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MARUFF, P., FALLETI, M. G., COLLIE, A., DARBY, D. and MCSTEPHEN, M. (2005), Fatigue-related impairment in the speed, accuracy and variability of psychomotor performance: comparison with blood alcohol levels. Journal of Sleep Research, 14:21–27.

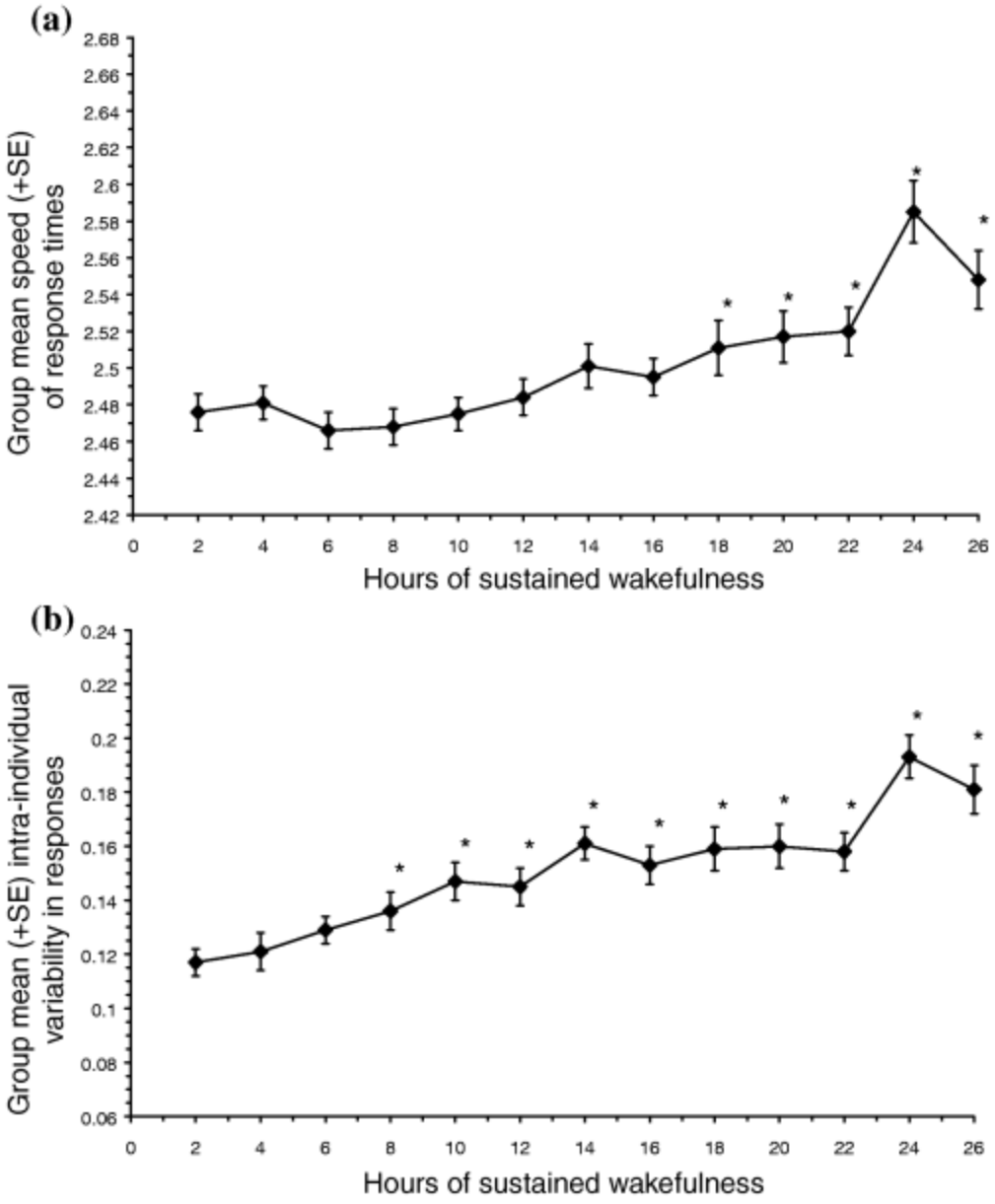
Cognitive performance is impaired by fatigue arising from sustained wakefulness and alcohol. Three recent papers directly compared the effects of increasing fatigue and blood alcohol concentration (%BAC) to provide a framework for understanding fatigue-related cognitive impairment. While the expression of fatigue-related cognitive impairments in terms of %BAC equivalents is sound, the methodology in each study was flawed in that the statistics used to compare the effects of %BAC and fatigue on cognition did not account for variation between or within each condition. The point estimates of the difference between a baseline and any level of fatigue or %BAC provided no indication of the size of difference that could reasonably be expected by chance. Importantly, all studies showed that variation increased as cognitive performance declined because of both increasing fatigue and %BAC. The current study compared the effect of increasing levels of %BAC and fatigue on the simple reaction task from the CogState test battery on 40 healthy adults using statistical methods that account for intra-individual and within-group variability in performance. After 24 h of sustained wakefulness and with 0.08%BAC, individuals showed maximal cognitive impairment; however, the magnitude of impairment found for fatigue was equivalent only to that observed for 0.05%BAC. Re-analysis of the data using percentage change scores indicated that the magnitude of fatigue-related cognitive impairment was much greater than that detected for 0.08%BAC. This suggests that previous studies that have not accounted for variability in the performance data have overestimated the effect of fatigue on cognitive performance.

