Predicting vulnerability to sleep deprivation using diffusion model parameters

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SUMMARY
We used diffusion modelling to predict vulnerability to decline in psychomotor vigilance task (PVT) performance following a night of total sleep deprivation (SD). A total of 135 healthy young adults (69 women, age = 21.9 ± 1.7 years) participated in several within-subject cross-over design studies that incorporated the PVT. Participants were classified as vulnerable (lower tertile) or non-vulnerable (upper tertile) according to their change in lapse rate [lapse = reaction time (RT) ≥ 500 ms] between the evening before (ESD) and the morning after SD. RT data were fitted using Ratcliff’s diffusion model. Although both groups showed significant change in RT during SD, there was no significant group difference in RT during the ESD session. In contrast, during ESD, the mean diffusion drift of vulnerable subjects was significantly lower than for non-vulnerable subjects. Mean drift and non-decision times were both adversely affected by sleep deprivation. Both mean drift and non-decision time showed significant state × vulnerability interaction. Diffusion modelling appears to have promise in predicting vulnerability to vigilance decline induced by a night of total sleep deprivation.

INTRODUCTION
Degradation of vigilance is probably the most robust alteration of neurobehavioural performance in healthy, sleep-deprived young adults (Lim and Dinges, 2010). The psychomotor vigilance task (PVT) (Dinges and Powell, 1985) is a proven assay for evaluating vigilance. Its simplicity makes it attractive for mathematical modelling of how performance fluctuates according to the time of day, most commonly using the two-process model or one of its variants (Mallis et al., 2004; Rajdev et al., 2013). However, the modelling of behaviour within trials has received considerably less attention (Ratcliff and Van Dongen, 2011).

The drift diffusion model of perceptual decision-making, or simply the diffusion model, allows decomposition of the processes underlying simple reaction time (RT) tasks (Ratcliff, 2002). For example, decision and non-decision components can be separated using this model. The non-decision component refers to time spent encoding the sensory input (pre-decision time), as well as time spent in executing the decision (post-decision time). Decision-making itself is conceived to be a noisy process involving the accumulation of information over time (Ratcliff, 1976; Ratcliff and Rouder, 1998) that can be modelled mathematically as a diffusion process. The diffusion model has been used to explain behaviour in a growing number of cognitive experiments (Heekeren et al., 2008; Krajbich et al., 2012; Menz et al., 2012; Ratcliff et al., 2003; Tegenthoff et al., 2005).

An attractive feature of diffusion modelling is that it can predict the response time distribution under different contexts (Ratcliff, 2002) and varying levels of noise (Ratcliff and Tuerlinckx, 2002). The model has been tested by manipulating various facets of the decision process and then observing the corresponding change in diffusion parameters (Voss et al., 2004). Among the numerous studies using the PVT to characterize performance in sleep-deprived people, only one (Ratcliff and Van Dongen, 2011) used diffusion modelling to explain behaviour. Diffusion parameters in the sleep deprived (SD) condition were compared to those obtained in the non-deprived condition. Although SD was found to negatively affect several diffusion model parameters, only the effect on the drift parameter was statistically significant.

In this study, we ascertained if the diffusion model could differentiate persons according to their vulnerability to sleep deprivation as measured by a decline in psychomotor...
vigilance. The present study was motivated by previous research showing alterations in behavioural performance by SD to be trait-like and reproducible across three experimental sessions (Van Dongen et al., 2004a,b). The feasibility of predicting vulnerability to SD using neuroimaging during the well-rested state has been demonstrated by some previous experiments (Chuah et al., 2006; Mu et al., 2005; Rocklage et al., 2009) but not in others (Lim et al., 2007).

To fill these gaps in our understanding of behaviour following SD, we posed two questions: (i) are the parameters of the diffusion model affected differentially in vulnerable and non-vulnerable participants? And (ii) can diffusion parameters determined prior to SD predict performance following SD?

METHODS

Subjects
A total of 135 participants (69 females, mean age 21.9 ± 1.7 years) from five different functional magnetic resonance imaging studies (fMRI) (Chee and Chuah, 2007; Chee et al., 2010; Chuah and Chee, 2008; Chuah et al., 2010; Venkatraman et al., 2007) on sleep deprivation contributed behavioural data to this report. The five studies shared common recruitment criteria and protocol for sleep deprivation. Volunteers had to: (i) be right-handed, (ii) be aged between 18 and 35 years, (iii) have habitual good sleeping habits (6.5–9 h of sleep every day), (iv) have no history of sleep or psychiatric or neurological disorders and (v) have no history of severe medical illness. All participants indicated that they did not smoke or consume any medications, stimulants, caffeine or alcohol for at least 24 h prior to the sessions. Informed consent was obtained from all participants in accordance with study protocols approved by the National University of Singapore Institutional Review Board.

