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Effects of modafinil on cognitive and meta-cognitive performance

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The stimulant modafinil has proved to be an effective treatment modality for narcolepsy and related sleep disorders and is also being studied for use during sustained military operations to ameliorate the effects of fatigue due to sleep loss. However, a previous study reported that a relatively large, single dose of modafinil (300 mg), administered to already sleep-deprived individuals, caused participants to overestimate their cognitive abilities (i.e. 'overconfidence'). Because the predominant application of modafinil is in otherwise healthy, non-sleep-deprived individuals, the present study investigated the generality of modafinil-induced overconfidence in a group of 18 healthy, non sleep-deprived adults. The design involved a double-blind, placebo controlled, fully within-subjects manipulation of placebo and modafinil (4 mg/kg: approximately 300 mg, on average) over three 50-min cognitive testing sessions (i.e. before drug ingestion, and at 90 and 180 min after drug ingestion). The cognitive task battery included subjective assessments of mood, fatigue, affect, vigor and motivation, and cognitive assessments of serial reaction time, logical reasoning, visual comparison, mental addition and vigilance. In addition, trial-by-trial confidence judgements were obtained for two of the cognitive tasks and more global, task level assessments of performance were obtained for four of the cognitive tasks. Relative to placebo, modafinil improved fatigue levels, motivation, reaction time and vigilance. In terms of self-assessments of cognitive performance, both the placebo and modafinil conditions were 'well calibrated' on trial-by-trial confidence judgements, showing neither marked over- nor under-confidence. Of note, the modafinil condition displayed a non-significant tendency towards 'overconfidence' for task-level assessments of performance. The present findings highlight the need for continued research on the many complex interactions involving fatigue states, occasional versus long-term stimulant use, and subjective assessments of fatigue and cognitive performance. Copyright © 2004 John Wiley & Sons, Ltd.

KEY WORDS — modafinil; cognitive performance; confidence; calibration; meta-cognition

INTRODUCTION

The stimulant modafinil (2-[(diphenyl-methyl)-sulfinyl]acetamide) has been shown to promote vigilance and arousal without toxicity, tolerance (Laboratoire L. Lafon, 1994) or significant sleep disturbances (Buguet *et al.*, 1995; Saletu *et al.*, 1989). In addition, the findings of several studies suggest that modafinil is biochemically and pharmacologically distinct from prototypical stimulants such as d-amphetamine (Ferraro *et al.*, 1996b, 1997) and does not produce subjective effects that are typically associated with dependency (Warot *et al.*, 1993; Jasinski, 2000; Rush *et al.*, 2002). Moreover, unlike amphetamines, which display widespread brain activation, modafinil has shown specificity for hypothalamic structures involved in sleep regulation and circadian rhythms (Capotot *et al.*, 2003; Lin *et al.*, 2000). Although the precise mechanism of action of modafinil is not fully understood, early studies suggested that it acts centrally as an α1-adrenergic agonist (Duteil *et al.*, 1979, 1990). More recent work suggests that both increased dopaminergic transmission (Ferraro *et al.*, 1996a, 1997; Mignot *et al.*, 1994; Wisor *et al.*, 2001) and decreased GABAergic activity (Ferraro *et al.*, 1996b; Fuxe *et al.*, 1996; Scammell *et al.*, 2000) may play critical roles by which modafinil promotes wakefulness.

Despite the lack of a substantiated theory of modafinil's underlying mechanism, the relatively benign

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pharmacological effects of the drug reported to date, coupled with its vigilance-promoting properties, have stimulated several important lines of research dedicated to human application. Most notably, modafinil has been demonstrated to be a safe and effective, long-term treatment modality for narcolepsy (e.g. Bastuji and Jouvet, 1988; Boivin *et al.*, 1993; Billiard *et al.*, 1994; Broughton *et al.*, 1997; Laffont *et al.*, 1994; Moldofsky *et al.*, 2000) and related clinical sleep disorders [e.g. idiopathic hypersomnia and excessive daytime sleepiness (EDS) associated with obstructive sleep apnoea (OSA)]. Currently, the recommended daily adult dose range for the treatment of narcolepsy and EDS is 200–400 mg, either as two divided doses in the morning and at noon, or as a single morning dose (Provigil®, 1997).