Both alcohol intoxication (Brust, 1993 for review) and fatigue arising from sustained wakefulness (Broadbent, 1958) have long been known to have detrimental effects on cognitive function. However, three recent and provocative studies directly compared the effects of fatigue and alcohol intoxication on performance in the same cognitive tests (Dawson and Reid, 1997; Lamond and Dawson, 1999; Williamson and Feyer, 2000). The findings from the all three studies agree that as little as 18–24 h of sustained wakefulness could induce impairments in the speed and accuracy of cognitive performance that were equal to or greater than the severity of impairment seen in individuals with blood alcohol concentrations (BAC) of 0.1%. While there were differences in the extent to which the high levels of alcohol and fatigue affected different cognitive functions, measures of performance speed were always impaired by both conditions.

The expression of fatigue-induced performance deficits in terms of BAC equivalents provides a framework for both understanding and communicating the severity of such impairment. This is because BAC is a metric used commonly in social and legal settings (e.g. driving laws) and most adults understand the effects of alcohol intoxication on cognitive performance. Consequently, these findings have had considerable influence on safety policy and practice (Dawson et al., 2001). However, each of the studies that compared the severity of cognitive impairment between fatigue and alcohol suffers from three limitations in the data analysis that may have led the authors to draw incorrect conclusions about the magnitude of cognitive impairment observed with increasing levels of %BAC and fatigue and also about the similarity of performance impairment between these two conditions. First, in all the three studies, the magnitude of impairment associated with each level of the fatigue and %BAC was expressed using only a percentage change score in which the group mean performance at each trial was subtracted from the group mean score at the related baseline trial and expressed as a percentage. As difference scores derived by subtracting one group mean from another do not take into account the variability associated with the different trials, it is not possible to determine whether the changes in performance detected reflect true change or merely normal variability in performance across different trials (Collie et al., 2002; Zakzanis, 2001). Inferences about the presence and magnitude of any differences cannot be based solely on simple subtractive techniques (Winer, 1971). Meaningful estimates of an experimental effect must be derived by expressing the difference between two group mean values as a function of the pooled variance associated with each (e.g. Cohen's d; Cohen 1988).

A second and related limitation is that all the three studies failed to appreciate that variability in cognitive performance also increased substantially as levels of fatigue and %BAC increased. For example, it is clear from the figures in Lamond and Dawson (1999) (Figure 6) and Dawson and Reid (1997) (Figure 2) that in addition to the decreasing accuracy and slowing reaction time, increased levels of fatigue and %BAC also resulted in larger within-group variability. For most performance measures, the standard error of the mean at 25-h sustained wakefulness was greater than double that observed for trials closest to the baseline. Thus, fatigue-related increases in the variability of group performance are substantial, yet these have not been compared with the fatigue-related changes found for response speed or accuracy. Furthermore, no studies have compared directly the effect of fatigue and %BAC on variability in performance.

Figure 2. (a) Group mean (+SE) speed of responses on the simple reaction time task across the baseline and four repeat trials in the alcohol (diamonds) and placebo (circles) conditions. (b) Group mean (+SE) intra-individual variability in responses on the simple reaction time task across the baseline and four repeat trials in the alcohol (diamonds) and placebo (circles) conditions. *Significant difference ($P < 0.01$) between alcohol and placebo.



The third and related limitation is that it is impossible to determine from any of the published studies whether increasing levels of fatigue and %BAC affected the variability of performance to the same extent. If the performance variability associated with increasing %BAC was different from that associated with increasing fatigue, then once again, it is meaningless to compare the magnitude of any change score between the alcohol and fatigue conditions without taking into account the different estimates of variability. For example, a decrease in performance of 10 ms, relative to a pooled standard deviation of 100 ms (i.e. Cohen's d = 0.1), detected for 25-h fatigue would be significantly smaller than the same decrease detected relative to a pooled standard deviation of 20 ms for a BAC of 0.1% (i.e. Cohen's d = 0.5). Without any estimate of variability, these two difference scores would be interpreted as being equal. In all of the studies conducted to date, performance variability has been ignored in the comparison of cognitive impairments associated with fatigue with those associated with alcohol.

