Effects of two nights sleep deprivation and two nights recovery sleep on response inhibition

SEAN P. A. DRUMMOND 1,2, MARTIN P. PAULUS 1,3 and SUSAN F. TAPERT 1,2

1Department of Psychiatry, University of California San Diego, 2Psychology Service and 3Psychiatry Service, VA San Diego Healthcare System, San Diego, CA, USA

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SUMMARY This study examined the effects of two nights of total sleep deprivation (TSD) and two nights of recovery sleep on response inhibition. Thirty-eight young, healthy adults performed a Go-NoGo task at 14:00 after: (1) a normal night of sleep; (2) each of two consecutive nights of TSD; and (3) each of two consecutive nights of recovery sleep; they also performed the task at 05:00 during the first night of sleep deprivation. We hypothesized that TSD would lead to an impaired ability to withhold a response that would be reversed with recovery sleep. Subjects did experience a significant increase in false positive responses throughout all of TSD, errors of omission (i.e. missed ‘go’ targets) were not significant until after the second night of TSD. Both components (withholding a response and automatic responding) of the task returned to baseline levels after one night of recovery sleep. These data suggest that individuals experience difficulty in withholding an inappropriate response during TSD, even when they are able to attend to the incoming stimuli and respond accurately to appropriate stimuli.

KEYWORDS attention, inhibition, NoGo, recovery sleep, sleep deprivation

INTRODUCTION

Response inhibition is the cognitive process necessary to stop oneself from engaging in a prepotent response when that reaction is not appropriate. Response inhibition involves two cognitive components: attention to incoming stimuli and prevention of an automatic response (Lezak et al., 2004). Poor response inhibition has been reported as one of the cognitive symptoms of a variety of conditions, such as schizophrenia (Weisbrod et al., 2000), substance use disorders (Fillmore, 2003), and attention deficit/hyperactivity disorder (Wllcull et al., 2005).

Response inhibition is often measured with a Go–NoGo task. Such a task requires frequent automatic responding to stimuli interspersed with the need to withhold a response from a specific, less frequently occurring, stimulus. It is well established that sleep deprivation can affect performance such that automatic responding is slowed and more variable during sleep deprivation (Doran et al., 2001; Dorrian et al., 2005).

The effect of sleep deprivation on withholding a prepotent or automatic response, though, has not been extensively studied. The few published studies in this area have reported inconsistent results. One reason for the inconsistency is that most studies have used fairly complex cognitive tasks involving a number of demands beyond withholding a response. For example, some studies have employed stimulus-response incompatibility paradigms that required not only inhibition of an automatic response but also initiation of a less salient response (Harrison and Horne, 1998; Jennings et al., 2003; Smulders et al., 1997). Studies have also used complex choice reaction time tasks (Jennings et al., 2003; Smulders et al., 1997), negative priming (Harrison and Espelid, 2004), or tasks with vague inhibitory demands (Fallone et al., 2001). Another reason for the inconsistent findings is that with a few exceptions, the aims of these studies were not specifically to examine response inhibition. Rather, withholding a response was but one part of a larger set of cognitive demands, all of which influenced the behavioral outcome.

Thus, it remains unclear whether total sleep deprivation (TSD) affects the ability to withhold a response specifically or whether errors of commission result from deficits in other task demands. Here, we used a Go–NoGo task to address this issue.
This task is ideal for focusing on withholding of an automatic response because of the simplicity of the design. Subjects performed the task at baseline, three times during TSD, and after each of two nights of recovery sleep. We hypothesized that (a) TSD would impair response withholding; (b) this impairment would be greater than that seen for automatic responding; and (c) recovery sleep would reverse the expected performance decrements.

METHODS

Subjects and conditions
Thirty-eight young healthy adults (18 females; age: 24.1 ± 5.0; education: 15.3 ± 1.6) free of medical and psychiatric disorders participated in this study after providing written informed consent. All subjects reported habitually obtaining 7–9 h of sleep. They completed sleep diaries and wore actigraphs for 1 week before the study to verify adherence to a regular sleep–wake schedule. After an adaptation night in the laboratory, subjects returned the next night and were then sequestered in the laboratory until completion of the study. The subjects slept according to their normal schedule on night 2, underwent TSD for the next two nights (about 64 h total), and then were given two nights of recovery sleep (again, according to their habitual sleep–wake schedule).

Testing procedures
At 14:00 on each day starting after night 2, plus at 05:00 during the first TSD night, subjects performed a Go–NoGo task. Thus, the task was administered at an average of 21.75, 30.75 and 54.75 h TSD (standard deviation of each = 0.44 h), as well as 6.75 ± 0.44 h after waking on the baseline day and after each recovery night. The computer-administered task involved viewing stimuli presented individually in the center of the screen in a semi-random order for 200 ms with a 1300 ms interstimulus interval. A total of 181 stimuli were shown during the 4.5 min task. Stimuli consisted of two geometric shapes in each of two sizes (see Fig. 1 for examples). Subjects were instructed to respond ‘as fast as possible’ with a button press on the keyboard to all shapes except the target shape and to withhold a response for the target shape. The task directions emphasized both speed and accuracy of responding. To develop a prepotent tendency to respond positively with a button press, the need to respond quickly was emphasized repeatedly in the directions, 68.5% of the stimuli were ‘go’ stimuli, and the ‘NoGo’ stimulus shared a perceptual feature in common with two of the Go shapes (size or geometric shape, respectively).

