Effects of Modafinil and Amphetamine on tracking performance during sleep deprivation

M. M. Taylor[1], DCIEM, Box 2000, North York, Ontario, Canada M3M 3B9; (mmt@ben.dciem.dnd.ca)

Introduction

This study was part of a comprehensive study of the effects of the drug modafinil on various aspects of human performance during sleep deprivation (Pigeau et al., In Press). In military operations, the behaviour of various elements and aspects of a situation often must be tracked continuously, perhaps by sleep-deprived personnel. The study reported here simplifies the problem of tracking a complex evolving situation down to its minimum, a single item that is affected by influences outside the control of the observer.

In each of six tracking tasks, the subject was required to maintain the relation between an on-screen cursor and a marker during a period of 50 sec. In any one task, either the cursor position or the marker position was affected by a disturbance generated from a number sequence previously computed. The subject could use the mouse either to compensate for a disturbance added to the cursor, or to cause the cursor to follow the movements of a marker that was affected by the disturbance.

According to the experimental design, twelve subjects were to be given modafinil three times during the sleep deprivation period, twelve were to be given amphetamine, which is believed to counter the effects of sleep deprivation, and twelve were to be given a placebo. One subject in the placebo group declined at the last minute to participate, and one subject in the amphetamine group fell ill midway through the sleep deprivation period, leaving eleven whose data could be used in each of those two groups.

Tasks

There were six different tasks, only five of which are included in the results described here; the sixth task was characteristically different in that it employed two markers and two cursors.

In two of the tasks, the marker and the cursor were vertical lines approximately 3 cm long. In one, the disturbance affected the marker, and the subject used the mouse to keep the cursor aligned with it vertically (pursuit tracking); in the other, both the disturbance and the marker affected only the cursor, and the subject was required to compensate for the disturbance in order to keep the cursor vertically under the marker (compensatory tracking).

The third task presented the subject with a circle of about 10 cm diameter, and a small disk of about 0.5 cm diameter that progressed slowly counterclockwise around the perimeter of the circle. The disturbance moved the small disk radially, and the subject used the mouse to compensate so as to keep the disk on the circle perimeter. The mouse affected the radial position of the disk, which meant that as the disk moved around the circle a left-right mouse movement might make the disk move left, right, up or down.

The fourth task presented what looked like a pendulum swinging from a point near the top-middle of the screen. Outside the arc of the pendulum bob, a disk moved in an arc at a speed that was affected by the disturbance. The mouse also affected that speed, and the subject's task was to keep the disk aligned with the shaft of the pendulum as the pendulum swung back and forth.

The fifth task was visually quite different, in that the display consisted only of a two-digit (or three-digit) number with digits about 2 cm tall. The disturbance added a positive or negative increment to the number, as did the mouse movement, and the subject used the mouse to keep the number as close to "50" as possible. In this task, both cursor and marker are conceptual numeric values, rather than being physical locations. The cursor is the value of the number represented by the digits on the screen, and the marker a memory for the value "50."

Each task was run with three different kinds of disturbance, two of which varied smoothly, and the third in jumps. Each kind was run at two difficulty levels. With six tasks and six combinations of disturbance type and difficulty, there were 36 distinct task-disturbance combinations, 6 of which were run during each individual hour of the experiment, in two group of three. Each group of three had one of each kind of disturbance, and each group of six had one of each task type and one of each disturbance-difficulty

---

[1]The studies reported here were conceived and programmed by W. T. Powers, whose Perceptual Control Theory (Powers, 1973) provides the conceptual background for the tasks and the analyses. Powers was also responsible for much of the analysis, and provided valuable assistance by e-mail, but generously declined participation in the authorship of this paper. The author assumes responsibility for all errors and omissions.

combination. Over each 6-hour experimental block, all 36 task-disturbance combinations were run once. The results reported here concern only 30 of these, ignoring the task with two markers and two cursors.

Conceptual Background

The tracking tasks were designed in the context of Perceptual Control Theory (PCT; Powers, 1973). PCT is based on the idea that people try to bring various environmental conditions to desired (possibly dynamically changing) states, but that the only access anyone has to an environmental condition is through the senses. Accordingly, it is the perception of an environmental condition rather than the condition itself that is brought to the desired state, or "controlled." In the case of the present experiment, the desired environmental condition is that the cursor match the marker, and the "controlled perception" is that of the deviation between the cursor and the marker. It is assumed that the subject wants the cursor to match the marker (though in the actual experiment, there were clearly occasions late in the sleep deprived period when this was not true).

