The Effects of Caffeine, Dextroamphetamine, and Modafinil on Humor Appreciation During Sleep Deprivation

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Study Objectives: Sleep loss consistently impairs performance on measures of alertness, vigilance, and response speed, but its effects on higher-order executive functions are not well delineated. Similarly, whereas deficits in arousal and vigilance can be temporarily countered by the use of several different stimulant medications, it is not clear how these compounds affect complex cognitive processes in sleep-deprived individuals.

Design: We evaluated the effects of double-blind administration of 3 stimulant medications or placebo on the ability to appreciate humor in visual (cartoons) or verbal (headlines) stimuli presented on a computer screen following 49.5 hours of sleep deprivation.

Setting: In-residence sleep-laboratory facility at the Walter Reed Army Institute of Research.

Participants: Fifty-four healthy adults (29 men, 24 women), ranging in age from 18 to 36 years.

Interventions: Each participant was randomly assigned to 1 of 3 stimulant medication groups, including caffeine, 600 mg, n = 12; modafinil, 400 mg, n = 11; dextroamphetamine, 20 mg, n = 16; or placebo, n = 14.

Measurements and Results: Humor appreciation for cartoon stimuli was enhanced by modafinil relative to both placebo and caffeine, but there was no effect of any stimulant medication on the appreciation of verbal humor during sleep loss. In contrast, all 3 stimulants improved psychomotor response speed, whereas only caffeine and dextroamphetamine improved ratings of subjective sleepiness.

Conclusions: Findings suggest that, despite similar alerting and vigilance-promoting effects, these 3 compounds have significantly different effects on those highly complex cognitive abilities mediated by the prefrontal cortex.

Keywords: Sleep deprivation, modafinil, performance, caffeine, dextroamphetamine, cognitive function, humor appreciation

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INTRODUCTION

SLEEP IS AN ESSENTIAL BIOLOGIC PROCESS THAT REVERSES THE DECREMENTS IN COGNITIVE FUNCTIONING THAT INVARIABLY OCCUR AS A RESULT OF extended wakefulness. In humans, the importance of sleep for normal functioning becomes increasingly apparent after 18 to 24 hours of continuous wakefulness as decrements in basic cognitive functions including alertness, attention, vigilance, and simple response time begin to emerge.[1-4] Without adequate sleep, some types of higher-order cognitive abilities also show deficits. For instance, sleep deprivation impairs decision making,[5] divergent thinking, mental flexibility,[6,7] and production of novel responses.[8] These types of complex cognitive abilities are believed to be mediated predominantly by the prefrontal cortex, a region of the brain important for executive functions, including attention, planning, problem solving, and decision making.[9] There is also evidence that the cognitive processes mediated by the prefrontal cortex may be particularly vulnerable to the detrimental effects of sleep loss.[5,6,8,10-12] Findings from functional neuroimaging research have helped clarify some of the underlying neurobiological mechanisms whereby sleep deprivation may exert detrimental effects on executive functions. For instance, a study using positron emission tomography showed decreased glucose metabolism within the prefrontal cortex following 24 hours of sleep deprivation, and these decreases correlated with decrements on several tests of cognitive abilities.[13] Furthermore, when a sleep-deprived individual attempts to solve a problem or engage in a cognitively demanding task, the brain appears to recruit additional prefrontal regions in order to maintain adequate performance.[14-16] Together, existing data converge to suggest that the prefrontal cortex and its associated cognitive functions are particularly vulnerable to sleep loss.

Considerable research effort has been devoted to determining the efficacy of stimulants for maintaining alertness.[17-24] Caffeine, modafinil, and dextroamphetamine are 3 of the most extensively evaluated stimulants for sustaining alertness and cognitive performance.[25] These 3 stimulants have been shown to be highly effective for restoring lower-order cognitive functions (e.g., vigilance, attention, reaction time) during sleep deprivation.[19,21,23,26,27] However, their relative effectiveness for countering the detrimental effects of sleep loss on complex executive functions is relatively unexplored. Limited data suggest that modafinil may have some effectiveness in enhancing executive functions in sleep-deprived volunteers,[28] but there have, as yet, been no comparable studies evaluating the relative effectiveness of stimulants on higher-order cognitive processes.