In addition to research involving application to various sleep disorders, the potential utility of modafinil is also being investigated in the context of sustained military operations (Buguet *et al.*, 2003; Lyons and French, 1991; Lagarde and Batejat, 1995) as a potential countermeasure to the debilitating effects of sleep deprivation on human cognitive performance (for reviews of the sleep loss and performance literature, see Krueger, 1989; Dinges and Kribbs, 1991; Harrison and Horne, 2000). Once again, modafinil is being considered as an alternative to 'gold-standard' stimulants such as D-amphetamine (Cornum *et al.*, 1996; Emonson and Vanderbeek, 1995), precisely because it is non-addictive and exhibits far fewer negative side effects (Lyons and French, 1991; Pigeau *et al.*, 1995). In this context, several studies to date have documented the effectiveness of modafinil to ameliorate cognitive performance under conditions of sleep deprivation (Bensimon *et al.*, 1991; Lagarde and Batejat, 1995; Pigeau *et al.*, 1995; Baranski *et al.*, 1998, 2002; Caldwell *et al.*, 2000; Wesensten *et al.*, 2002). These studies typically fall into one of two applications related to military scenarios: recuperation and maintenance (see Babkoff and Kreuger, 1992). In recuperation studies (e.g. Pigeau *et al.*, 1995; Wesensten *et al.*, 2002), participants are permitted to become extremely fatigued and then are administered a (typically) large dose (e.g. 300–400 mg) to determine if, and to what extent, cognitive performance can be restored to baseline levels. On the other hand, in maintenance studies (e.g. Caldwell *et al.*, 2000; Baranski *et al.*, 1998, 2002; Legarde and Batejat, 1995), participants are given smaller, more frequent doses (e.g. 3×100–200 mg/24 h) in an attempt to maintain cognitive performance at (or near) baseline levels throughout a period of sleep derivation (cf. Brun *et al.*, 1998).

The present study focuses on the effects of modafinil on simple and complex cognitive task performance. Whereas the cognitive enhancing effects of modafinil have recently been documented in non-sleep deprived subjects (Turner *et al.*, 2003), our main concern in this research is with the effects of modafinil on the so-called 'self-monitoring' or 'meta-cognitive' abilities (i.e. the ability to accurately self-assess one's own cognitive performance). The latter issue is important because Baranski and Pigeau (1997) reported that a high/normal dose of modafinil (300 mg), administered in a recuperative paradigm to individuals who were already sleep-deprived, induced 'overconfidence'; i.e. subjective estimates of performance exceed actual cognitive performance. Specifically, their findings revealed that cognitive performance was slightly improved upon administration of modafinil (300 mg) but subjective estimates of performance increased disproportionately. Interestingly, comparison groups in that study participating under placebo and d-amphetamine (25 mg) did not show overconfidence: The placebo condition appropriately 'calibrated' their subjective estimates to match their lower performance; the d-amphetamine condition, on the other hand, showed a marked increase in subjective estimates of performance which was matched by an appropriately large increase in actual performance. In a more recent study, Baranski *et al.* (2002) found no evidence of overconfidence when modafinil was administered in small doses throughout a period of sleep deprivation (i.e. 3×100 mg/24 h; i.e. every 6 h); i.e. in a maintenance paradigm.

The objective of the present study was to examine further the effect of a large, single dose of modafinil on cognitive and meta-cognitive functioning, employing a wider range of cognitive tasks than was examined by Baranski and Pigeau (1997) and in a population of otherwise healthy, non-sleep deprived individuals. To date, the effects of modafinil on meta-cognitive functioning have not been studied in a non-sleep deprived population and thus it is important to determine if modafinil *per se* causes overconfidence or if the Baranski and Pigeau (1997) results are limited to conditions involving a sleep deprived state. Importantly, as the above discussion has outlined, the overwhelming majority of modafinil users are not sleep-deprived military personnel but otherwise normal, healthy adults who may be taking single doses in the high/normal range for clinical sleep disorder application. In addition, it is also important to understand the meta-cognitive effects of modafinil for the potential, occasional, non-clinical use of the stimulant to combat 'normal fatigue states' in the

general population (e.g. truck drivers, pilots, students, shift-workers, etc).

MATERIALS AND METHODS

Subjects

Participants were 18 adult students recruited from local universities by advertisement. Participants were males[†] aged 18–40 years (mean = 24.2 y; SD = 6.4) and the mean weight of the participants was 79.8 kg (SD = 6.6) with a range of 66.7–93.0 kg. Subjects were pre-screened by a physician and satisfied the following criteria: (a) were healthy (b) were medication free, (c) abstained from alcohol or caffeine for 48 h prior to testing, and (d) had no allergies or haematological, cardiovascular, neurological, psychiatric or sleep-related disorders. All subjects were fully informed about the purposes of the study and the procedures to be employed, signed informed consent forms for participation, and were given a full debriefing and a medical examination upon completion of the study. The experiment was approved by the DRDC-Toronto ethics committee for research involving human subjects.