The "control" in "PCT" is precisely that of engineered control systems, and all the tools that are applied to artificial control systems are also be applied to living ones. The "canonical circuit diagram" of an elementary control unit is shown in Figure 1, and a variant used in the actual analysis is shown in Figure 2.

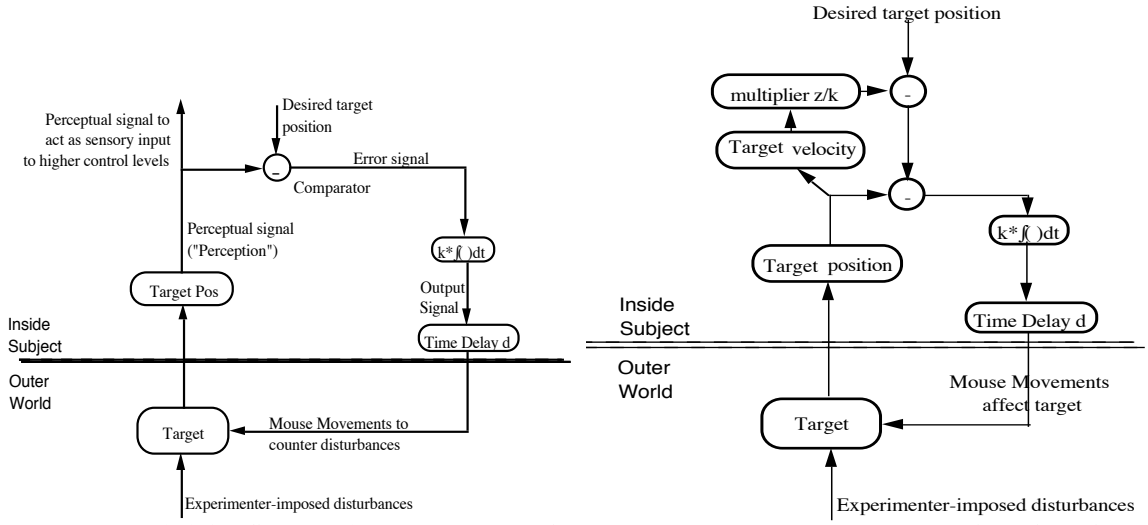

Figure 1.(left) Canonical control unit with two parameters, k and d. Figure 2.(right) Three-parameter control loop used to fit the experimental data:,using the target velocity to affect the momentary reference level for the target.

There are two inputs, the desired "reference" value of the perceptual signal and the sensory input from the environment. There are two outputs, the perceptual signal, which can act as a sensory input to other control systems, and an output signal that affects the environment by some means that may impose some delay. We will not consider the up-going perceptual signal any further, except as shown in Figure 2, and we will assume that the output delay incorporates all the delay around the loop. This latter assumption is clearly false, but is mathematically equivalent to introducing delays at each stage of processing.

The output signal affects the environmental variable that gives rise to the perceptual signal. For example, in the present study, the output signal affects the movements of the mouse, which result in movements of the cursor on the screen, thereby affecting the relation between cursor and marker that the subject perceives and attempts to maintain at its desired value. If the result is to bring the perceptual signal nearer to its reference value, the loop has negative feedback, and the perceptual signal is being controlled more or less effectively. If the output moves the perceptual signal away from its reference value, the loop has positive feedback; the error will increase, further increasing the output, to a degree limited only by saturation somewhere in the loop. Living systems use loops with negative feedback; positive feedback implies loss of control.

The output signal is generated by a function that acts on the error signal, which is the difference between the intended and actual value of the perceptual signal. In the canonical control loop of Figure 1, the output function is shown as a pure integrator with a gain factor "k", which has the dimension of sec^{-1}. Other functions are possible, but the pure integrator has several merits, not the least of which is the fact that

using it produces a model that often correlates over 0.99 with the performance of trained and motivated human subjects in a tracking task. In Figure 1, the "target" is taken to that aspect of the environment that corresponds to the controlled perception. In the experiment, the "target" would ordinarily be the relationship between the cursor and the marker; the reference value for the intended perception would be, for example, for the cursor to be aligned with the target, or for the displayed number to be "50."