Among the most complex forms of higher cognition is the ability to appreciate humor.[29] This capacity appears to be uniquely human and requires a host of complex integrative processes, including attention, working memory, mental abstraction, and divergent thinking, as well as the ability to link these cognitive processes with an affective state of mirth or amusement.[30] While neuropsy-

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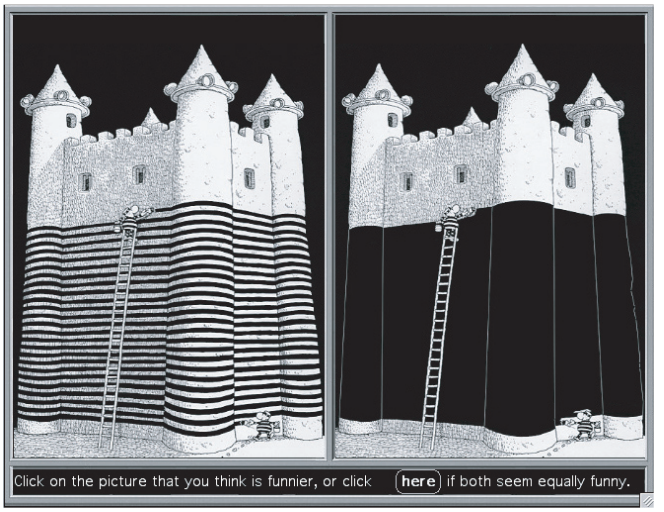

Figure 1—An example of a visual cartoon item from the University of Pennsylvania Humor Appreciation Test. Participants viewed pairs of cartoons or news headlines that were similar in most respects, but which differed in a subtle but critical element that usually added an element of humor to the situation. Participants were asked to decide which cartoon or headline was "funnier" or whether the two options were equally funny (image reprinted with permission of Dr. Ruben Gur).

chological and functional neuroimaging studies have suggested that humor appreciation involves the interaction of several cortical and subcortical regions, the ventromedial prefrontal region appears to be most associated with the cognitive-affective integration of humorous information,[29-31] and functional activity within this region correlates positively with subjective assessments of a joke's amusement value.[32] Although the prefrontal regions most associated with humor appreciation appear to overlap with those areas that show significantly decreased metabolic activity during sleep deprivation, no studies have examined the effect of sleep loss and stimulant medications on the ability to appreciate humor. In the present study, we evaluated the effects of caffeine, modafinil, dextroamphetamine, or placebo on humor appreciation in volunteers following 49 hours of sleep deprivation.

METHODS

Participants

Fifty-four (29 male, 24 female) healthy, predominantly right-handed [Edinburgh Handedness Inventory—10 item form; mean = +53.6, SD = 49.3;[33]], adult volunteers ranging in age from 18 to 36 years (mean = 23.5, SD = 4.0) remained awake for 66 hours as part of a larger study of the effects of sleep deprivation on cognitive performance. Preliminary data from other aspects of that study have been presented elsewhere.[34] The education level of the participants ranged from 11 to 18 years, and all volunteers were within the normal range of intellectual functioning on the Wechsler Abbreviated Scale of Intelligence (mean full-scale IQ = 106.2, SD = 12.1; range = 84-129). Participants were excluded if they had any history of psychiatric, neurologic, or other significant medical problems that could pose a health risk during the course of the investigation, as determined by the study physician. Participants were also excluded if they reported daily caffeine consumption above 400 mg per day, and/or used tobacco products within the past 36 months. In fact, these participants were all low to moderate habitual users of caffeine, with a mean estimated daily intake of 51.7 mg (SD = 64.3; range = 0 mg-243 mg) based on self-reported use of coffee, tea, soft drinks, and other caffeine-containing products. There were also no significant differences in average daily caffeine intake across the 4 experimental groups ($F_{3,53}$ = 0.94, p = .43). Participants were instructed to abstain from alcohol, stimulants, and other psychoactive substances for 48 hours prior to arrival at the laboratory, and compliance was monitored by regular urine drug screening conducted at intake and every 24 hours throughout the study. Following a thorough description of the study and procedures, all participants provided written informed consent. This study was approved by the Walter Reed Army Institute of Research Human Use Review Committee and the U. S. Army Human Subjects Research Review Board.

