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Pharmacological Optimization of Performance: Memory and Cognition

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Abstract

Decrements in reasoning, vigilance, and memory will surely occur under extremely stressful circumstances. Recent advances in the neurochemistry and neurophysiology of cognitive processes suggest that it may be possible, in the foreseeable future, to improve or maintain these abilities under severe conditions. No currently available compounds have been shown to reliably and unambiguously improve cognitive functioning in normal rested individuals. A few compounds show some evidence of effectiveness in aged or dysfunctional individuals. These and other treatments should be examined for effectiveness in normal but severely challenged individuals. Emphasis should be on attenuating the performance deficits that result from stressful situations rather than on improving the performance of normal individuals under optimal circumstances.

Introduction

"This is One-six. I'm at coordinates 298028, over." "This is Delta Six. Are you sure of that? . . . According to what you gave me, you're in the South China Sea, over." . . . Goddamn! I've done this a million times . . . "Concentrate", I said to myself while staring at the meaningless blob of colors, whirls, and numbers. Suddenly, everything jelled in perfect clarity. "Delta Six, this is One-six. You're right, my coordinates are 288028. I need a dustoff fast, over." . . . Two lessons: claymores and thunderstorms do not mix, and reading a map under pressure is not like reading one in a training exercise. (Downs, 1978).

Lieutenant Downs learned the hard way that even well practiced mental tasks can suddenly become confusing or even impossible under extreme conditions. Hunger, physical and mental fatigue, fear, pain, hypoxia, intoxication and many other stressors can reduce cognitive efficiency. Memory, ability to concentrate, and reasoning ability can all be drastically impaired under severe circumstances. Often, the consequences of such changes are worsened by occurring without being obvious to the affected individual. With the incredible complexity of a modern battlefield soldiers now are faced with mental tasks of enormous difficulty. Advances in the technology of warfare dictate that intense battles can now continue during darkness, bad weather and other conditions that previously would have brought about at least a lull in the battle. Both armaments and doctrine now call for soldiers to be engaged in sustained operations lasting as long as several days without significant rest. The missing element in these scenerios is likely to be the inability of even well trained, highly motivated soldiers to satisfactorily perform their assigned tasks for such extended periods. This paper examines issues involved in and approaches to enhancement of cognitive performance under challenging conditions.

The search for ways to improve performance is not new. Recent advances in neuroscience have however resulted in many new approaches. These same advances have resulted in an increased awareness of the extent to which neural functions do not operate independently but are quite interrelated. It is, therefore, important that we carefully

consider the trade-offs when seeking to optimize any one aspect of performance.

The analysis of cognitive functioning can be considered to have three essential phases: First a training phase where some new skill or information is acquired; second, a delay period; and finally a testing phase. For the purposes of studying performance during sustained operations we would consider the delay period to be disruptive. Interventions might be effective during any or all of these phases. Treatments are evaluated by the degree to which they reverse or attenuate the disruption in performance usually seen under the test conditions. Most animal research screening for cognitive enhancing agents uses single day paradigms. A typical procedure is for animals to be trained on an avoidance task in the morning. These animals are then exposed to an intervention which would normally lower subsequent avoidance performance. Such interventions are most often electrically induced seizures or hypoxia. The effectiveness of various treatments in minimizing this induced loss of performance is taken as an indication of their possible effectiveness (Gamzu, 1984). Human research normally uses persons who have suffered serious declines in mental abilities due to normal aging or disease. Seldom does research concerning enhancement of cognitive functioning use normal, well trained subjects (animal or human) performing under sub-optimal conditions. Proper evaluation of any potential interventions for military use during sustained operations must include such tests.

Potential Performance Enhancers: Memory and Cognitive Functioning

Nootropics:

These recently developed "mind-activating" drugs are purported to have selective activity on telencephalic structures and to have a very low incidence of toxicity and undesired effects. The mechanism of action is not well understood but may work at least in part by improving the ATP/ADP ratio. A large number of related compounds have been synthesized and several of these drugs are currently in use (in Europe) for the treament of various dementias. Results of these clinical studies have been mixed, but there have been enough positive findings to encourage continued research. A few studies have even demonstrated small but reliable improvements in cognitive performance in normal young adults. Piracetam, a prototypical example of the nootropic class, has been shown to improve mental performance in aged but clinically normal individuals (Mindus, et al, 1976) and in young adults (Dimond & Brouwers, 1976).

Stimulants:

Caffeine, and to a lesser extent in recent years nicotine, have been fixtures of life in the U.S. Army for decades. Coffee has in fact been a staple of Army rations since 1832. Though widely viewed as a mild stimulant helpful in temporarily relieving minor fatigue and boredom with little risk, laboratory studies have reported improvements in tasks ranging from vigilence and reaction time to complex verbal tasks like the Graduate Record Exam (Sawyer, Julia, and Turin, 1982), although effects on the more purely cognitive tasks seem to be dependent upon personality. Nicotine, in tablets as well as cigarettes, has repeatedly been shown to help sustain performance on monotonous tasks, and to improve both speed and accuracy on a variety of information processing tasks (Wesnes and Warburton, 1983). It is clear that, given the social acceptibility of these drugs, any proposed stimulant will have to show marked advantages over these two to merit much consideration.