Despite the high correlation often found between human performance and simulations based on the canonical model, there often remain discrepancies, some of which can be reduced substantially by introducing a second half-loop involving the control of the perceived target velocity (rate of change of the relationship between cursor and marker) as shown in Figure 2. This is the model that was used to analyze the experimental data.

The second loop can be considered as a "predictor" loop, which augments or reduces the output signal depending on whether the error is increasing or decreasing, by using the perception of the derivative to modify the reference value for the target relation between cursor and marker according to the rate at which that relation is changing.[2] Ideally, the perceived target location should be unchanging and at its externally provided reference value. In simulating the performance of the human subjects in the experiment, the relative degree to which subjects relied on the predictor loop was affected by the drugs.

Data and analysis

The raw data consisted of the precomputed disturbance waveform that was used to influence the target, together with the actual cursor position sampled at 60 Hz over the 50 seconds of the tracking run. An "error" waveform can be derived by comparing the cursor position with what it should have been at each sample moment if the "target" relationship between cursor and marker had been held to its intended value. The mean-square error provides a theory-independent view of the results, but is of secondary interest for the present report. Of greater interest is the fitting of the control model to the peculiarities of the individual tracks, as the sleep deprivation period progressed under the different drug conditions.

To fit the model for a particular trial, a computer simulation was run, using the same sequence of disturbance values, comparing the output values with the actual cursor values produced by the human subject. The three parameter values were optimized by a simple gradient-search technique based on the sum of squared differences between actual and simulated values, and the resulting correlation between the mouse and the model output was taken as a measure of the goodness of fit. For most of the tracks, the model of Figure 2 fitted the actual mouse movements reasonably well, many of the correlations being above 0.95 and about 1/4 being above 0.99.

As the sleep deprivation period progressed, subjects sometimes would seem to fall asleep for one or more seconds, as indicated by their failure to move the mouse. These periods are called "microsleeps." Some subjects described hallucinations which may have affected their tracking; for example, the pendulum was described as swinging into and out of the screen rather than left to right. And on other occasions the subject seemed to oscillate the mouse with no regard to the screen. The more blatant of these instances were removed from the data before attempts were made to fit the model, but undoubtedly less obvious instances of related phenomena remain and affect the quality of the fit during the period of severe sleep deprivation. Despite these problems, only occasional tracks yielded data that could not be well fit by the model.

Results

For the purposes of this report, we emphasize the effects of the test drugs on the fitted model parameters, and ignore all differences among the tasks. All values are normalized to the means of the values over the first four six-hour blocks, one on the practice day and three, ending at 02:00 the first night, on the experimental days. The first drug dose was administered two hours before the end of the fourth block. The effect on the normalization of including these two hours, if any, is to reduce the apparent effects of a drug.

The main results are shown in Figures 3 to 6. Figure 3 shows the effects of the different drugs on position gain or "insistence on precision of tracking" (k in Figure 1 and 2), Figure 4 the effect on delay (d in Figures 1 and 2), and Figure 5 the effect on predictor gain or "reliance on prediction" (z in Figure 2). The data during microsleep periods was excluded from the model fits that are shown in Figures 3 to 5. The effects on the number of microsleeps per 50 second run is shown in Figure 6.

---

[2]This relationship was pointed out by R. S. Marken in a message on the CSG-L mailing list April 13, 1995. (CSG-L@-vmd.cso.uiuc.edu)