Stimulant Medications

Participants were randomly assigned to 1 of 4 drug groups: placebo (n = 14), caffeine 600 mg (n = 12), modafinil 400 mg (n = 11), or dextroamphetamine 20 mg (n = 16) in a double-blind manner. These specific dosages were chosen based on previous research from our own laboratory showing that they are essentially equivalent for restoring alertness and cognitive performance during sleep deprivation.[23,35,36] The study medications or placebo were administered in identical opaque capsules prepared by the Walter Reed Army Medical Center Pharmacy. All medications were administered 5.5 hours prior to the Humor Appreciation Test. According to available literature, the 3 medications differ in their respective time to peak plasma concentrations and elimination half lives. Specifically, caffeine has been suggested to have a highly variable half life, ranging from 1.5 to 9 hours,[37,38] with most reports averaging between about 3 to 5 hours, depending on the population studied.[39,40] According to the product monograph for Provigil, the average half life for modafinil is about 15 hours. The product monograph for dextroamphetamine (Dexedrine) states that the average half life of that medication is approximately 12 hours.

Test Materials

University of Pennsylvania Humor Appreciation Test

The Humor Appreciation Test is one of the many available tests within the University of Pennsylvania Computerized Neuropsychological Battery[41-43] and can be obtained from the University of Pennsylvania Department of Psychiatry website at: (http://www.med.upenn.edu/bbl/pubs/downloads/nptasks_desc.html). The Humor Appreciation Test presented participants with 40 pairs of stimuli in a randomized order. Each pair was presented as a single unit on the computer screen at the same time. Twenty of the scenarios were visual in nature (i.e., they presented 2 nearly identical nonverbal cartoons), and 20 of the scenarios were verbal in nature (i.e., they present 2 nearly identical fictitious newspaper headlines). In each pair of nearly identical stimuli, 1 scenario differed subtly from its counterpart so as to make it funny or humorous, while the other nearly identical picture or statement was not designed to be funny. An example of a visual cartoon item is shown in Figure 1. An example of a verbal headline item is as follows: Headline 1—"Veterinarian Investigates Failed Panda Mating;" Headline 2—"Panda Mating Fails; Veterinarian Takes Over." Participants made a forced

choice for each pair, deciding whether the stimulus on the right was funnier, the one on the left was funnier, or whether the 2 stimuli were equally funny.

Psychomotor Vigilance Testing

Subjects also completed a variation of the psychomotor vigilance test (PVT) at regular intervals (every 2 hours) throughout the study. The present variation of the PVT was administered on a palm-held computer and assessed simple reaction time/psychomotor speed.[44] It should be noted that the current palm-based version differs in timing and appearance from the standard 10-minute version of the PVT that is typically administered on a desktop computer or self-contained hand-held device.[45] The duration of the palm-based PVT was 5 minutes, during which time the participants were required to watch the screen and press a response key with their dominant hand each time a target stimulus appeared. The time delay between each stimulus presentation was pseudorandomly assigned across trials so that each of the response intervals was presented an equal number of times throughout the task.[44]

Stanford Sleepiness Scale

The Stanford Sleepiness Scale was administered in conjunction with the PVT at regular intervals throughout the study. The scale presents participants with a series of statements indicative of increasing subjective sleepiness.[46] Scale items range from a score of 1 ("Feeling active, vital, alert or wide awake") to 7 ("No longer fighting sleep, sleep onset soon, having dream-like thoughts"). Participants simply select the statement that most closely describes their current subjective state of alertness.

Facilities

Participants were studied in groups of 4, and all procedures were conducted in-residence at the sleep laboratories of Walter Reed Army Institute of Research. Each participant was tested individually by a trained psychometric technician in a noise-insulated private room that contained a bed and computer work station. The temperature in the sleep laboratory was maintained at 73ºF (22.7ºC), with humidity controlled through a well-ventilated, centralized air-conditioning system. Lighting within the laboratory testing area was maintained at approximately 500 lux, and ambient noise was set to 65 dB using white-noise generators. Participants were allowed to eat only food provided by the laboratory. Although a wide variety of foods were available, choices were controlled to maintain uniformity of nutritional intake and ensure that no caffeine or other stimulants were available in the diet.