The heaviest reported use of other stimulants is the extensive use of amphetamines by the Soviet Red Army during World War II. Reported benefits included

not only reduction of fatigue and drowsiness but also improvements in memory and concentration (Jones, 1985). Amphetamine and related stimulants (methylphenidate -- Ritalin) do in fact improve performance in routine tasks requiring vigilance. The tradeoff is perseverative stereotypic behavior. Complex reasoning and decision making will likely be adversely affected.

Hormones:

Several investigators, including Kety (1972), McGaugh (1973, 1983) and de Weid (1974) have implicated a role for endogenous hormones as modulators of memory processes. In particular, catecholamines and endorphins seem to effect memory storage. Adrenocorticotropic hormone (ACTH) has also been shown to modulate memory storage processes. All of these systems are activated during arousal and so would be especially important when considering cognitive functioning under challenging circumstances. Although there is usually a "U" shaped function to the effects, moderate increases in ACTH, increases in catecholamines, and blockade of endorphins have all been shown to enhance memory in laboratory animals. The main lesson from this work might be that there is an optimal level of arousal for a given behavior at a specific stage of training. Too much or too little arousal will result in lower performance.

Enhancers of Neurotransmitter Systems:

The discovery of decreased levels of cholinergic activity in Alzheimier patients prompted a great deal of research into the effectiveness of treatments which would increase cholinergic functioning. There are two basic permutations of this approach. The first approach is to increase the levels of acetylcholine (ACH) in the brain by increased systhesis. Various dietary precusors such as choline and lecithin have been tried with minor effects at best. The other permutation involves more direct manipulation of the cholinergic system, either by direct use of agonists or by using cholinesterase inhibitors to prolong the action of what ACH is available (Bartus, et al, 1984). Physostigmine and other drugs increasing the duration of action of ACH have been shown to improve memory in laboratory animals,and, under certain conditions, in humans. Non-specific neural excitants such as strychnine have also been found to improve memory under certain conditions (Crabbe & Alpern, 1973).

Blood Flow/ Metabolism Enhancers:

Under some severe conditions an increase in the amount of blood flow to the brain might improve performance. Several types of drugs are available for accomplishing this. Pentoxifylline (Trental) increases the flexibility of blood cells so that more blood can get into areas having low blood flow (Petrie, 1985). Compounds of this type are suggested to be effective against the primary symptoms of senility such as disorientation, confusion and memory loss. Their effectiveness in normal individuals under stressful conditions should be evaluated. Calcium channel blockers (e.g. Nifedipine, Verpapamil, Diltiazem) can prevent spasms in muscles and blood vessels. This type of drug might be useful in maintaining effective cognitive functioning at high altitudes, in aircraft with low-cabin pressures or other circumstances leading to brain oxygen debt.

Anxiolytics:

Beta-adrenergic blockers (e.g. Propranolol) have proven useful for reducing performance anxiety in concert musicians and actors as well as competitive shooters (Noyes, 1985). These might improve cognitive performance under the stressful conditions of combat as well.

RNA Synthesis:

Increasing rates of RNA synthesis was thought to be a mechanism for improving memory. Magnesium Pemoline was intially purported to increase RNA synthesis and a number of studies followed investigating its effectiveness in improving memory. After the initial unbridled enthusiasm it has become evident that the effects are small if they exist at all (Eisenstein & D'Amato, 1975).

Future Directions

Our laboratories at Walter Reed are currently conducting a number of research projects concerned with optimization of cognitive functioning. Animal studies include projects investigating: performance decrements in rats living in a chronic stressful environment; performance changes occurring under the influence of chemical warfare antidote compounds; and circadian patterns of cognitive performance. Human studies include: ongoing studies concerned with performance changes under the influence of chemical warfare antidote compounds; continuing studies investigating performance changes with sleep loss; and planned studies of the effects of nootropic and alerting agents on performance changes accompanying prolonged sleep loss.

Summary

* When the going gets tough, anybody can get stupid.
* Naturally occuring hormones, including ACTH, epinepherine, and endorphins, play an important role in memory acquisition, consolidation and retrieval.
* Training should be under conditions of physiological and emotional arousal similar to those under which the tasks are likely to be performed.
* Consideration must be given to performance variables: These include: attention and perception, motivation, degree and type of required repsonse, and task complexity.
* Although a few reports have shown minor performance improvements in normal individuals, there are no known pharmacologic compounds that are generally regarded as be useful for improving congnitive functioning in rested, normal individuals. A number of agents have shown some effectiveness in improving functioning in aged or dysfunctional individuals; their effectiveness in improving degraded performance in normals should be systematically studied.

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