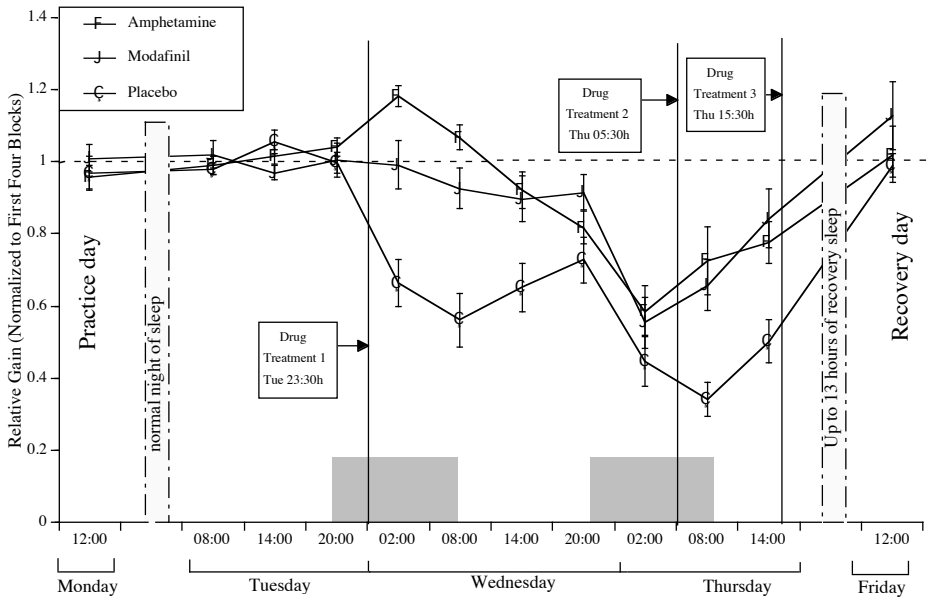

Figure 3. The effects of the three drugs on the position gain (insistence on precision) of the best fit model parameters over the period of sleep deprivation. All curves normalized to unity over the average of the first four blocks.

Figure 3 shows a pattern for the Placebo group that is also seen in some other parts of the larger study (Pigeau et al. 1995), a precipitous drop of 40% during the first night, some recovery during the second day, and a further precipitous drop by 40% of the daytime value during the second night with again some recovery during the next day. Of the 11 subjects in this group, only one showed a substantially different pattern. That subject showed no decline, and perhaps even an improvement, over time up to the start of the second night. Modafinil mitigated or eliminated the effect of sleep loss until the drug wore off after about 24 hours, whereas amphetamine improved the subjects' insistence on precision for 6-12 hours. The second dose of each drug improved performance relative to that before the dose, whereas during the same period, the performance of the placebo group continued to decline.

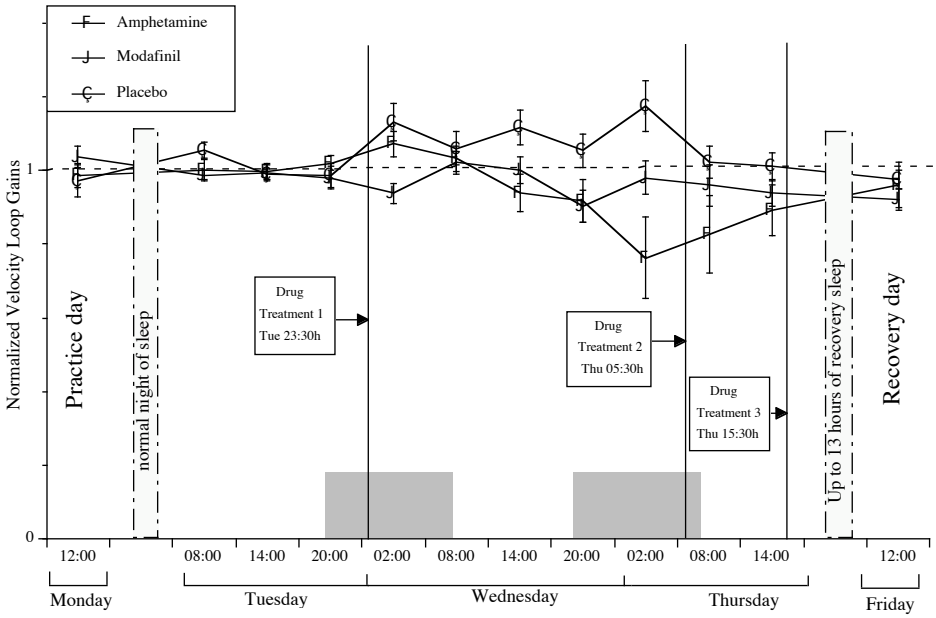

Figure 4. The effect of the three drugs on the delay parameter of the best fitting model, over the course of sleep deprivation. All data normalized to the mean of the first four blocks.