Instead, the absolute difference between performance at baseline and 23-h sustained wakefulness has been inferred as being the same as the absolute difference between baseline and 0.1%BAC (e.g. Lamond and Dawson, 1999). Therefore, as for within-condition comparisons (e.g. baseline versus 0.07%BAC), the significance of between-condition comparisons (e.g. 25-h sustained wakefulness versus 0.01%BAC) must be determined with reference to some estimate of the variability in performance associated with each condition.

The first aim of the current study was to replicate the finding that increasing %BAC and sustained wakefulness independently lead to impairments in cognitive function. Secondly, we investigated the effects of both fatigue and %BAC on the variability in performance, in addition to the effects on the speed and accuracy of performance. Thirdly, we used a measure of effect size to express the magnitude of performance impairment associated with increasing fatigue and %BAC that takes into account differences between group means as within-group variability. Effect sizes provide a reliable estimate of performance change when used to compare the performance change associated with increasing levels of fatigue and %BAC. Finally, for the levels of fatigue and %BAC that yielded the maximum cognitive impairments, we calculated percentage change scores based on simple subtraction of group means (e.g. Dawson and Reid, 1997) to determine whether the use of this inappropriate statistic would have resulted in overestimation or underestimation of the experimental effect detected.

A total of 40 healthy young participants (16 males, 24 females) were recruited from two university campuses to participate in this study. The average age of participants was 21.64 years (SD = 3.79, range = 18–40 years). The average education level was 14.92 years (SD = 1.42 years, range 13–20 years). Inclusion criteria for the study included age >18 years and normal neurological function as determined by a consultant neurologist. Exclusion criteria included a history of loss of consciousness, psychiatric or neurological illness, dementia, head-injury, insomnia or other sleep disorders, the presence of significant health-related (including emotional) disorders and the use of medications that might have altered cognitive status. Participants were also excluded if they regularly used drug and alcohol substances, or reported difficulties sleeping in the two nights before each experimental session. Each participant was paid $40 for each experimental condition completed. All participants were naïve to the aims and hypotheses of the experimental conditions, and gave informed consent prior to enrolment. The experimental protocol was approved by the Institutional Ethics Committee prior to the commencing study.

The simple reaction time (SRT) task from the CogState computerized cognitive test battery (version 1.0) (CogState Ltd., Melbourne, Australia) was administered on Apple Macintosh iMacs in a large assessment laboratory containing 15 computers. This test was chosen because it has been shown to be sensitive to very mild cognitive changes in young adults following anaesthesia (Maruff et al., in press), concussion (Makdissi et al., 2001) and alcohol (Maruff et al., 2001). Once individuals are familiar with the test, it shows no practice effects, is quick to administer and score (Collie et al., in press). Overall, CogState measures a range of cognitive functions (e.g. psychomotor and memory function) using a number of different tests (e.g. choice reaction time, one-back memory; for full task descriptions see Falleti et al., 2003); on its own, the SRT task measures psychomotor speed. This task consists of 45 trials presented at the beginning of the test battery, halfway through the battery (after approximately 6 min) and then at

the end of the battery (after approximately another 6 min). On each occasion, the task can last up to 2 min (totalling to 6 min overall).

The stimuli for the SRT consist of playing cards. Subjects were instructed to press the space bar on the computer keyboard as soon as the card turned face up. A buzzer indicated incorrect responses, i.e. failures to respond or responses faster than 100 ms. Incorrect responses were omitted from analysis. Correct responses received no auditory feedback. A self-rated fatigue questionnaire was also administered to subjects during the fatigue condition. This questionnaire required each participant to rate their current level of fatigue on a scale from 0 to 100, where 0 indicated 'not fatigued at all' and 100 indicated 'very fatigued'.

All subjects completed all the three experimental conditions (fatigue, alcohol and placebo). One week before the study, all participants completed a familiarization phase in which they performed the test four times in a 3-h period. Once the study began, participants then completed an alcohol or fatigue condition in which the order of alcohol and fatigue conditions was randomized across participants with each of the three experimental conditions (fatigue, placebo and alcohol) given 1 week apart. For the fatigue condition, participants were assessed every 2 h during a 24-h period, starting at 09:00 hours one morning and finishing at 09:00 hours the following morning. All participants were instructed to arise from bed at 07:00 hours on the morning of testing, therefore by 09:00 hours on the morning following the first testing session, subjects had been awake continually for 26 h. Once they arrived at the laboratory, participants remained at the premises until after the 09:00 hours testing session on the following morning. All participants were supervised for the entire testing period and were forbidden from taking any physical exercise, showers or consuming food or drinks that contained caffeine or other stimulants.