Procedure

The participants arrived at the sleep laboratory on the evening of Day 1. At that time, the volunteers were fitted with electroencephalographic electrodes for continuous ambulatory monitoring, provided a urine sample, and were given a demonstration of the PVT and Stanford Sleepiness Scales. Each volunteer was administered the Wechsler Abbreviated Scale of Intelligence[47] by a trained psychometrician. Participants retired to their private bedrooms at 11:00 PM and were provided with 8 hours time in bed. On the morning of Day 2, volunteers were awakened at 7:00 AM and remained awake in the laboratory for the next 66 hours, passing time watching television, playing games, and taking occasional scheduled cognitive tests. At 2:50 AM-3:00 AM on Day 3 (after 44 hours awake), participants ingested an oral dose of dextroamphetamine 20 mg, caffeine 600 mg, modafinil 400 mg, or placebo in a double-blind fashion. Participants then engaged in a variety of cognitive tasks over the next several hours. From 8:20 to 8:40 AM on Day 3 (following 49.5 hours awake), participants completed the PVT, Stanford Sleepiness Scale, and the Humor Appreciation Test. This time period was deliberately chosen to maximize potential deficits associated with homeostatic sleep and circadian rhythm drives in order to provide the most effective test of the stimulant medications.

Humor Appreciation Test scores were tabulated by determining the number correct for the 20 verbal items and the 20 cartoon items separately, with higher scores indicating better performance on each scale. These raw scores were then compared to normative data for 17 non–sleep-deprived healthy normal volunteers provided by the test's developer (Ruben C. Gur, personal communication, August 29, 2005). Based on the normative data, the raw scores were transformed into standard T-scores, with a mean of 50 and a standard deviation of 10 [i.e., T = [((raw score – normative mean)/normative SD) × 10)+50]. Thus, a score of about 50 is comparable to the average score of the non–sleep-deprived controls. Scores falling below a T-score of 40 (i.e., -1 SD below the mean) can be considered as "below average." Scores for the PVT were calculated as response speed (1/reaction time × 1000). These response speed scores were then normalized as a percentage of the mean speed performance for the 8 PVT administrations on the baseline day (8:20 AM to 10:20 PM on Day 2). Higher scores represent better performance (i.e., faster response speed). Scores on the Stanford Sleepiness Scale represent subjective sleepiness and range from "1" (wide awake) to "7" (sleep onset soon), so higher scores represent greater subjective sleepiness. Scores on these 4 tasks (Visual Humor, Verbal Humor, PVT, Stanford Sleepiness Scale) were entered as dependent variables into a multivariate analysis of covariance with drug group (dextroamphetamine 20 mg, caffeine 600 mg, modafinil 400 mg, or placebo) as a between-groups variable. Several covariates were also included to control for factors that have been related to the ability to appreciate humor. Because intellectual functioning can affect the capacity to appreciate humor,[48-50] we included Verbal IQ and Performance IQ as separate covariates to correspond to the verbal and visual humor conditions. Level of education has also been associated with humor appreciation[51] and was, therefore, included as a covariate. Finally, humor appreciation has been shown to be related to lateralized brain function.[52-55] Hence, we included the Laterality Score from the Edinburgh Handedness Inventory as a covariate as well.

RESULTS

After covarying for the effects of verbal and performance IQ, education, and laterality, the omnibus multivariate analysis of covariance revealed that there were significant differences among the drug groups on the 4 dependent variables ($F_{12,132} = 1.89$, $p = .04$). Univariate analyses of covariance, utilizing the same covariates, were undertaken for each dependent variable.

Humor Appreciation Test

Visual Humor

With intelligence, education, and laterality statistically con-

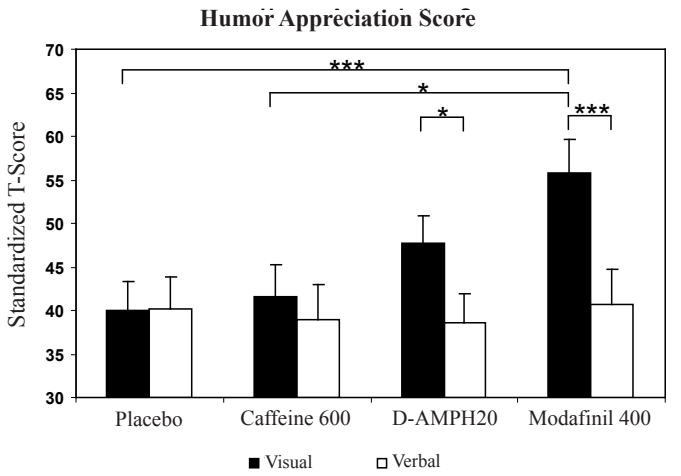

Figure 2—Mean standardized T-scores for visual and verbal items of the Humor Appreciation Test for each drug condition following 49.5 hours of sleep deprivation. T-scores were derived by comparing the raw score performance to normative data for each task. The average T score for the normative group (healthy, non–sleep-deprived) is 50 with a standard deviation of 10 points. Scores below 40 reflect below average performance and those above 60 reflect above average performance on the Humor Appreciation Test. Error bars represent 1 standard error (SEM). The placebo group generally performed below average. Modafinil significantly enhanced performance on visual humor items relative to placebo and caffeine. Modafinil and dextroamphetamine (D-AMPH) also enhanced performance on visual humor items relative to verbal humor items. In contrast, none of the drugs enhanced verbal humor performance beyond placebo. *p< .05, ***p<.005.

