index of the amount of pupil dilation (array processing effort) that accounts for amount of light exposure during stimulus presentation, there was a significant effect of processing load (array size), with greater dilation found at higher loads. The main effect of sleep deprivation was not significant, but consistent with our hypothesis, there was a significant session by array interaction. Follow-up paired samples t-tests indicated significantly greater pupil dilation following TSD relative to normal sleep only in the three-letter array condition ($t(19) = -2.76$, p = .012, d = .62). A similar pattern of results was found for array dilation amplitude, whereby the session by array interaction just missed significance (p = .050), and significantly greater pupil dilation was found following TSD relative to normal sleep only in the three-letter array condition ($t(19) = -2.60$, p = .018, d = .58; Figures 3 and 4). As expected, given differences in the amount of array light, the array size effect was significant for array constriction amplitude, with greater constriction responses in the 10-letter array, but the session effect and session by array size interaction were not significant.

With regard to fixation constriction amplitude (preparatory effort), there was a significant main effect of TSD, such that less constriction (greater pupil dilation/effort) was found after TSD relative to normal sleep, but the array size effect and the session by array size interaction were not significant (Figure 4). Finally, there was an array size effect for latency to constriction and latency to dilation, such that there was shorter latency to constriction for the 10-letter array and shorter latency to dilation for the 3-letter array. However, there were no significant effects of session or session × array interactions.

Discussion

This study examined the effect of sleep deprivation on effort (pupil dilation) and performance on a task of attention and processing speed efficiency at varying levels of task difficulty in a sample of healthy college-aged adults. Consistent with our hypothesis, significantly poorer detection accuracy was found following a period of TSD (~55 hours), with marginally longer response times across both arrays (both 3- and 10 items). Also consistent with our hypothesis, greater cognitive effort (pupillary dilation) was found following TSD, though only at lower but not higher processing loads. Finally, we found significantly greater preparatory pupil dilation following TSD in both processing load conditions, suggesting greater preparatory effort overall. These findings suggest that sleep deprivation is associated with more variable cognitive effort both prior to and during stimulus presentation.

In the context of Massar et al.'s [8] neuroeconomic framework of motivational decline under sleep deprivation, we might have expected that less effort would be put forth for both processing load conditions following TSD. However, within this framework, participants are expected to be more likely to put forth effort when there is greater probability of reward [8]. We predicted and found reduced array processing effort only in the higher processing load condition, which had lower probability of success. Conversely, we found greater effort in the lower-load condition, which had greater probability of reward/successful performance. These results suggest that the greater perceived probability of success when they saw three-letter arrays was sufficiently motivating for participants to put forth greater effort to complete the task following TSD. This decision to engage with the low-load condition may also have been influenced by prior experience with these stimuli at pre-test under NS, which resulted in nearly perfect performance accuracy for the three-letter condition. This expectation for success may have added additional motivation to engage in this task. Conversely, although there was increased preparatory effort prior to array onset in both conditions, there was a nonsignificant decline in pupillary responses from NS to TSD for the 10-letter array, suggesting potential differences in processing load-dependent effort allocation. Taken together, the findings also suggest that as perceived task difficulty increases following sleep deprivation, the decision to engage with the task will depend on whether the level of cognitive resources required to complete the task is worth it, given the perceived probability of success.

The findings in our study that there were more errors and moderately slower reaction time following sleep deprivation may be partially explained by greater recruitment of less efficient processing resources, making focused attention and cognitive control slower and more error prone, despite increases in cognitive effort. While we did not directly assess neurological activation patterns in our participants and thus cannot confirm hypotheses about our findings in terms of their relationship to neuroanatomical studies, prior research provides insights that are important to consider. Neurological control over attention and general cognitive effort are dependent on efficient communication between a complex array of neural networks. For instance, cortical inputs from the orbitofrontal and anterior cingulate cortices—which are associated with decision-making [46] and cognitive control [47]—to the LC are important in task-related behaviors, such as engagement or disengagement from an activity [24] and are particularly vulnerable to SD [17].

Moreover, in their meta-analysis of neuroimaging studies in sleep deprivation, Ma and colleagues found decreased activation within frontal and parietal regions during an attentional task following sleep deprivation; however, there was increased activation within the bilateral thalami [28]. Further, on an attention task, Chee et al. identified cognitive "lapses" following sleep deprivation characterized by interspersed periods of normal neural activation with periods of reduced cognitive control and lower cortical arousal [29]. These changes in arousal patterns to being less predictable or efficient following TSD compared to NS may help to explain, in part, why cognitive exertion feels more effortful after a period of sleep deprivation. Other studies have posed that changes in cognitive performance and increased difficulty in task performance are related to variability in sustained attention and vigilance related to mounting sleep pressure, microsleeps, and local sleeps (i.e. neurons that have been active for prolonged periods go "offline" in some cortical regions during tasks following TSD) [6, 12, 30, 48].