Six different versions of the test were constructed. A previous pilot study, not designed as a direct control for this study, with 21 subjects from the same demographic as those reported here examined the practice effects and comparability of task versions. In that pilot, each subject took five of the six different versions of the Go–NoGo task, once each on five separate days after normal sleep. These test administration days were either consecutive or included two non-testing days (i.e. Saturday and Sunday) when the 5-day testing period included a weekend. Briefly, with respect to practice effects, only false positive rate showed a main effect of time (P = 0.018), with an improvement from test 1 to test 2, and no significant changes thereafter. Overall, these data suggest that the practice effects for this task are

![Figure 1. Examples of task stimuli. Each row shows the stimuli from 1 of the 6 matched versions of the task. In each case, the first three shapes represented ‘go’ stimuli where subjects were required to press a button as quickly as possible when they appeared. The far right shape was the ‘NoGo’ stimulus where subjects were required to withhold a response. Note that to increase the tendency to respond with a button press, the NoGo shape shared a perceptual feature with each of two Go shapes (size or geometric shapes, respectively). While the shapes are shown in gray scale here, the actual stimuli were in color (all shapes of a given version were the same color).](image)

modest and largely resolved after the first administration (Table 1). With respect to version compatibility, analyzes showed no differences in any version of the task on any variable (Table 2).

**Data analysis**

The outcome variables for task performance included (1) hit rate (correct button press for Go stimuli); (2) response time (RT) for correct hits; and (3) false positive rate (error of commission for NoGo stimuli). Automatic responding was measured with hit rate and RT for hits, while response withholding was measured with false positive rate (i.e. errors of commission). All variables were analyzed with one-way repeated measures ANOVA. Posthoc follow-up tests were done with Dunnett’s test corrections using the baseline scores as the comparator. Hit RT data for six subjects was lost due to technical errors, so $n = 32$ for that analysis.

**RESULTS**

Figure 2 shows the results of the three outcome variables. Each variable showed a significant effect of Time in the omnibus ANOVA ($P < 0.001$ with Greenhouse–Geisser correction). Hit rates were significantly different from baseline only after two nights TSD (55.75 h). Hit RT was significantly slower than baseline after both 31.75 and 55.75 h TSD. False positive rates, on the other hand, were elevated during all TSD testing sessions. Each of these variables returned to baseline values after one night of recovery sleep. Hit RT and false positive rates continued to decline after the second recovery night, but this change was significant only for hit RT.

**Table 1** Practice effects from a previous pilot study

<table>
<thead>
<tr>
<th></th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 3</th>
<th>Time 4</th>
<th>Time 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hit rate</td>
<td>0.97</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>False + rate</td>
<td>0.14</td>
<td>0.10</td>
<td>0.09</td>
<td>0.09</td>
<td>0.10</td>
</tr>
<tr>
<td>Hit RT (ms)</td>
<td>602.18</td>
<td>614.30</td>
<td>622.75</td>
<td>589.54</td>
<td>589.08</td>
</tr>
</tbody>
</table>

Data for each variable are presented as mean (top) and standard deviation (bottom).

**Table 2** Version comparability from a previous pilot study

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Hit rate</td>
<td>0.98</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>False + rate</td>
<td>0.08</td>
<td>0.12</td>
<td>0.14</td>
<td>0.12</td>
<td>0.09</td>
<td>0.09</td>
</tr>
<tr>
<td>Hit RT (ms)</td>
<td>584.25</td>
<td>607.98</td>
<td>601.47</td>
<td>603.39</td>
<td>610.16</td>
<td>615.21</td>
</tr>
</tbody>
</table>

Data for each variable are presented as mean (top) and standard deviation (bottom).
DISCUSSION

Here, we report the effects of two nights TSD and two nights of recovery sleep on response inhibition as measured by a Go–NoGo task. Given the simple nature of the task design, we were able to more directly test the effects of TSD on the ability to stop oneself from performing an automatic response than many previous studies examining inhibition during TSD. We found that throughout TSD, subjects showed an impaired ability to withhold an automatic response. In contrast, hit rates remained stable early in TSD and only showed significant declines after the second night of TSD. This pattern suggests that during most of TSD subjects could initiate a response normally when appropriate (although somewhat slower than usual), but the inability to withhold an inappropriate response was impaired. Performance on all outcome variables returned to baseline levels after a single night of recovery sleep.

The main goal of this report was to evaluate whether the ability to withhold a response is impaired by TSD. As stated above, these data suggest that is indeed the case. One possible explanation for why subjects made more errors of commission than errors of omission during TSD may be they sacrificed accuracy in favor of speed. The emphasis on speed in the task directions may have led subjects to emphasize this outcome over the need to not respond during the NoGo stimuli. However, the RT data does not support this hypothesis. Such a focus on speed over accuracy should have favored intact RTs during correct hits with TSD. However, as Fig. 2 shows, that is not the case since RTs actually slowed during TSD.