trolled, there was a significant effect of stimulant medications on the percentage of correctly identified items on the visual cartoon portion of the Humor Appreciation Test ($F_{3,52}$ = 3.67, p = .019; see Figure 2). The modafinil 400-mg group (mean = 55.86, SD = 12.65) demonstrated significantly better performance on the cartoon items than both the placebo group (mean = 39.97, SD = 12.62, p = .004) and the caffeine 600 mg group (mean = 41.58, SD = 12.62, p = .011). None of the other groups differed significantly.

Verbal Humor

As evident in Figure 2, once the covariates were statistically controlled, there were no significant differences among any of the medication groups on the verbal headline portion of the Humor Appreciation Test ($F_{3,52}$ = 0.69, p = .98). Within each medication group, we also compared volunteer performance on the Visual and Verbal Humor items. For participants given modafinil 400 mg, Visual Humor (mean = 47.94) scores were significantly higher than Verbal Humor (mean = 39.09) scores (p < .001; see Figure 2). Similarly, for participants receiving dextroamphetamine 20 mg, Visual Humor (mean = 55.06) performance was also significantly higher than Verbal Humor (mean = 39.13) performance (p = .013).

Psychomotor Vigilance Test

Response speed scores were transformed to reflect each participant's performance as a percentage of their baseline performance from the first day of the study. As evident in Figure 3, after con-

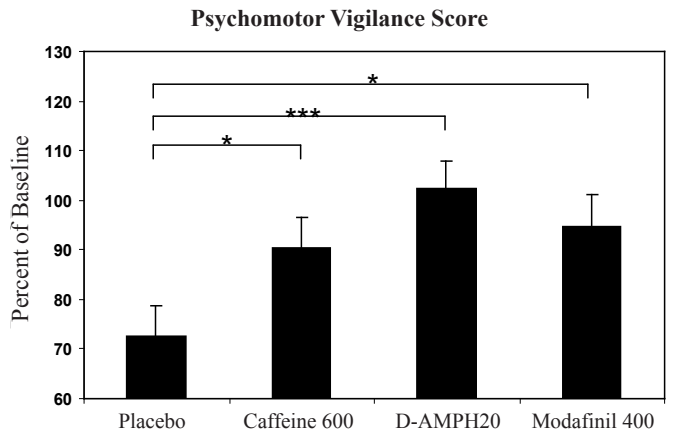

Figure 3—Mean performance on the palm-based psychomotor vigilance test (PVT) following 49.5 hours of sleep deprivation (expressed as a percentage of performance relative to the baseline day). Higher scores equate to faster response speed. Each of the 3 stimulants produced faster response speed scores on the PVT relative to placebo. None of the 3 stimulants differed from one another. *p< .05, ***p<.005. D-AMPH refers to dextroamphetamine.

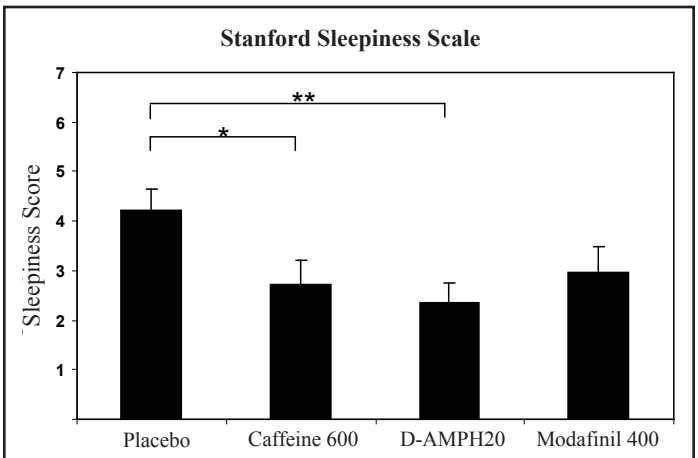

Figure 4—Mean scores on the Stanford Sleepiness Scale following 49.5 hours of sleep deprivation. Scores range from zero to seven. Higher scores equate to greater subjective sleepiness. Relative to placebo, both dextroamphetamine (D-AMPH) and caffeine were associated with reduced sleepiness scores, whereas sleepiness ratings for modafinil did not differ from placebo. *p< .05, **p<.01.