Participants visited the laboratory three times. They first attended a briefing session, during which they were informed of the study protocol and requirements and practised the study task. At the end of this session, each participant was given a wrist actigraph to wear throughout the study. The first experimental session took place approximately a week later. The order of the two experimental sessions (rested wakefulness and sleep deprivation) was counterbalanced across all the participants and separated by 1 week. This was to minimize the possibility of residual effects of sleep deprivation on cognition for those participants whose sleep-deprivation session had preceded their rested–wakefulness session (Van Dongen et al., 2003). Sleep duration was verified by actigraphic data and data from non-compliant subjects were not analysed.

Experimental details
In the rested wakefulness (RW) session, participants arrived at the laboratory on the scheduled date at 07:30 hours. The PVT was administered at 08:00 hours. In the sleep deprivation sessions subjects arrived at the laboratory on the scheduled date at 19:30 hours. Participants underwent a night of SD under supervision of a research assistant. The PVT (Dinges and Powell, 1985) was administered every hour from 20:00 to 5:00 hours the next morning (10 test periods). For this report, only data from the first two epochs at 20:00 and 21:00 hours during the wake maintenance zone of the SD session and two test periods at 4:00 and 5:00 hours following a night of total sleep deprivation were analysed. We did not compare RW with SD directly, because only one ‘RW’ data point was available. The first two evening sessions were labelled ‘evening before sleep deprivation’ (ESD) and the last two sessions were labelled ‘sleep deprivation’ (SD). Participants also rated their subjective sleepiness on the nine-point Karolinska Sleepiness Scale after each PVT test. Throughout the night, they were allowed to engage in non-strenuous activities such as reading, watching videos and conversing. When performing the PVT, participants were instructed to respond as quickly as possible. RTs <150 ms were regarded as false alarms, and were excluded from analysis. All PVTs administered were of 10-min duration.

Diffusion parameters estimation
For each participant, the single boundary drift diffusion model was applied to two sessions of RT data in each state. The estimated parameters for each group in each state were then aggregated for further statistical analysis. The model divided RT into two components: decision time and non-decision time, with the latter consisting of sensory encoding (the pre-decision time) and decision execution (the post-decision time); see Fig. 1a. Non-decision time was assumed to vary from trial to trial according to a uniform distribution with mean $T_{mn}$ and width $S_r$. Decision time was modelled using a single boundary diffusion process with a drift parameter. Evidence was assumed to accumulate from the starting point until the boundary a was reached. The drift parameter was also allowed to vary across trials according to a normal distribution with mean $\xi$ and standard deviation $\eta$ (Fig. 1b). This differs from most perceptual decision-making models that involve two choices, in that these have used a two-boundary model. Due to the difficulty in uniquely identifying model parameters in single boundary tasks (Ratcliff and Van Dongen, 2011), we followed Ratcliff’s suggestion to use uniquely identifiable parameter ratios ($\xi/a$ and $\eta/a$). This resulted in a model with four parameters: $\theta = \xi/a$, $\eta/a$, $T_{mn}$, $S_r$. In other words, the drift parameters of one subject cannot be compared with another without first normalizing their estimated boundary values. For the sake of simplicity, from this point onwards we will use drift and drift ratio interchangeably. When comparing the drift parameters across group, it is implicit that they were normalized by the estimated boundary parameter.

To estimate the model parameters, we followed the strategy described in detail by Ratcliff and Van Dongen (2011) (Fig. 2). The RT distribution was simulated using a
Figure 1. Schematic illustration of the one choice Ratcliff diffusion model. (a) Reaction time (RT) can be divided into two distinct components—decision time and non-decision time. Non-decision time may be broken down into pre-decision time, referring to stimulus encoding time and post-decision time, which corresponds to response-output time. (b) Non-decision time was modelled as a uniform distribution with mean $T_{er}$ and range $St$. Decision time was modelled as a one-boundary diffusion process with drift $\xi$, which captures the mean rate of information uptake and is assumed to vary across trials with a standard deviation $\eta$. The decision process ends when the diffusion process reaches the boundary located at $a$. Note that while drift is symmetrically distributed about $\xi$, drift angle is not.