Materials

Subjects participated in the study in groups of 3–4 but the cognitive testing sessions were performed independently and in separate testing rooms. The cognitive test battery was performed on PC compatible computers, each with a 14 in. screen. A PC mouse was used as an input device on all tasks and subjective questionnaires.

Procedure

The study employed a double blind, fully within-subjects manipulation of modafinil and placebo. Subjects were randomly assigned to the order of drug condition (placebo or modafinil) and testing phases were separated by a (minimum) 1-week drug 'wash-out' period. Modafinil (4 mg/kg; i.e. approximately 300 mg, on average) or placebo (Metamucil) was prepared for each subject and administered in opaque gelatin capsules.[‡]

The experiment involved three cognitive testing sessions per day on each of two testing days, where each testing day was separated by the washout period. Each cognitive testing session lasted approximately 50 min. The first occurred 90 min prior to drug ingestion and the second and third sessions occurred 90 min and 3 h post-drug ingestion, respectively. According to Lafon (1994), maximal blood concentrations of modafinil occur 2–3 h post ingestion (see also Wong *et al.*, 1999). In addition to the formal cognitive testing sessions, all participants performed four practice sessions that were completed during a familiarization phase of the study (i.e. at least 1 week prior to the start of the formal study). These sessions served to stabilize performance on the various tasks and thus to minimize the effects of practice on cognitive task performance.[§]

Cognitive test battery

The cognitive test battery included a subset of tasks used extensively in previous human performance studies in our laboratory (Baranski *et al.*, 1994, 1998, 2002; Pigeau *et al.*, 1995). The specific tasks selected for the present study permit the investigation of a diverse range of fundamental cognitive processes and have been shown to be extremely sensitive to cognitive performance changes. The tasks that comprised the cognitive test battery were always performed in the same order and included the following.

[†]At the time this study was conducted (i.e. 1998), it was anticipated that the use of modafinil in military applications would be considered only for 'special forces' personnel, which were all male. We have since conducted several studies involving modafinil which were open to male and female participants. In none of those studies were any systematic effects observed due to gender.

[‡]This dosing level was chosen for several reasons. First, it approximates that used in the Baranski and Pigeau (1997) study where overconfidence was observed in sleep-deprived individuals. Second, it was unnecessary to examine lower doses since a previous study found that overconfidence does not occur at doses lower than that investigated here (Baranski *et al.*, 2002). Third, the present dose would certainly produce subjective effects on alertness and energy levels in non-sleep deprived participants (Turner *et al.*, 2003), which provides a logical, potential basis for misattribution of cognitive performance levels. Finally, it seemed unnecessary to examine dosing levels that exceed the maximum single dosage for the treatment of narcolepsy and related sleep disorders. Hence, if overconfidence occurs in the present study, then the results would be applicable and thus relevant to populations currently employing modafinil therapeutically.

[§]In order to examine the effects of modafinil on physical work capacity, the design of the study included four exercise periods, each of 5 min duration, during which the subjects completed various 'ride-to-exhaustion' protocols on a stationary bicycle. The exercise periods were strategically placed so as not to interfere with the cognitive testing sessions (i.e. at least 1 h separated exercise and cognitive testing). These data, and the associated physiological measures of physical performance (e.g. heart rate, blood pressure, and blood and urine samples) are not reported here.

Subjective questionnaires (approx. 3 min). The questionnaire included items that probed the subjects' current level of mental and physical fatigue, motivation and mood. In addition, the global vigor affect (GVA) scale (Monk, 1991) was administered. This scale was subsequently scored on the vigor and affect subscales according to the procedure outlined in Monk (1991). All scale questions involved a visual analogue scale (VAS) from 0 to 10, which was anchored at both ends by a short verbal description (e.g. 'Not at all tired' vs 'Very tired'). To enter a rating the subject 'hooked' a visual pointer on a sliding scale with the computer mouse and dragged the pointer on the monitor to the appropriate location on the scale.