Figure 4 shows that there is very little effect of sleep deprivation on loop delay, though there may be a small shift to longer delays during and after the first night, until the end of the second night. These changes should not be considered reliable, in that several subjects did not show the same pattern. For the same reason any apparent drug effects must be considered with caution.

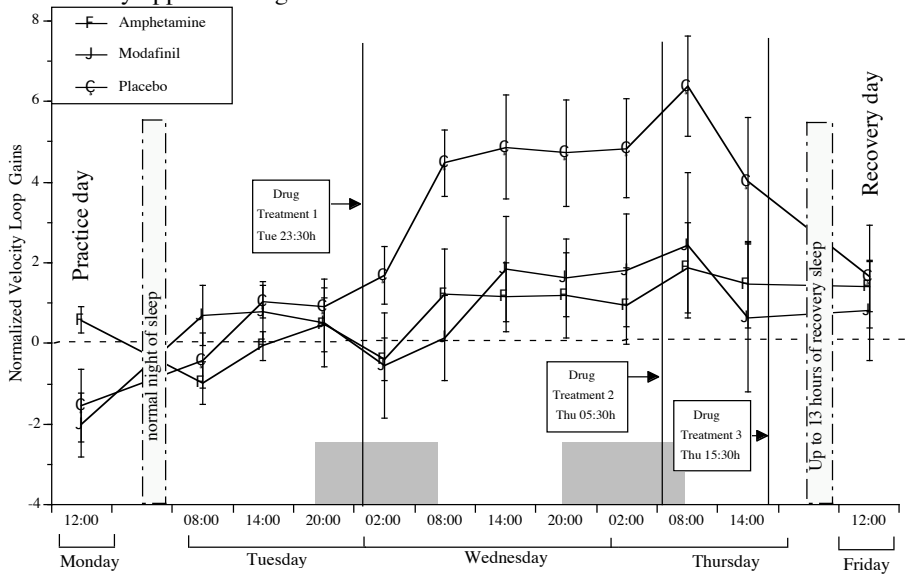

Figure 5. The effect of the three drugs on the reliance on prediction in the best fit model parameter (z in Figure 2). All data normalized to the mean of the first four blocks.

Figure 5 shows for the Placebo group a rapid rise during the first night in reliance on predicted rather than observed target position (one interpretation of increasing gain of the velocity loop, z in Figure 2). There is no recovery during the second day, but a further rise during the second night, with recovery of that second rise during the following day. The effect is diminished or eliminated by both drugs, but there is no difference in this respect between the two drugs.