The adaptive gain theory (AGT) of LC activation proposed by Aston-Jones and Cohen [24] suggests that phasic LC activation is associated with task-related decision-making and performance optimization, whereas tonic activity correlates with task disengagement and a search for alternatives. Tonic activity in the LC is generally linked to inter-trial pupil diameter (baseline) and phasic activity is thought to be brought on by the introduction of a stimulus or task-evoked change, with less pre-trial dilation and greater task-evoked dilation associated with better task performance [10, 24]. In our study, inter-trial baseline pupil

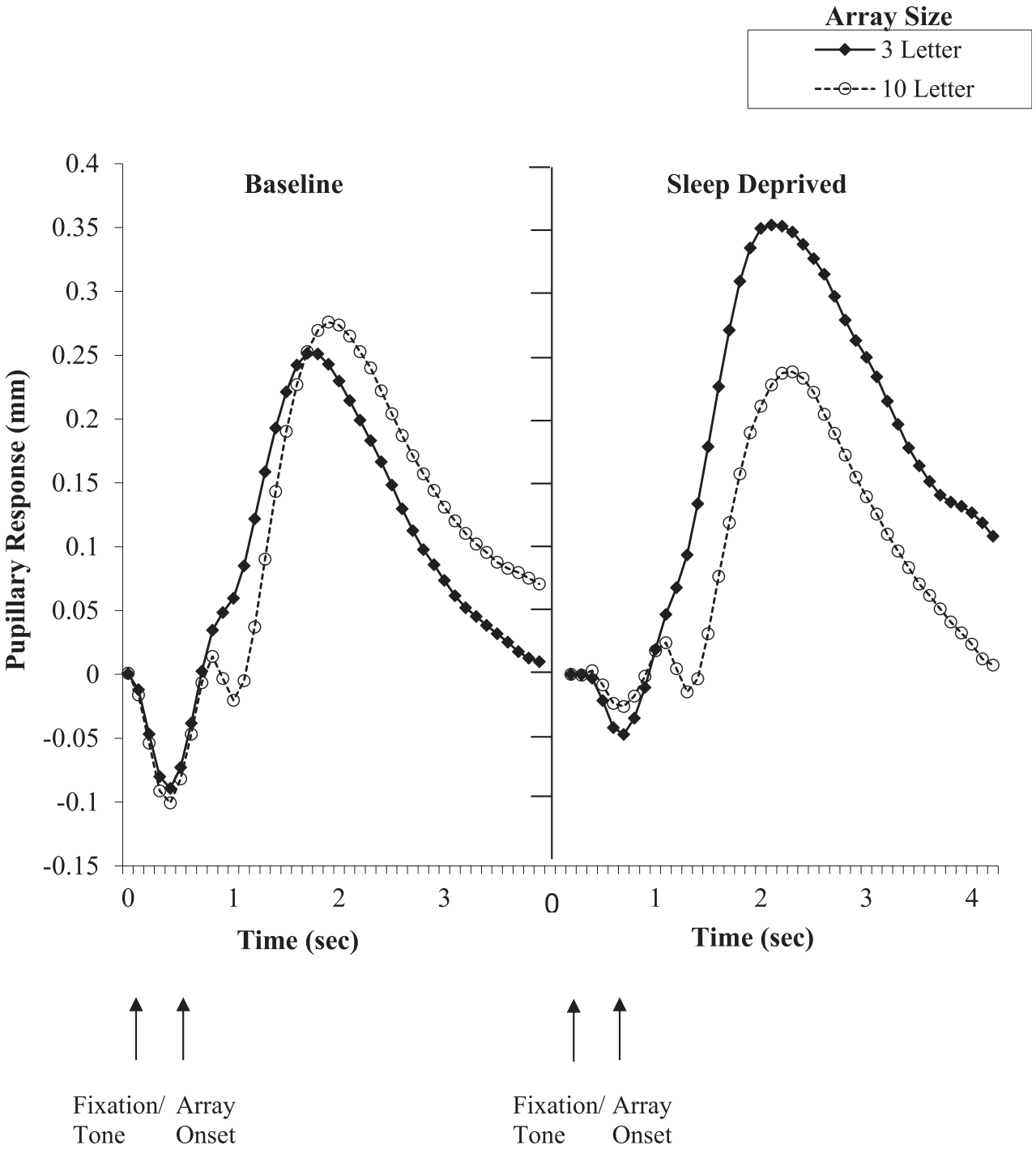

Figure 3. Pupillary response patterns to stimuli between normal sleep (baseline) and sleep deprivation conditions. The dashed line with diamonds represents changes in pupil dilation in response to the 3-letter span of apprehension (SOA) array and the dashed line with circles shows response patterns to the 10-letter array. The response to the 3-letter condition was significantly larger in the 3-letter condition following total sleep deprivation (TSD). In contrast, pre-stimulus, preparatory pupillary responses (the initial constriction from time 0) were significantly larger on both arrays from normal sleep to TSD conditions.