Four-choice serial reaction time (3 min). This task is based on a variation of a well-known task employed by Wilkinson and Houghton (1975) and used extensively in sleep loss and performance experiments. On each trial of the serial reaction time (SRT) task, four response buttons (P, G, L and S) were presented on the computer monitor in a square configuration (i.e. two above and two below). Directly above the displayed letters, a probe letter (P, G, L or S) was presented. The subject's task was to move a visual pointer with the mouse over the response button corresponding to the probe letter and to depress the mouse button as quickly and as accurately as possible. The probe letter varied on each trial and was randomly generated by the program. Accuracy of response and response time was measured on each trial. The latter was recorded from the appearance of the probe letter to the depression of the response button on the mouse.

Mental addition (9 min). This task is based on a similar task employed by Wilkinson (1969). This version of the mental addition (ADD) task required subjects to add a random sequence of eight numbers (between 1 and 16), which were presented on the computer monitor at a rate of 1 number every 1.25 s. The sequence was terminated by the presentation of a visual prompt ($\Rightarrow$) at which time subjects typed in their response using the mouse and a visual keypad presented on the monitor. Upon entering their response, subjects were prompted for a subjective confidence rating which should reflect their subjective probability of a correct response, from 0 (certain of an error) to 100 (certain of a correct response). Judgement confidence and accuracy were measured on each trial.

Detection of repeated numbers (DRN) vigilance task (8 min). The detection of repeated numbers task is based on a variation of a similar task employed by Smith and Miles (1986) and used extensively in human performance studies. Three-digit numbers are presented on a video monitor at a rate of 1 per second. The DRN vigilance task requires subjects to detect, by pressing a mouse button, when the same three-digit number occurs in succession. In total, eight repeated numbers occur randomly distributed within each minute of the task. Correct detections occur when the subject presses the mouse key within 2 s of a repeated number; misses occur when repeated numbers are presented but the mouse button is not pressed; false alarms occur when the mouse button is pressed but successive numbers were not presented.

Logical reasoning task (3 min). The logical reasoning task (LRT) is based on Baddeley (1968). On each trial, a pair of letters is presented at the top of the screen: A B or B A. Directly below the pair of letters is a statement concerning the spatial arrangement of the letters: e.g. A precedes B; B does not follow A, etc. . . . There were 16 such statements in total. The subject's task is to determine if the statement is true or false, by pressing with the mouse the appropriate response button (T or F) on the screen. Response time and response accuracy were measured on each trial.

Visual perceptual comparison (5 min). This task is a variation of the classic two-alternative forced choice line-length discrimination task (Henmon, 1911). Each trial of the comparison (CMP) task began with the presentation of an instruction ('LONGER' or 'SHORTER'), which was displayed near the top of the computer monitor. One second later, the visual display appeared which consisted of two horizontal lines, divided by one short vertical line. The display remained on the screen until the subject responded. The subject's task was to determine which of the two lines was longer or shorter, depending on the instruction. Subjects responded by depressing either the left or the right button on the mouse to indicate that the left or right line was the longer or the shorter. Four levels of judgement difficulty were randomly presented to the subjects; the difficulty was defined *a priori* on the basis of the ratio of the longer to the shorter line: 1.01, 1.03, 1.05 and 1.07. All lines appeared black on a white background. Subjects were encouraged to respond as quickly and as accurately as possible. As with the addition task, subjects were prompted, after each response, for a subjective confidence rating. Because the line task is a 2-alternative forced choice task the confidence scale ranged from 50% (guess) to 100% (certain of a correct response). Response time, response accuracy and confidence ratings were recorded on each trial.

Self-monitoring

Self-monitoring of cognitive task performance was assessed at two levels: Trial-by-trial, confidence 'calibration' analyses and task-level analyses. For the former, a large number of trial-by-trial confidence judgements are required and thus only two of the tasks permitted such analyses (i.e. visual comparison and mental addition). The methods of analysis for trial-by-trial confidence judgements will be described in the relevant part of the Results section. For the latter, task-level analyses, a common and quantitative index of response accuracy is required (i.e. percentage of correct responses) in which performance is not errorless or nearly errorless. Hence, four cognitive tasks were examined for self-monitoring at the task level: mental addition, perceptual comparison, logical reasoning and detection of repeated numbers (vigilance). In order to assess the extent to which subjects were able to accurately assess their own cognitive abilities at the task level, each of these four tasks were preceded with a single question, which asked subjects to estimate the percentage of correct responses that they would achieve (i.e. pre-task estimate). In addition, each task was followed by a similar question that asked subjects to estimate the percentage of responses that they answered correctly (i.e. post-task estimate). Subjects' self-monitoring ability was assessed by comparing the subjective estimates of performance with actual performance accuracy. When the estimates exceed or fall below actual performance we conclude that subjects are overconfident or underconfident in their assessments, respectively. When assessments closely match performance, we conclude that subjects are 'well-calibrated' (see Baranski and Pigeau, 1997).