Figure 2. Parameter estimation process. (i) Initial values for the parameter $\theta$ were estimated from the data using a maximum likelihood estimate (MLE). (ii) 20,000 samples of reaction time (RT) were generated and compared with the actual observed RT using a $\chi^2$ test for goodness-of-fit. This process was repeated and the fit successively improved using a Nelder-Mead simplex algorithm until there was no further improvement (tolerance criteria was set at 0.5).
combination of random walk approximation (Tuerlinckx et al., 2001) and shifted inverse Gaussian distributions (Michael et al., 1976). This was compared to experimental RT data using the χ² statistic for goodness-of-fit. We started with an initial estimate for the parameters using a maximum likelihood-based estimator and utilized an iterative algorithm based on simple minimization routine (Nelder and Mead, 1965) to successively improve the model fit (see Patanaik et al., 2014 for details).

The Ratcliff model leaves several free parameters that can be altered depending on the data. For the simulation process, 20 000 RTs per distribution were obtained. We used a step size of 0.1 ms for the random walk approximation and stepped through 0.05, 0.1, . . . , 0.95 quantiles of the RT distribution to obtain model fits. These quantile RTs were used to find the proportion of responses in the model RT distribution lying between quantiles. To derive expected values (E), the proportion of responses was multiplied by the number of observations. The observed values, (O), were multiplied by 0.05 and the number of observations. A χ² statistic was then computed as Σ(O – E)²/E. Our estimator was validated using two sessions of simulated 10-min PVT data obtained from 100 subjects. We found the estimates to be unbiased.

Statistical analyses

Group differences were evaluated using an independent-samples t-test. To assess the interaction effect of state (ESD or SD) and group (vulnerable or non-vulnerable) on relevant diffusion parameters, a 2 × 2 factorial design analysis of variance (ANOVA) was employed. Alpha was set at 0.05. To assess the discriminative power of the diffusion parameters a binary logistic regression analysis was performed to classify subjects into vulnerable and non-vulnerable groups using baseline data. We used vulnerability as a dependent variable and diffusion model parameters measured in ESD as independent variables. We also tried introducing baseline standard RT metrics to the set of independent variables, anticipating any increase in accuracy. In the set of standard RT metrics, we also included the slowest 10% RS. The slowest 10% RS is known to be correlated strongly with drift parameter based on simulations (results not shown). The independent variables were introduced one at a time sequentially, using the forward selection method, until the addition of an extra variable resulted in no statistically significant increase in accuracy. A receiver operating characteristic (ROC) curve was obtained by varying the threshold of the logistic function. All analyses were conducted using SPSS version 20 (IBM, Chicago, IL, USA) and Matlab 2013b (The MathWorks, Inc., Natick, MA, USA).

RESULTS

Identification of vulnerable and non-vulnerable subjects

Based on the change in the number of lapses between SD and ESD (δl = lSD - lESD), subjects were identified as non-vulnerable if they belonged to the lower tertile and as vulnerable subjects if they belonged to the upper tertile. A lapse was defined as a trial with RT ≥ 500 ms. Non-vulnerable subjects (n = 43) had δl < 4 and vulnerable subjects (n = 45) had δ > 12.

The two groups were similar in age [mean age for non-vulnerable group = 22.0 years, standard deviation = 1.97 years; mean age for vulnerable group = 22.0 years, standard deviation = 1.68 years; t = 0.43, NS] and gender (18 females in non-vulnerable group, 22 females in vulnerable group; χ² = 0.43, NS). As expected, across the entire group, sleep deprivation (SD) elicited significant changes in mean and median RT, the reciprocal of RT and lapses compared to the evening before sleep deprivation (ESD) state (Table 1). SD had a significant effect on diffusion model parameters (drift, non-decision time) other than within-trial variability in drift. Importantly, during ESD, there was no significant difference in any of the traditional RT metrics between the two groups (smallest P = 0.08, for mean RT; Fig. 3).