diameter declined, but nonsignificantly, following sleep deprivation, and significant task-evoked effects of sleep deprivation were found for both preparatory (after the trial onset at the warning tone but before the array onset), and array processing (constriction-dilation difference and dilation amplitude). This may suggest a (nonsignificant) decline in tonic (exploration) firing and significant increase in phasic (task-focused) firing, in an attempt to maintain performance, although unsuccessfully given that performance declined following TSD. Future studies combining pupillometry with direct assessments of neurological firing patterns within the LC and related systems (e.g. PFC) would be needed to confirm this hypothesis.

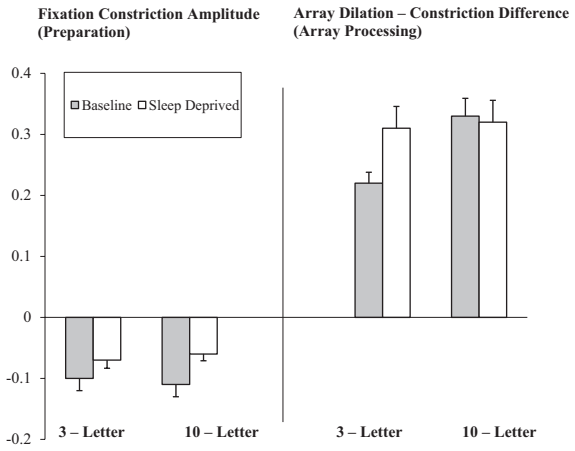

Figure 4. Differences in preparatory pupillary constriction and dilation in response to stimulus presentation across arrays and conditions are shown here. On the left, the gray boxes represent fixation constriction amplitude (preparatory pupillary responses) following normal sleep and the white boxes show responses following total sleep deprivation (TSD). Preparatory pupil size was significantly larger in the TSD condition across both arrays compared to baseline. On the right side, the total dilation-constriction difference (total pupil dilation accounting for ambient light introduced by the stimuli) in response to stimuli is illustrated. While there was significantly more dilation following TSD to the 3-letter array, there was no significant change in dilation in the 10-letter condition.

Limitations

This study had several limitations. First, the sample size was small. Although power analysis suggested that the sample size for this study provided enough power to detect medium to large effects, we may have been underpowered to detect small to medium effects. Second, due to significant artifacts during pupillometry introduced by factors such as drooping eyelids and excessive blinking following sleep deprivation, about one-third of the participants were dropped from final analyses as a result of unusable pupil data. However, excluded participants did not perform differently than included participants on baseline pupillometry measures or post-TSD performance measures on the SOA or PVT after TSD. Thus, excluded participants did not show a generalized impairment during TSD, reducing potential concern about our results being biased toward individuals resilient to the attention or sleepiness impacts of TSD. Nonetheless, the high proportion of data loss does illustrate the difficulty in using pupillometry analyses in sleep-deprived individuals. Third, although linear interpolation is commonly used to correct for trial-by-trial artifacts often inherent in pupillometry studies, this method may occasionally result in lost variability to examine fluctuations or instability effects following sleep deprivation. Fourth, we did not include functional neuroimaging or decision-making assessments that would have been helpful in further confirming changes in decision-making processes and underlying cognitive resources activated during these tasks. Fifth, the time window used for our fixation duration was 800 ms, which is at the lower end of suggested ranges in prior literature (500–1000 ms). However, given that the light reflex emerged at 150 ms and was immediately followed by a preparatory "bump" in pupil size, we are confident that this interval was of sufficient length to detect changes in preparatory cognitive effort. Lastly, our sample was a relatively homogenous group with primarily White individuals. There is some early evidence to suggest differences in mydriatic response based on iris color [49], which was not accounted for in this study. To our knowledge, there is not substantial evidence for differences in pupillary response patterns across ethnic/racial groups, but this may be a factor to consider for future research.

Despite these limitations, the study found that TSD significantly impacted cognitive performance and was associated with changes in the patterns of task-evoked pupillary responses (cognitive effort) under low- and high-processing loads. The findings suggested a complex load-dependent decision-making process about whether to increase or decrease cognitive effort to compensate for processing limitations imposed by sleep deprivation, which was consistent with frameworks relating changes in cognitive resource allocation in the PFC, parietal, and LC-NA networks after sleep deprivation [17, 20, 50, 51]. Future work may expand on these findings with functional neuroimaging to better delineate activation patterns following sleep deprivation as they relate to pupillary responses to stimuli.

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