trolling for intelligence, education, and laterality, there was a significant effect of the stimulant drugs on PVT performance ($F_{3,52}$ = 4.54, p = .007). Overall, all 3 stimulants resulted in significantly faster response speeds relative to placebo (mean = 72.7%, SD = 22.10%), with dextroamphetamine, 20 mg, producing the fastest performance (mean = 102.4%, SD = 21.74%, p = .001) followed by modafinil, 400 mg, (mean = 94.6%, SD = 22.15%, p = .02) and caffeine, 600 mg, (mean = 90.3%, SD = 22.10%, p = .05). None of the 3 stimulant groups differed from each other in PVT performance, however.

Stanford Sleepiness Scale

Figure 4 shows that there was also a significant main effect of stimulant drug on subjective ratings of sleepiness after accounting for the variance associated with the covariates ($F_{3,52}$ = 3.23,

p = .03). Relative to the sleepiness scores of the placebo group (mean = 4.20, SD = 1.66), those participants receiving dextroamphetamine 20 mg reported significantly lower subjective sleepiness (mean = 2.36, SD = 1.63, p = .004). Similarly, caffeine 600 mg (mean = 2.73, SD = 1.66) also yielded significantly lower subjective ratings of sleepiness compared with placebo (p = .03). In contrast, the sleepiness ratings of the modafinil group (mean = 2.97, SD = 1.66) did not differ significantly from that of placebo (p = .077). Stanford Sleepiness Scale scores did not differ significantly among the 3 stimulant groups.

DISCUSSION

Following 49.5 hours of continuous wakefulness, the means for both verbal and visual humor within the placebo group were essentially 1 standard deviation below the average performance of healthy, normal, non–sleep-deprived individuals, suggesting that sleep loss adversely affects the capacity to appreciate humor. Interestingly, administration of modafinil, 400 mg, significantly enhanced the ability to detect humor in cartoons, relative to placebo or caffeine 600 mg, but did not enhance performance significantly beyond that of dextroamphetamine 20 mg. Both modafinil and dextroamphetamine, however, were more effective at improving the appreciation of visual humor than verbal humor. In fact, the ability to discriminate humorous from nonhumorous newspaper headlines was not enhanced by any of the stimulant medications relative to placebo. While the 3 stimulants showed differential enhancement of the appreciation of visual humor, all 3 were comparably effective at maintaining psychomotor vigilance performance relative to placebo. These findings suggest that mere enhancement of alertness and vigilance was not itself sufficient to improve the complex cognitive processes involved in humor appreciation. Furthermore, as evidenced by the lack of an effect of modafinil on Stanford Sleepiness Scale scores relative to placebo, maintenance of subjective alertness was also neither necessary nor sufficient to produce improvement in the appreciation of humor. Apparently the enhancing effect of modafinil on humor appreciation involves more than simple stimulation of alertness and arousal systems.

The ability to detect and appreciate humor represents an extraordinarily complex integrative process within the human brain, involving many of the most well-developed executive functions. In fact, humor appreciation has been suggested to be among the "highest and most evolved human cognitive functions."[29] While there are likely to be specific subsystems, such as linguistic and visuospatial processing networks that may be particularly important for comprehending different types of humor (e.g., verbal versus visually presented jokes),[29] the higher-order cognitive skills involved in appreciating an idea, scene, or story as humorous are believed to be mediated predominantly by the multimodal association regions of the prefrontal cortex, particularly within the right ventromedial regions.[29-31] Humor appreciation requires the confluence of multiple cognitive and affective processes, including simple attention, working memory, mental flexibility, set shifting, long-term memory retrieval, verbal abstraction, and the integration of these cognitive components with affective and somatic state information[30]—capacities that are unique to the heteromodal association regions of the prefrontal cortex.[56] Recent neuroimaging research has demonstrated that functional activity within the ventromedial prefrontal cortex during comprehension of a joke is positively correlated with the perceived humor or funniness of the joke.[32] Patients with damage to this region of the brain typically have deficits in complex social-emotional situations, such as in the ability to identify sarcasm in verbal comments,[57] to detect irony and social faux pas,[58] and to feel empathy for the plight of another person.[59,60]