RESULTS

One subject did not complete the second week of testing and thus his data were not used. Accordingly, the data to be reported are based on the 17 subjects who provided full data sets. The results are presented in three sections. The first reports the effects of the drug manipulation on subjective estimates of mood, performance, and physical and mental fatigue. Section two provides a view of the effects of the drug manipulation on cognitive performance and section three presents the results of the self-monitoring analyses. For sections one and two, data were analysed by repeated measures analysis of variance (ANOVA) with two levels of drug (placebo and modafinil) and three sessions as within-subjects factors. Analyses for section three are described below. Throughout this paper, statistical significance was set at the 0.05 level and the Huynh-Feldt epsilon correction was used to adjust for potential violations of compound symmetry assumptions, although the degrees of freedom reported in the text are based on the design. Finally, for all cognitive performance measures reported below, observations on which response times were greater then 3 SD of the mean were trimmed as outliers. In no cases did this account for more than 1.0% of the data.

Subjective measures

The mental fatigue scale revealed a reliable effect of drug condition ($F(1, 16) = 7.35$), with significantly lower fatigue ratings in the modafinil condition ($M = 2.18$, $P = 2.66$). No other main effects or interactions were reliable. The physical fatigue scale revealed a significant effect of sessions ($F(2, 32) = 5.50$); as expected, physical fatigue was higher for session 3, following the exercise. In addition, there was a reliable effect of drug ($F(1, 16) = 5.77$), with lower fatigue ratings in the modafinil condition ($M = 2.42$, $P = 3.10$). The interaction between drug and sessions was not reliable. The motivation scale revealed a reliable drug $\times$ session interaction ($F(2, 32) = 5.29$). As is evident in Figure 1a, motivation increased in the modafinil condition relative to the placebo condition. A Tukey HSD post-hoc test confirmed a reliable difference between placebo and modafinil for session 3 (HSD, $p < 0.002$). There were no main effects or interactions involving the mood scale; indeed, subjects were quite amicable throughout the study.

The GVA scale was analysed on the dimensions of affect and vigor, following the procedure outlined in Monk (1991). There were no main effects or interactions on the affect scale. The vigor scale revealed a main effect of session ($F(2, 32) = 6.19$); ratings increased monotonically over sessions 1–3. The main effect of drug was also reliable ($F(1, 16) = 11.32$) with higher vigor ratings reported in the modafinil condition ($M = 63.4$, $P = 61.2$). The interaction was not reliable.

Summary of the subjective measures. Overall, the subjects' mood remained fairly positive throughout the study and was independent of drug condition. Fatigue levels were lower and vigor was higher in the modafinil condition and motivation displayed a clear interaction between Session and Drug Condition.

Cognitive performance measures

For the SRT, LRT and CMP tasks, response time and response accuracy (i.e. % correct) were dependent

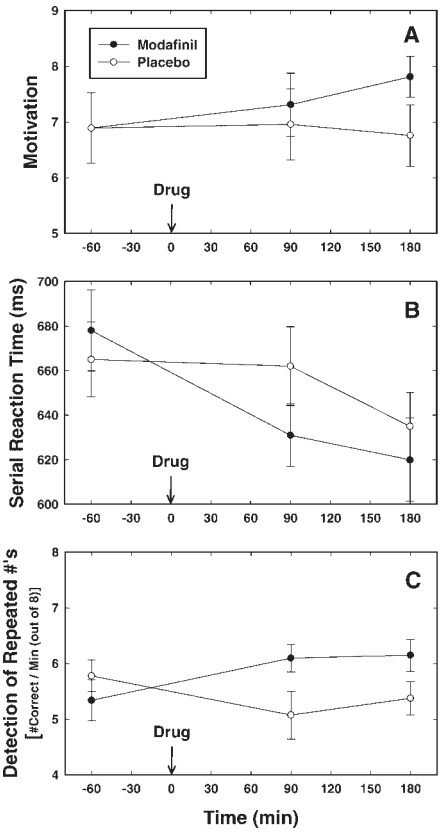

Figure 1. Motivation ratings (A), serial reaction time (B) and vigilance scores (C), separately for the placebo and modafinil conditions. Error bars denote the standard error of the mean across subjects

measures. For the ADD task, the experimental program controlled stimulus presentation; consequently, only response accuracy was used as a dependent measure. For the DRN (vigilance) task, responses were required within a specific 2 s interval and, as such, the number of correct detections, misses and false alarms provided the critical measures.