For the alcohol condition, the order of placebo and alcohol administration was randomized. Following the baseline session, participants were required to ingest a glass of orange juice of which 40% was vodka at half hourly intervals for 2 h or until their %BAC reached 0.80. Twenty minutes after the consumption of each drink, %BAC was estimated using a standardized alcohol breathometer accurate to ±0.002% BAC (AlcomasterTM, Australian Dynamic Technologies Pty Ltd, Castle Hill, NSW, Australia). Participants were not informed about their %BAC at any stage of testing. For the placebo condition, timing of drinks and tests was identical to that of the alcohol condition, however all drinks contained only orange juice. To maximize the potency of the placebo, the rim of the glass that contained the orange juice was sprayed with vodka mist. In addition, in each testing session the number of participants who received alcohol was equivalent to the number that had received placebo.

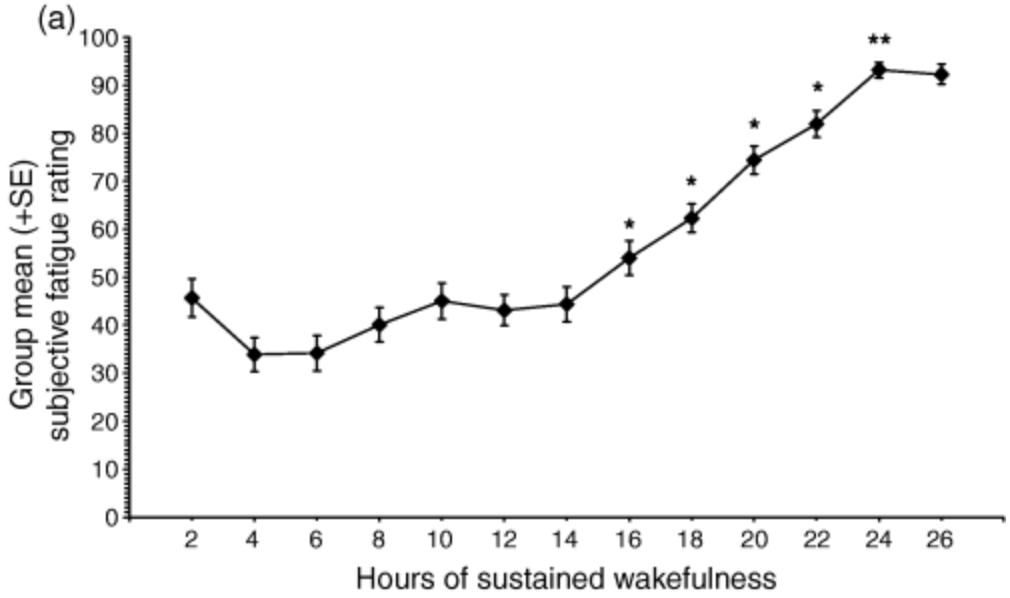
For each test, the accuracy of responses was calculated as the number of correct responses. Anticipatory or abnormally slow responses were counted as errors and excluded from further analysis. Inspection of the distributions of response times for correct trials in individuals indicated a positive skew in all distributions. This is a common feature of response time distributions and therefore these distributions were normalized for each participant through the application of a log10 transformation to the individual response times (Luce, 1986). For each participant, the mean of these log10-transformed

distributions was used to express the speed of responses, the standard deviation of these log10-transformed distributions was used to define the intra-individual variability in performance.

The group average %BAC was calculated for each trial in the alcohol condition (Fig. 1) and was compared between each assessment using a series of t-tests with adjacent trials set as planned comparisons within a one-way repeated measures anova. The mean subjective rating of fatigue was also calculated for each trial in the fatigue condition (Fig. 2) and each trial was compared with baseline using pairwise t-tests set as planned comparisons within a one-way repeated measures anova. For both measures, the significance was determined using the multivariate F and Wilk's lambda from the manova to minimize the effects of any violation of the homogeneity of covariance assumption.

Figure 1. (a) Group mean (+SE) percentage blood alcohol for each trial in the alcohol condition. Group mean blood alcohol concentration (%BAC) for baseline is not shown as individuals showed a 0.0 %BAC. (b) Group mean (+SE) subjective fatigue rating for each trial in the sustained wakefulness condition.

*Measure on the trial changed significantly from the trial immediately previous.



The SRT data for the alcohol and fatigue conditions were analysed separately before being compared. First, the effect of increasing %BAC and placebo on performance was compared by submitting the measures of response speed, accuracy and intra-individual variability for each participant at each level of the alcohol and placebo condition to a series of 2 (group) × 4 (trial) repeated measures anovas. The significance of any effect where degrees of freedom were >1 were determined using the multivariate F to minimize the effects of any violation of the homogeneity of covariance assumption. Significant interactions were decomposed using t-tests. For each performance measure, Cohen's d was used to express the magnitude of impairment associated with increasing %BAC relative to the baseline performance.