<table>
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<tr>
<th>Table 1</th>
<th>Standard reaction time and diffusion parameter statistics of study participants</th>
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<tr>
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<td>ESD (n = 135)</td>
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<tr>
<td>Reaction time (RT) statistics</td>
<td></td>
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<tr>
<td>Mean RT, ms</td>
<td>266 ± 34</td>
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<tr>
<td>Mean response speed, 1/s</td>
<td>4.0 ± 0.4</td>
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<tr>
<td>Median RT, ms</td>
<td>249 ± 26</td>
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<tr>
<td>Total lapses</td>
<td>2.6 ± 3.7</td>
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<tr>
<td>Diffusion parameter statistics</td>
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<tr>
<td>Normalized drift $\tilde{\alpha}$</td>
<td>10.9 ± 2.7</td>
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<tr>
<td>Across standard deviation in drift $\tilde{\beta}$</td>
<td>2.8 ± 1.7</td>
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<tr>
<td>Mean non-decision time $T_{\text{nc}}$, ms</td>
<td>157 ± 17</td>
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<td>Range of non-decision time $S$, ms</td>
<td>47 ± 16</td>
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Overall χ² fit for evening before sleep deprivation (ESD) state was 16.8 ± 7.2 and sleep deprivation (SD) state was 17.7 ± 9.7. Critical value for χ², df = 14 is 26.1.
Effects of state and group on diffusion parameters

**Mean diffusion drift**

There was a significant main effect of state on mean diffusion drift $\xi$ ($F_{1,172} = 69.4; P < 0.001$). Averaged across the two tertiles, diffusion drift was significantly lower in the SD state compared to ESD state. There was a significant main effect of group on drift, with vulnerable participants having a lower mean diffusion drift than non-vulnerable participants, $F_{1,172} = 45.1; P < 0.001$. Vulnerable subjects had significantly lower diffusion drift in both ESD ($t_{86} = 2.44; P < 0.05$) and SD ($t_{86} = 7.65; P < 0.001$) compared to non-vulnerable subjects.

The interaction of state and group was significant, ($F_{1,172} = 8.33; P < 0.005$) (Fig. 4). Thus, while both groups showed significant declines in mean diffusion drift following sleep deprivation (vulnerable $t_{88} = 9.02; P < 0.001$; non-vulnerable: $t_{84} = 3.3; P < 0.005$), decline in drift rate was greater in vulnerable than in non-vulnerable subjects.

**Mean non-decision time**

There was a main effect of state on mean non-decision time $T_{\text{err}}$ ($F_{1,172} = 7.47; P < 0.01$), with $T_{\text{err}}$ being faster in ESD than during SD. This was modulated by group [group $\times$ state interaction ($F_{1,172} = 6.1; P < 0.05$)], such that the decline in non-decision times was also significant in vulnerable subjects ($t_{88} = -3.54; P < 0.001$), but not in non-vulnerable subjects ($t_{84} = 0.11; P = 0.91$). There was no main effect of group on $T_{\text{err}}$, $F_{1,172} = 1.45; P = 0.23$.

**Predicting vulnerability from baseline data**

We observed a classification accuracy of 69.3% at a sensitivity of 65.1% and specificity of 73.3% using baseline normalized diffusion drift ($\zeta$), diffusion signal-to-noise ratio ($\eta$) and mean non-decision time ($T_{\text{err}}$). The baseline slowest 10% RS was observed to be highly correlated ($r = 0.77, P < 0.001$) with baseline mean diffusion drift. Despite this, no improvement in classification was observed by the addition of any traditional RT measures. The ROC curve is presented in Fig. 5. The area under the curve was 0.74.

**DISCUSSION**

**Effect of sleep deprivation on diffusion parameters**

Our results replicate and extend the previous finding that single boundary diffusion drift ratio is reduced with sleep deprivation on the standard PVT. Diffusion drift has also been found to be reduced on a numerosity discrimination task (Ratcliff and Van Dongen, 2009). However, these sleep deprivation-related changes in diffusion drift may be context- and/or task-dependent. Menz et al. (2012), for example, observed that drift reduced with a decision task in SD for easy but not for difficult decisions. Additionally, SD appears to affect non-decision diffusion parameters (mean and variance of non-decision times). The latter finding is possibly a result of the greater power of the present study ($n = 135$ versus $n = 19$ for one of the original studies) and is consistent with the notion mooted by those authors that SD can affect multiple cognitive processes (Ratcliff and Van Dongen, 2009).
Difference in diffusion parameters between vulnerable and non-vulnerable subjects
The most interesting finding of the present work is that the drift parameter on the evening before sleep deprivation predicted greater vulnerability to SD, something that was not anticipated by merely observing PVT performance. The latter may have arisen because, in the ESD state, diffusion drift rate and non-decision time were affected in opposite directions—vulnerable subjects had longer decision times but shorter non-decision times.