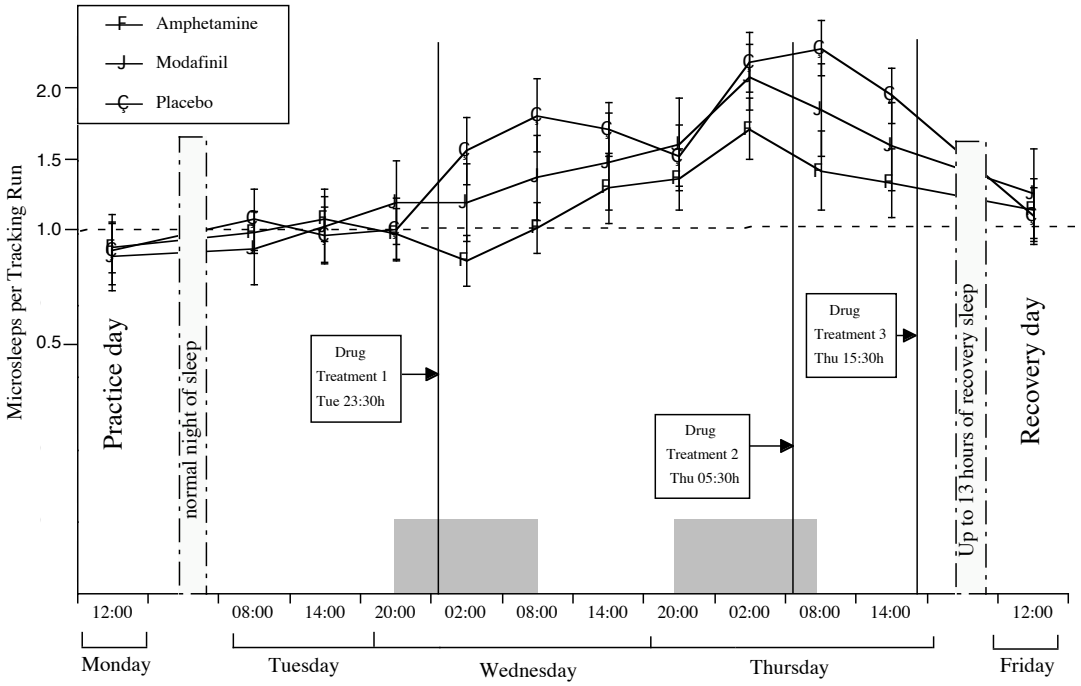

Figure 6. Effects of the three drugs on the average number of microsleep periods per tracking run.

Figure 6 shows the effects of the drugs on the average number of microsleeps per 50 second run. As with all the graphs, the data are normalized to the mean of the first four blocks. The data correspond fairly well to the results for insistence on precision (Figure 3). But unlike Figure 3, amphetamine seems to be a little better than modafinil at reducing the tendency to microsleep.

Overall, then, the effect of sleep deprivation seems to be to reduce the care and precision of the tracking (position loop gain) and to compensate by putting more reliance on predicting where the target is going and moving the mouse accordingly.

The most prominent effect of the drugs seems to be that they maintain the care and precision attempted by the subjects, and amphetamine even increases it, while both drugs reduce or eliminate a tendency for sleep deprived subjects to increase their reliance on what they expect to happen as opposed to what is actually happening at the moment.

Apart from the fitting of the model, there are questions relating to the way the model does not fit, the most prominent of these being the tendency of sleep deprived subjects to engage in what might be called "microsleep," manifest in a cessation of mouse movement. In the analyses, a microsleep was defined as any period in which the mouse did not move for at least 60 samples (1 sec).

Microsleeps happened throughout the study, including during the practice and first trial day and the recovery day, but they were more numerous and tended to be longer as the period of sleep deprivation continued Each group showed a pattern very like their pattern for position gain (insistence on precision) in the model fit, except that the modafinil group seemed to be intermediate between the placebo and amphetamine groups throughout.

Summary

In a variety of tasks with very different kinds of display, subjects deprived of sleep were asked to maintain a fixed relationship between a cursor and a marker, when one or the other was being disturbed according to a precomputed waveform. The actual movements that they produced were simulated by a three-parameter control loop that incorporated prediction of the changes of the target relationship. In casual terms, sleep loss affected mainly the insistence of the subjects on precise control and their tendency to use prediction of the future position rather than observation of the present error. It also affected the tendency of subjects to fall into "microsleep," defined as a period of one or more seconds with no activity when activity might normally be expected.

The effects of sleep deprivation were reduced or eliminated by amphetamine or modafinil. Instead of the reduction in "insistence on precision," modafinil subjects maintained their insistence essentially unchanged for about 24 hours after the first dose, and recovered somewhat from the second-night decline after the second drug dose. Amphetamine subjects showed an increase rather than a decline in "insistence" after the first dose, but the effect was short-lived, so that 24 hours later their performance was between that of the placebo and of the modafinil subjects.

Both drugs nearly eliminated the change in reliance on prediction shown by the placebo subjects. Even when their insistence on precision based on the current error dropped during the second night, they did not compensate by increasing their reliance on prediction, as the placebo subjects did. Both drugs reduced the tendency to microsleep, amphetamine perhaps more so than modafinil.

One finding that should be of importance in military sustained operations is the relatively increased reliance by the placebo subjects on prediction as opposed to direct observation (Figure 3). During and after the first night, the placebo subjects based their tracking actions increasingly on what they believed to be happening rather than on their observation of what was actually happening. Both drugs more or less eliminated this tendency.

References

Pigeau , R., Naitoh, P., Buguet, A., McCann, C., Baranski, J., Taylor, M., Thomson, M. & Mack, I. (In Press). Modafinil, d-Amphetamine and Placebo during 64 hours of sustained mental work. I: Effects on mood, fatigue, cognitive performance and body temperature. *Journal of Sleep Research*.

Powers, W. T. (1973). *Behavior: the control of perception*. Chicago: Aldine.