The fact that both automatic responding and withholding a response were impaired during TSD (albeit at different rates) raises the possibility that both functions rely on the same cognitive processes and/or brain regions. While it is clear that the automatic responding component of this task requires attention, it remains unclear whether withholding a response also relies mainly on the attention system or an inhibitory system independent of attention. Manly and colleagues, through a series of experiments, argue that both task components require endogenous attention (Manly et al., 1999). Evidence for this includes the fact that subjects scoring high on a measure of ‘absent mindedness’, but not those scoring low, showed greater false positive rates when the task was made longer or the proportion of NoGo stimuli was reduced (both manipulations should increase attentional demands). Additionally, they found that faster hit RTs were correlated with increased false positives and suggested this means that ‘inefficient’ use of attention or an ‘inattentive approach to the task’ produces both speeding of responses and errors of commission (Manly et al., 1999). However, given that there are many different types of attention (e.g. sustained, selective, spatial, divided, etc.) that each engage different brain regions (Itti et al., 2005; Posner, 2004), possibly the two very different behaviors of automatic responding and withholding a response rely on distinct aspects of the attention system. Consistent with this idea are the facts that (a) during TSD our subjects showed a slowing of RT to Go stimuli along with an increase in false positive responding; and (b) both variables showed reversals after Recovery sleep. These relationships are opposite those of Manly et al. If Manly et al.’s findings argue in favor of a single attention process underlying both types of responding, our data would have to be seen as arguing against that idea. Thus, our data may suggest that TSD produces a dissociation between the types of attention responsible for automatic responding and response withholding that Manly et al.’s manipulations did not.

Moreover, consistent with the notion that automatic responding and withholding a response may rely on at least slightly different cognitive processes is the fact that each seems to activate different regions within the prefrontal cortex. The vulnerability of the prefrontal cortex to TSD has long been debated (Binks et al., 1999; Harrison and Horne, 1996; Horne, 1993; Wimmer et al., 1992). The prefrontal cortex, though, is composed of many sub-regions, and it is likely those regions respond somewhat differently to TSD. The region within the prefrontal cortex most commonly implicated in response withholding during neuroimaging and lesion studies is the right ventral prefrontal cortex, typically within the inferior frontal gyrus (Aron et al., 2004; Fassbender et al., 2004; Kelly et al., 2004; Matthews et al., 2005). This suggests that impaired response withholding during TSD may result from impaired function of this specific region. Automatic responding, on one hand, typically activates sustained attention regions within the right dorsolateral prefrontal cortex (Culham et al., 2001; Yamasaki et al., 2002). Impaired automatic responding during TSD, then, may relate to impaired function of this region, possibly due to an impaired ability to appropriately allocate cognitive resources to within the brain (Drummond et al., 2005). Significant errors of omission were not evidenced here until after two nights of TSD. However, if a more subtle deficit in resource allocation was present earlier in TSD, that may have contributed to potential dysfunction within the prefrontal region required for successful inhibition. A caveat to this possible consequence of TSD is that some tasks rely less on the prefrontal cortex after sufficient practice (Beauchamp et al., 2003; Sayala et al., 2005). If that occurs for response withholding, then the task may rely more heavily on other brain systems, such as the posterior portion of the attention system.

The simplicity of the task design, while largely a strength, did not allow us to evaluate all aspects of response withholding. Specifically, we only examined motor inhibition, as opposed to speech inhibition. We also did not evaluate the ability to stop a response that has already been initiated, as can be done with the Stop Task (Brown and Braver, 2005; Matthews et al., 2005). However, as described above, our aim focused on the ability to withhold a motor response and this Go–NoGo task allowed us to do that relatively free of other cognitive demands. A second limitation is that we did not use a pure measure of sustained attention (e.g. the psychomotor vigilance task (PVT)) to contrast with response withholding. However, given the emphasis on speed, the Go stimuli here served as a reaction time task for which we could assess both errors of omission and speed, the two most

common measures used in sustained attention analyzes. Another limitation of the study is the lack of an explicit control group who received all study procedures except TSD. While our pilot data provide information regarding practice effects, this is an imperfect control. Nonetheless, it is interesting to note that the practice effects in the pilot study were in the opposite direction of the TSD effects seen here, suggesting that the true TSD effects may be even greater than what we report.

In summary, we utilized a Go–NoGo task to assess the impact of two nights TSD and two nights of recovery sleep on the ability to withhold a motor response. The design of our cognitive task allowed us to study this outside the context of more complex cognitive demands. We found that subjects experienced significant impairment in response withholding throughout all of TSD, while automatic responding was not significant until after the second night of TSD. Both components of the task returned to baseline levels after one night of recovery sleep. These data suggest that individuals experience difficulty in withholding an inappropriate response during TSD, even when they are able to attend to incoming stimuli and respond accurately to appropriate stimuli. Thus, operational settings might consider installing safeguards to prevent mistakes and accidents from occurring as a result specifically of impaired response withholding among sleep deprived personnel.

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REFERENCES