In the ESD state, when the diffusion drift was high, the mean drift and non-decision parameters traded-off without affecting overall observed performance. The effects of varying levels of mean diffusion drift and mean non-decision time on median RT can be modelled (Fig. 6). The figure was generated by simulating 30-min PVTs for each pair of diffusion-drift and non-decision time parameters while holding constant variability parameters. The modelled RT of two representative subjects, one vulnerable and one non-vulnerable to SD, are shown overlaid on the plot. During ESD the mean diffusion drift and non-decision parameters of these participants differed even though they had the same median RT. Modelling showed that as the diffusion drift was reduced, median RT became dominated by the drift parameter and the trade-off between the parameters became less apparent.

Interaction effect of state and group on diffusion parameters
Both mean diffusion drift and mean non-decision time showed statistically significant group × state interaction. The results suggest that in terms of decision time (i.e. drift parameters) subjects with better performance in ESD state were less affected after sleep deprivation. Furthermore, those with faster decision time performance but slower non-decision times in the ESD state were also less affected by sleep deprivation.

The observation that all diffusion parameters were less affected by SD in non-vulnerable participants suggests that they may have greater cognitive reserve (Stern, 2002) compared to vulnerable subjects (Bell-McGinty et al., 2004; Chuah et al., 2006). This concept has been applied primarily to cognitive ageing, but has also been shown to be relevant in the context of sleep deprivation (Chee et al., 2006; Mu et al., 2005).
Possible neurocognitive accompaniments of reduced diffusion drift

Although a slower drift rate speaks to slower accumulation of evidence on which to base action, the present experiments and analyses were not designed to examine the possible contribution of this mechanism. An experiment that examined the rate of processing limitations in the sleep deprived state was one where sleep deprivation was accompanied by a leftward shift in frequency response profile of fMRI signal in higher visual cortex (Kong et al., 2014). This finding indicates that the maximal rate at which pictures are processed in higher (but not primary) visual cortex is lowered by sleep deprivation.

Sleep deprivation has been shown consistently to result in reduced recruitment of parieto-frontal and visual extrastriate brain regions during the performance of visual attention tasks (Chee et al., 2010; Lim et al., 2010; Tomasi et al., 2009) and even in the preparatory phase (Chee et al., 2011). The degree of reduction of activation generally corresponds to impaired accuracy in tasks, but only in two studies has greater baseline activation been found to mark individuals relatively more resistant to the negative effects of sleep deprivation (Chuah et al., 2006; Mu et al., 2005). As such, the neural correlates of predictors of vulnerability to sleep deprivation remain to be characterized further.

Predictive value of diffusion model parameters

Even though there were statistically significant differences between the vulnerable and non-vulnerable group in the baseline ESD condition, it remains to be seen if the diffusion parameters are useful in predicting vulnerability at an individual level. Estimated diffusion parameters are noisy at an individual level, especially with limited data. Despite this, logistic regression showed that diffusion parameters have reasonable discriminative power. The addition of traditional RT metrics to the classifier did not improve classification accuracy. Future work should consider using other easily derived physiological measures (for instance, heart rate variability; Chua et al., 2012), in combination with complex non-linear classifiers, to improve phenotypic characterization of vulnerability to psychomotor vigilance as a result of sleep deprivation. Another way to improve classification accuracy could be to improve the estimates of diffusion model parameters by aggregating more data from longer periods of PVT at baseline, keeping in mind that longer non-standard PVTs are affected strongly by time on task effects, which might negatively affect classification.

Strengths and limitations

One of the strengths of the present study is its large sample size. We also used an established estimator for model parameter estimation that was validated on simulated data. While having some utility in operational settings (Mu et al., 2005), the comparison between ESD and SD is less ideal
It should be remembered that while vigilance decrements are an important and robust measure of performance decline in sleep-deprived persons, other cognitive domains may not be similarly affected (Van Dongen et al., 2004a). Another potential limitation is that we were unable to uniquely identify all the model parameters of the Ratcliff model. This was because a large drift with a distant boundary is operationally the same as a small drift with a proximate boundary. The model has no way of determining the exact drift and boundary parameters separately; only drift ratios (c/a, n/a) can be estimated uniquely.

The study was carried out under the supervision of MWLC. The manuscript was written by AP under the guidance of VZ, CKK and MWLC.

CONFLICT OF INTEREST

No conflicts of interest declared.

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Predicting vulnerability to sleep deprivation


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Mean reaction time in ms across sessions. Error bars represent one standard error of the mean.