The effect of increasing fatigue on cognitive performance was determined by submitting the measures of response speed, accuracy and intra-individual variability for each participant at each level of sustained wakefulness to a series of one-way anovas. Repeated t-tests were used to compare performance at adjacent intervals where significant main effects occurred. Cohen's d was then used to express the magnitude of impairment associated with increasing levels of fatigue, relative to the baseline performance. The magnitude of change in performance on the three measures with increasing levels of fatigue was then superimposed on the magnitude of impairment found with increasing %BAC for the same measures. As a large number of comparisons were made in the current study type I, error rate for all analyses was set at $P < 0.01$.

Finally, to determine the extent to which percentage change scores can affect conclusions about the magnitude of performance change, the difference in performance between the level of fatigue and %BAC that yielded the maximum cognitive impairment and their respective baseline trials was expressed as percentage change (e.g. Dawson and Reid, 1997). For each individual, the mean reaction time was calculated from the distribution of raw reaction times at each assessment. These individual means were used to calculate a group mean for the 24-h sustained wakefulness trial, the 0.08%BAC trial and for their respective baseline trials. For both conditions, a percentage mean change score was calculated by subtracting the mean at baseline from that for the maximum impairment trial in the fatigue and %BAC conditions. This value was then expressed as a function of the group mean response speed at baseline and multiplied by 100. These percentage change scores were then compared with the overlap statistic derived from the Cohen's d from the analyses detailed above (e.g. Zakzanis, 2001).

The group mean %BAC increased significantly from the baseline to first assessment, from the first to the second assessment from the second to the third assessment and from the third to the fourth assessment. For subjective fatigue, the group showed no significant increase in subjective fatigue until the trial at 14-h sustained wakefulness (22:00 hours). After that, subjective fatigue increased significantly for every trial until the trial at 24-h sustained wakefulness (07:00 hours). The level of subjective fatigue remained equivalent between the trials at 24 and 26 h (09:00 hours) of sustained wakefulness.

For the speed of responses, manova indicated a significant condition × trial interaction ($Wilks'\lambda = 0.24$; $F(4,22) = 16.7$; $P < 0.001$) (Fig. 1a). Post-hoct-tests indicated significant differences between the alcohol and placebo conditions for the third and fourth trials. For the intra-individual variability of responses, manova indicated a significant condition × trial interaction ($Wilks'\lambda = 0.24$; $F(4,22) = 16.7$; $P < 0.001$) (Fig. 1b). Post-hoct-tests indicated significant differences between the alcohol and placebo conditions at the second, third and fourth trials. For the accuracy of responses, there was no main effect or interactions involving the trial factor, so no further analyses were conducted.

For the speed of responses, manova was significant [$Wilks'\lambda = 0.29$; $F(12,32) = 6.4$; $P < 0.001$]. Post-hoct-tests indicated that the speed of performance at the 16-h sustained wakefulness trial and for all trials beyond had increased significantly from baseline (Fig. 1a). For the intra-individual variability of responses, manova was significant [$F(12,32) = 9.9$; $P < 0.001$]. Post-hoct-tests indicated that the consistency of response times at the 6-h sustained wakefulness trial and for all trials beyond had

decreased significantly from baseline (Fig. 1a). For the accuracy of responses, manova was not significant [Wilks'λ = 0.52; F(12,32) = 2.5; P = 0.03], therefore no further analyses were conducted.

Figure 3a,b shows the magnitude of impairment in the speed and intra-individual variability of responses, expressed as Cohen's d relative to baseline, for the increasing levels of sustained wakefulness. These effects are superimposed on the magnitude of the impairment associated with increasing %BAC, also expressed as Cohen's d relative to baseline for the same measures in the same subjects. For each measure, performance reductions with increasing levels of fatigue and at the time of maximal impairment (24-h sustained wakefulness), this magnitude was approximately equal to that found for a 0.05%BAC.

Figure 3. (a) Group mean (+SE) speed of responses on the simple reaction time task with increasing hours of sustained wakefulness. (b) Group mean (+SE) intra-individual variability in responses on the simple reaction time task with increasing hours of sustained wakefulness. *Significant difference ($P < 0.01$) between that trial and the baseline.