The prefrontal cortex also appears to be particularly susceptible to the detrimental effects of sleep loss.[13,61] Interestingly, as little as 24 hours of total sleep deprivation is associated with significant reductions in regional cerebral metabolism within heteromodal association regions, including the prefrontal and parietal cortexes.[13] Sleep deprivation also impairs a host of executive functions believed to be mediated by the prefrontal cortex, including problem solving and divergent thinking,[7,62] supervisory control,[12] cognitive set shifting,[63] verbal creativity, flexibility, and inhibition.[8] Although humor appreciation is a highly complex cognitive ability involving prefrontal brain regions, we are not aware of any other research that has studied the effects of sleep loss or stimulant medications on this capacity. Participants who received placebo generally performed below the average range, whereas those receiving modafinil scored well within the average to high average range on the visual humor task, despite 2 nights without sleep. Furthermore, the fact that caffeine and dextroamphetamine increased subjective and objective alertness but failed to significantly improve performance on humor appreciation suggests that modafinil may have influenced additional neural systems not directly enhanced by these other 2 stimulants.

Modafinil has been shown to be effective at improving alertness[64] and performance on a variety of cognitive tasks, including simple vigilance and reaction time, working memory, and logical and grammatical reasoning,[21,65,66] as well as higher-order executive function tasks, including verbal fluency, mental flexibility, and creativity.[28] Few studies have specifically explored the neuroanatomic sites of action for modafinil in humans, but some recent neuroimaging evidence suggests that this compound may influence activity within the anterior cingulate gyrus, a cortical region adjacent to the medial prefrontal cortex.[67] Thus, the enhanced ability to detect humor by the modafinil group relative to placebo may be related to drug-induced alterations in activity within the prefrontal cortex and adjacent corticolimbic regions.

While the present data suggest that modafinil and, perhaps to some extent, dextroamphetamine may provide significant benefits in terms of simple alertness and vigilance as well as higher-order cognitive-affective processes such as the ability to appreciate humor in nonverbal cartoons, the present data are limited by several methodologic issues. First, the different elimination half lives of the 3 medications make it difficult to interpret data in a cross-sectional design such as that employed in the present study. It is quite plausible that the earlier peak concentration and more-rapid elimination of caffeine may have led to the poorer performance seen in that group in the present study. Had we been able to assess humor appreciation more proximal to drug administration, we may have obtained a better performance for caffeine. The schedule for the administration of the Humor Appreciation Test was designed as a compromise among several factors, including the time of maximal blood concentration of the stimulants, half lives of the stimulants, the time of maximal circadian drive for sleep, and logistic constraints posed by the need to assess multiple cognitive capacities following drug administration. Given that the performance and subjective-sleepiness effects of caffeine

were significantly enhanced relative to placebo but did not differ from the other 2 stimulants, we believe that the comparison among groups on the Humor Appreciation Test is reasonable and justified. Though not optimal, the timing of the administration of the Humor Appreciation Test did permit a reasonable comparison within a time window that would be considered to be operationally relevant for most occupational, aviation, and military scenarios. Second, the present study would have been strengthened had we been able to assess humor appreciation at multiple time points. Unfortunately, the Humor Appreciation Task is, by its very nature, not a repeatable task, and there are presently few if any psychometrically sound instruments of this type available with alternate forms. Given that our Humor Appreciation Test was not repeatable, we chose to maximize potential effects by testing at the nadir of the circadian rhythm. By restricting the assessment to a single time point, we were not able to disentangle the homeostatic need for sleep from the influence of the circadian rhythm. Future research will need to use repeatable measures at different phases of the circadian rhythm to disentangle these influences from the effects of sleep loss and to determine whether humor appreciation is effectively returned to baseline levels by stimulant medications. Finally, the present findings are limited by the use of only a single type of measure of humor appreciation. Subsequent research may benefit from the use of multitrait multimethod assessment of humor and related constructs to more effectively clarify the effects of sleep loss and stimulants on the complex higher-order cognitive processes involved in the ability to appreciate humor. Despite these caveats, the present findings suggest that various stimulant medications are not comparable with respect to their ability to enhance or sustain the capacity to detect and appreciate nonverbal humor, an executive function that is among the most complex and integrative cognitive capacities of the human brain.

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