Serial reaction time. ANOVA revealed no main effects or interactions for the accuracy measure. For response time, there was a main effect of sessions ($F(2, 32) = 38.71$) due to practice and a drug × session interaction ($F(2, 32) = 8.70$). As is evident in Figure 1b, RTs were significantly faster following modafinil administration. Indeed, a Tukey HSD post-hoc test revealed a reliable difference between placebo and modafinil for session 2 (HSD, $p < 0.004$).

Mental addition. There were neither main effects nor interactions for the ADD task.

Logical reasoning. ANOVAs revealed significantly higher accuracy ($F(1, 16) = 6.23$) and marginally faster response times ($F(1, 16) = 4.21$, $p = 0.056$) in the modafinil condition than for the placebo condition (Accuracy: M = 88.5%, P = 86.7%; RT: M = 3083 ms, P = 3219 ms). No other main effects or interactions were reliable.

Perceptual comparison. ANOVA conducted on response accuracy revealed no main effects or interactions. For response times, the only effect to achieve statistical significance was a main effect of session ($F(2, 32) = 13.24$); response times uniformly decreased with increasing practice.

DRN vigilance. ANOVA on the number of correct detections per minute (out of 8) revealed a significant main effect of Drug ($F(1, 16) = 10.50$) which was qualified by a reliable Drug × Session interaction ($F(2, 32) = 9.67$). As is evident in Figure 1c, in the modafinil condition, vigilance improved over sessions whereas for the placebo condition vigilance declined slightly. Tukey HSD post-hoc test confirmed reliable differences between placebo and modafinil for sessions 2 (HSD, $p < 0.003$) and 3 (HSD, $p < 0.05$). Subsequent analyses on the number of false alarms per minute and the number of misses per minute confirm that the principle finding was due exclusively to increased errors of omission (i.e. misses) in the placebo condition.

Summary of the cognitive measures. In each case where significant effects were obtained the effect of modafinil was uniformly positive with respect to cognitive performance. Thus, modafinil not only improves cognitive performance in sleep-deprived individuals—it can be viewed as a general cognitive enhancer (see also Turner *et al.*, 2003).

Self-monitoring analyses

The self-monitoring analyses are presented in two sections. The first examines the effects of modafinil on the accuracy, or 'calibration' (Lichtenstein *et al.*, 1982; Harvey, 1997) of trial-by-trial confidence ratings for the addition and comparison tasks—the two tasks that permitted the collection of a sufficient number of trials for such analyses. The second section, following Baranski and Pigeau (1997), examines the accuracy of more global self-assessments at the task level.

Calibration analyses. 'Calibration' analyses at the trial-by-trial level attempt to identify the effect(s) of

a variable on the accuracy of confidence judgements. One method of capturing this relationship is via analysis of the calibration function (Keren, 1991; Lichtenstein *et al.*, 1982; Harvey, 1997). The top panel of Figure 2 plots the proportion of correct responses associated with each level of confidence reported by the subjects in the mental addition task. These data are for the two sessions that followed drug administration, separately for the placebo and modafinil conditions. The figure represents a 'full-range' calibration plot, ranging from '0' (certain of an error) to '100%' (certain of a correct response), with 50% denoting a 'guess' response. Ideal, or perfect, calibration of confidence judgements is denoted by the solid identity line; over- and under-confidence are represented by points below and above the identity line, respectively. Although participants provided many 'certain error' ratings (i.e. confidence = 0%), confidence ratings of 10–40% were averaged to provide more reliable estimates of subjective errors in that range, thus resulting in the 8 data points provided in the figure. As is evident in the plot, participants were extremely well calibrated in the process of mental addition. More importantly for our present purposes, modafinil did not have an antagonistic effect on the calibration function. In addition, the frequency with which the various confidence levels were used was virtually identical in the two conditions. Overall, subjects in the modafinil condition were 86.10% (SEM = 2.65%) correct in the addition task and their mean confidence was 88.95% (SEM = 2.04%), resulting in a slight overconfidence of 2.85% (SEM = 2.38%). By comparison, subjects in the placebo condition were 84.57% (SEM = 2.37%) correct and their mean confidence was 87.67% (SEM = 2.18%), resulting in a slight overconfidence of 3.10% (SEM = 2.49%). T-tests conducted on the accuracy, confidence and over–under confidence measures confirmed that the placebo and modafinil conditions did not differ statistically.