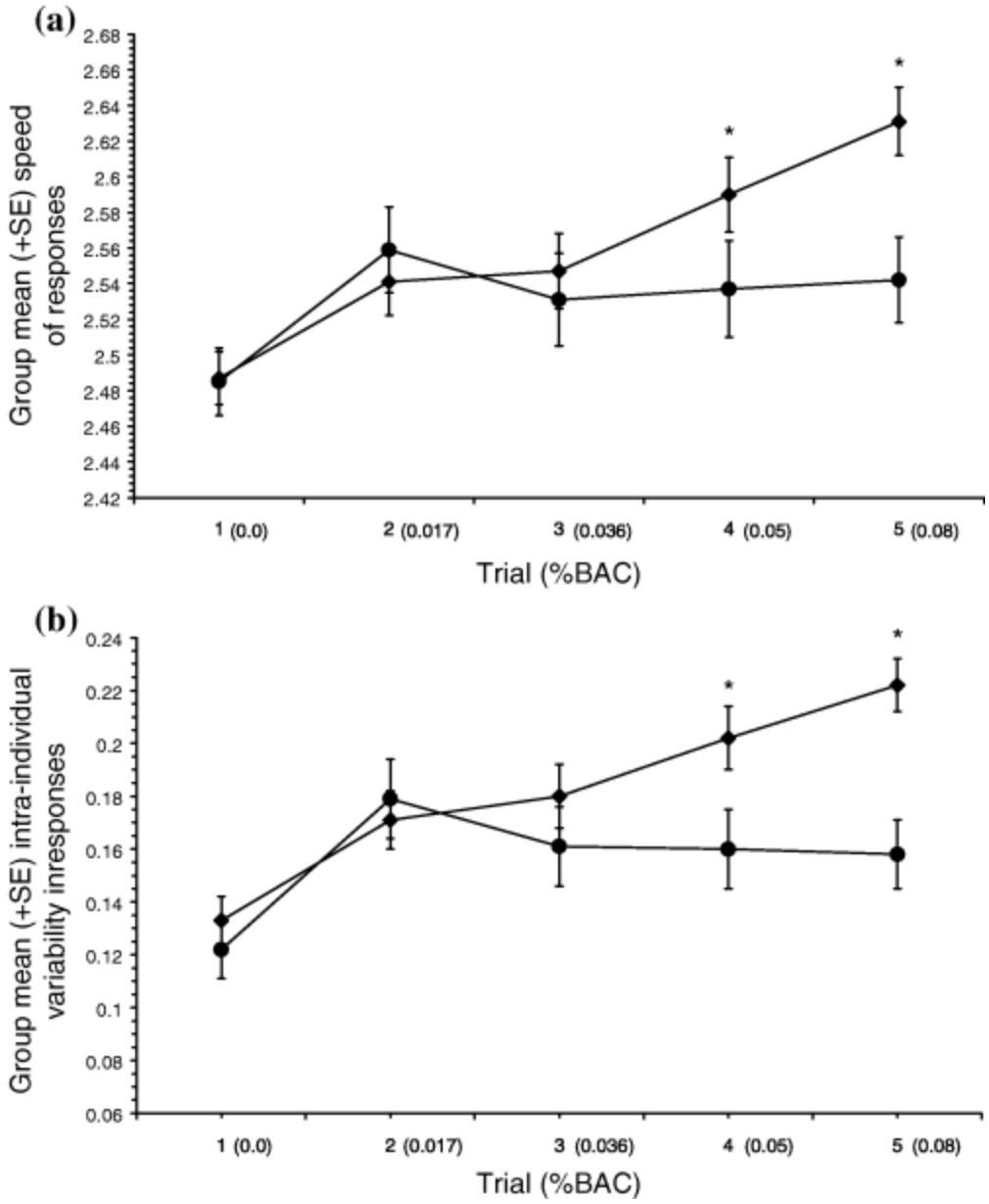
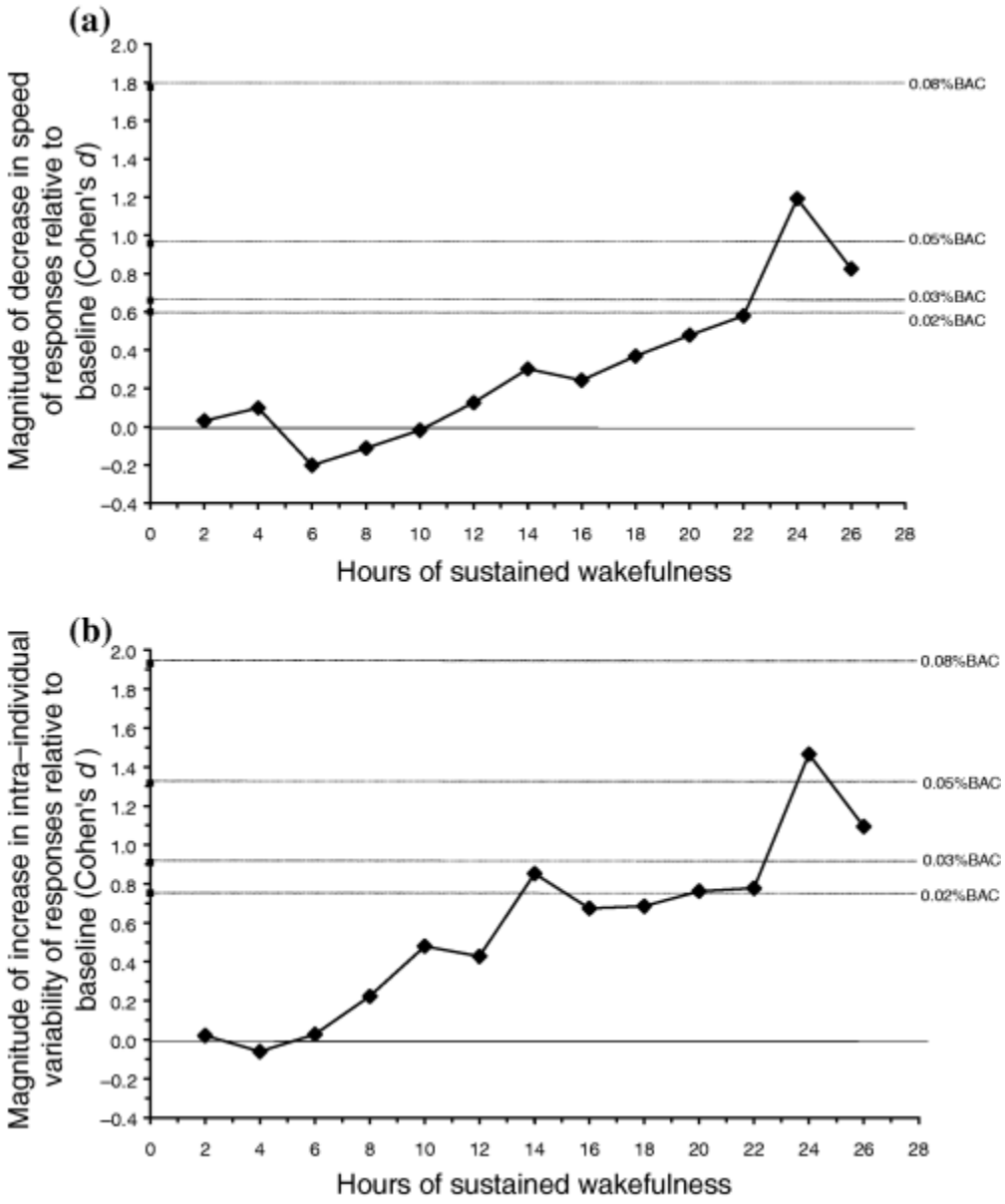


Table 1 shows the percentage change scores, Cohen's d and the non-overlap statistic computed for the difference between the 24-h sustained wakefulness and baseline trials and between the 0.08%BAC and baseline trials. Cohen's d shows that the magnitude of change for the maximum fatigue condition was less than that for the 0.08%BAC (Fig. 4). The non-overlap statistic indicates that for both conditions the distributions of performance had shifted with each condition so that the percentage overlap was quite low. Importantly, the percentage change scores indicated that the magnitude of change associated with 24-h sustained wakefulness was much greater than the impairment found for 0.08%BAC. In addition, when the percentage change was compared with the percentage non-overlap of distributions derived from the Cohen's d for the difference between the 24-h sustained wakefulness and 0.08%BAC conditions and their relative baselines, the magnitude of impairment according to the non-overlap statistic was considerably smaller than that indicted by the percentage change measure.

Table 1. Impairment in reaction time speed between baseline and the maximum level of fatigue-related cognitive impairment, and between baseline and the maximum percentage blood alcohol concentration (%BAC) expressed using Cohen's d, the distributional non-overlap statistic (%NOL) and the percentage change in group mean values

	Maximum subjective fatigue (24-h sustained wakefulness)	Maximum % BAC (0.08)
Cohen's d	1.19	1.77
%NOL	62.2	77.4
Percentage change in mean values	58.1	39.26

Figure 4. (a) Magnitude of impairment (Cohen's d) in the speed of responses on the simple reaction task with increasing hours of sustained wakefulness compared with the magnitude of impairment (Cohen's d) in the speed of responses on the simple reaction time task found with each increase in %BAC. (b) Magnitude of impairment (Cohen's d) in the intra-individual variability of responses on the simple reaction task with increasing hours of sustained wakefulness compared with the magnitude of impairment (Cohen's d) in the intra-individual variability of responses on the simple reaction time task found with each increase in %BAC.



The magnitude of the impairment in the speed and intra-individual variability of psychomotor function detected in individuals who had been awake continuously for 24 h was slightly greater than the impairment observed for the same individuals when they were rested but had a %BAC of 0.05. Importantly, for no aspect of psychomotor performance was the magnitude of impairment in psychomotor function equivalent to that found for 0.08%BAC. In contrast, increasing levels of fatigue and %BAC did not affect the accuracy of psychomotor function. These results are consistent with previous research indicating that serious cognitive impairments are associated with the fatigue that occurs after relatively short periods of sustained wakefulness (Dawson and Reid, 1997; Lamond and Dawson, 1999; Williamson and Feyer, 2000). However, our study suggests that the magnitude of the fatigue-related cognitive impairment is not as great as that estimated in previous studies that compared the cognitive consequences of fatigue and alcohol directly without considering the effects of either condition on the variability of performance.