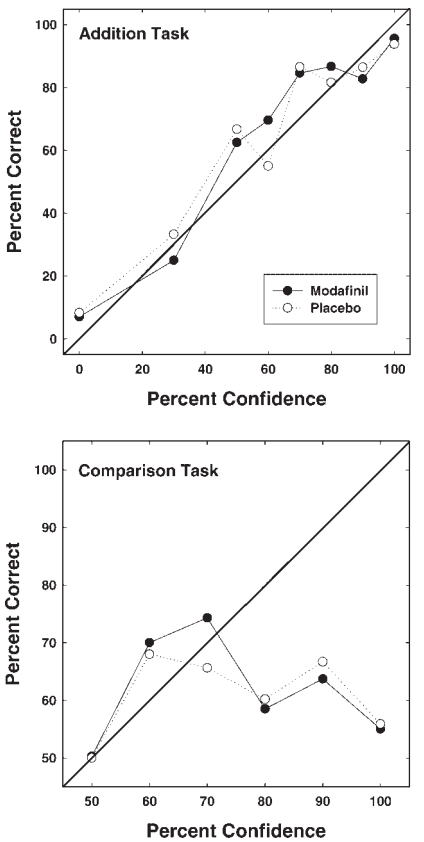

Figure 2. Calibration curves for the addition task (top panel) and the perceptual comparison task (lower panel), separately for the placebo and modafinil conditions. The top panel shows a 'full-range' calibration plot, ranging from '0%' (certain of an error) to '100%' (certain of a correct response); the lower panel shows a 'half-range' calibration plot, ranging from '50%' (guess) to '100%' (certain of a correct response). In each plot, the solid diagonal represents 'ideal' calibration

The lower panel of Figure 2 plots the calibration curves for the perceptual comparison task. As is typical for two-alternative forced choice tasks, the corresponding calibration plots represent a 'half-range' confidence scale, ranging from '50%' (guessing) to '100%' (certain of a correct response). In striking contrast to mental addition, subjects were not well-calibrated in sensory discrimination (Baranski and Petrusic, 1994, 1999). As in the addition task, however, modafinil did not have an antagonistic effect on the calibration function or on the frequency with which the confidence categories were used. Overall, subjects in the modafinil condition were 61.78% (SEM = 3.07%) correct in the comparison task and their mean confidence was 66.55% (SEM = 3.27%), resulting in an overconfidence of 4.77% (SEM = 4.66%). By comparison, subjects in the placebo condition were 61.49% (SEM = 3.01%) correct and their mean confidence was 65.23% (SEM = 3.02%), resulting in an overconfidence of 3.74% (SEM = 4.37%). Again, *t*-tests conducted on the accuracy, confidence and over–under confidence measures confirmed no difference between placebo and modafinil.

Task-level analyses. A repeated measures ANOVA was conducted using the difference between estimated (i.e. Pre- and Post task estimates) and observed performance (i.e. percent correct) for each session as the

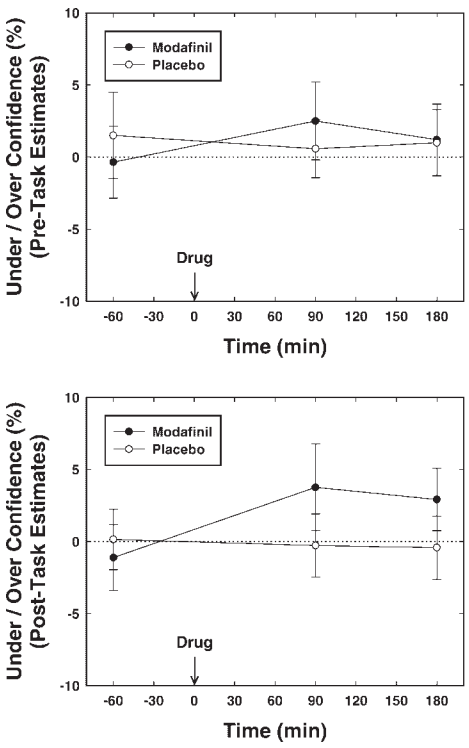

Figure 3. Degree of over- or under-confidence in the pre-task estimates (top panel) and the post-task estimates (lower panel), separately for the placebo and modafinil conditions. The index is based on the percentage difference between estimated and actual performance accuracy. Error bars denote the standard error of the mean across subjects

dependent measures. Hence, positive differences on this statistic denote overconfidence in the assessment, negative differences denote underconfidence, and little or no bias denotes that subjects are well calibrated at the task level. Drug (2 levels: modafinil vs placebo), Session (3), and Task (4 levels: CMP, LRT, ADD and DRN) were within subject factors.