Re-analysis of the data using percentage change scores instead of a metric that accounted for variability both within and between experimental conditions indicated that the use of absolute difference scores to both characterize and compare the cognitive impairment associated with fatigue and alcohol lead to an overestimation of performance impairment. Furthermore, by comparing these percentage change metrics between fatigue and %BAC without considering the variation associated with each, gives rise to conclusions that the impairment associated with fatigue is greater than the impairment associated with 0.08%BAC. This is opposite to that observed when the statistics used to compare conditions took into account differences in variability between experimental conditions in addition to differences between group mean values.

The importance of understanding the effect of fatigue on the variability of performance is evident in the effect size detected for increase in the intra-individual variability of performance at 24-h sustained wakefulness (compared with baseline, Cohen's d = 1.5). This was twice greater than that found for the impairment in the speed of performance for the same level of sustained wakefulness (24 h) (Cohen's d = 0.7), although both fatigue-related impairments were equivalent to that found for the same measure in the same individuals with 0.05%BAC. When considered with the minimal effect of increasing fatigue and %BAC on the accuracy of performance, it appears that increasing levels of fatigue and alcohol have qualitatively and quantitatively similar effects on simple psychomotor performance. That is, while increasing levels of fatigue and %BAC increase the reaction times and decrease the consistency of psychomotor performance without altering its accuracy, decreases in the consistency of performance are much greater than increases in its speed. The effect of fatigue in decreasing the consistency of task performance has been noted previously and was hypothesized to be the result of very brief losses of consciousness or microsleeps that increase with frequency as the hours of sustained wakefulness increase (Bills, 1931; Broadbent, 1958). The recording of brain electrical activity using the electroencephalograph while fatigued individuals perform cognitive tasks shows that during lapses in cognitive performance, subjects momentarily slip into a light sleep. Importantly, individuals are generally not aware of these microsleeps despite their deleterious effects on performance (Bonnet and Moore, 1982). However, we did not monitor brain electrical activity in the current experiment and therefore are unable to determine whether the increased variability we observed for psychomotor performance at 24 h of sustained wakefulness was actually because of an increase in the number or duration of microsleeps during testing. Even more interesting would be to determine whether the increased variability in psychomotor performance found for the same people when they were well-rested but with a %BAC of 0.05 was also because of microsleeps.

Despite our study detecting smaller impairments in fatigue-related cognitive impairment than has been reported previously, the magnitude of impairment we did observe is still serious. Even accounting for intra- and inter-subject variability, the cognitive impairment found at 24–26 h of sustained wakefulness was greater than that associated with %BAC levels at which many jurisdictions consider the operation of a motor vehicle to be unsafe and therefore illegal. As Williamson and Feyer (2000) point out, it is not uncommon for workers to stay awake for 24 h especially around the change of a shift pattern. It is therefore not surprising that time of day and driver fatigue is often reflected in fatigue crash studies (e.g. Folkard, 1997; Pack et al., 1995). Pack and colleagues examined the temporal distribution of

crashes judged by police to be fatigue related. The results showed a high peak between midnight and late morning and a smaller peak in the early afternoon. This distribution was consistent with the results of sleep studies by Lavie (1986) whereby the peak fatigue crash periods were similar to the amounts and distribution of sleep obtained by subjects in the sleep experiment. Similarly, Blower and Campbell (1998), in their investigation of fatalities and injuries of truck drivers in fatigue-related crashes, found fatigue-related crashes peaking between midnight and 06:00 hours. Our data are consistent with these studies and show the impairment in simple psychomotor performance, impaired beyond the limits deemed acceptable by society in individuals who have been awake for relatively short periods of time. Therefore, our study and the three previous ones provide direct experimental support for the proposal that individuals should not engage in cognitively demanding and high-risk activities, such as driving, when they have been awake for more than 20 h.

One limitation of the current study was that it investigated the effects of increasing fatigue and %BAC on simple attentional function. Nonetheless, the data gained and the analyses performed now provide a sound foundation for the investigation of more complex cognitive functions. Furthermore, as the magnitude of impairment was expressed using a measure of effect size, the results of future research also using effect sizes can be compared directly with those observed in the current study in meta-analyses. A second limitation of the current study and all those completed to date is that the comparison in cognitive impairment between fatigue and %BAC has been performed only for healthy young adults. It would be important to know whether these fatigue-related impairments become even greater as individuals become older or ill.

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