Figure 3 provides plots of the difference between the Pre- and Post-Task estimates and actual accuracy, separately for the modafinil and placebo conditions. The data were averaged over the four tasks that permitted a quantitative index of response accuracy (percentage correct), which could be compared directly with subjective estimates of performance (i.e. CMP, ADD, LRT and DRN). In each case, subjects in the placebo condition displayed close to perfect calibration in their task-level estimates (Baranski and Pigeau, 1997; Baranski *et al.*, 1994; and see Dorrian *et al.*, 2000). For the modafinil condition there was good calibration for the pre-task estimates and a mild tendency towards overconfidence in the post-task estimates.

The ANOVA revealed a significant effect of Task for both the pre- and the post-task estimates ($F(3,48) = 5.40$ and $F(3,48) = 3.21$, respectively). Post-hoc comparisons revealed that subjects were generally more underconfident on the logical reasoning task (-6.6%) and generally more overconfident on the vigilance task (7.3%). No other main effects or interactions were reliable for the pre-task estimates. For the post-task estimates, the main effect of drug condition approached reliability ($F(1,16) = 3.60$, $p = 0.07$), with slight overconfidence in the modafinil condition. Finally, the critical interaction between session and drug condition was not reliable ($F(2,32) = 2.60$, $p = 0.09$). As is evident in the lower panel of Figure 2, estimates in the placebo condition were well calibrated throughout, whereas the modafinil condition shows a 5% change in the direction of overconfidence, although this effect, as mentioned, did not achieve conventional levels of statistical significance.

DISCUSSION

The present study examined the effect of modafinil on cognitive performance and on the ability to assess one's own cognitive performance in non-sleep deprived individuals. Modafinil's effectiveness as a cognitive enhancer has been substantiated and extended by the present findings; i.e. results were uniformly positive with respect to subjective assessments of fatigue, motivation and cognitive performance. With respect to the effect of modafinil on self-monitoring ability, the present findings suggest that modafinil did not induce overconfidence in non-sleep deprived individuals, although the non-significant trend towards mild overconfidence in the task-level estimates may suggest that further investigation is warranted.

To date, the effects of modafinil on meta-cognitive processes have been examined on three occasions; the first two involving conditions of sleep deprivation (Baranski and Pigeau, 1997; Baranski *et al.*, 2002). The findings taken together suggest that modafinil *per se* does not cause overconfidence directly. However, for people who are already sleep deprived, the marked improvement in subjective sleepiness and increased vigor following a relatively large single administration of modafinil may be misinterpreted to imply a concomitant improvement in cognitive performance. Indeed, our research has demonstrated that people are adept at assessing their momentary levels of subjective fatigue and sleepiness (Pigeau *et al.*, 1995), and these assessments are (perhaps due to evolutionary mechanisms) correlated with actual

performance. Problems in overconfidence can potentially occur when: (a) unfamiliar tasks are performed for which there is limited explicit feedback from the environment to supplement or corroborate subjective assessments of performance, or (b) a person has had limited familiarity with the subjective experience of fatigue due to sleep loss and thus an improvement in subjective sleepiness (due to a stimulant, for example) may cause them to assume that they are performing better than they actually are.

This argument suggests that there should be less concern when using modafinil as a treatment for narcolepsy (and associated sleep disorders) because in clinical populations people are experiencing the world under continuous drug administration and thus are provided with ample feedback from the environment to learn how normal fatigue states and drug states interact and in turn are related to actual performance. Conversely, as the findings of Baranski and Pigeau (1997) showed, there may be concern about the effects of modafinil (or any treatment that acutely relieves subjective feelings of fatigue or sleepiness) for occasional users under 'normal fatigue states' where the vigilance enhancing properties of the drug may be misattributed. Indeed, such misattributions have previously been documented, most notably with amphetamine (see Smith and Beecher, 1960, 1964; and cf. Hauty and Payne, 1957). Our results highlight the need for more research on the many complex interactions involving normal fatigue states, occasional versus long-term stimulant use, cognitive performance, and subjective assessments of fatigue and performance.

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