Analysis:

Food for Thought: Dietary Nootropics for the Optimisation of Military Operators Cognitive Performance

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Abstract

Nootropics are compounds that enhance cognitive performance and have been highlighted as a medium-term human augmentation technology that could support soldier performance. Given the differing ethical, safety, and legal considerations associated with the pharmaceutical subset of nootropics, this analysis focuses on dietary supplementation which may enhance cognition during training and operations. Numerous supplements have been investigated as possible nootropics, however research is often not context specific or of high quality, leading to questions regarding efficacy. There are many other complex cofactors that may affect the efficacy of any dietary nootropic supplement which is designed to improve cognition, such as external stressors (e.g., sleep deprivation, high physical workloads), task specifics (e.g., cognitive processes required), and other psychological constructs (e.g., placebo/nocebo effect). Moreover, military population considerations, such as prior nutritional knowledge and current supplement consumption (e.g., caffeine), along with other issues such as supplement contamination should be evaluated when considering dietary nootropic use within military populations. However, given the increasing requirement for cognitive capabilities by military personnel to complete role-related tasks, dietary nootropics could be highly beneficial in specific contexts. Whilst current evidence is broadly weak, nutritional nootropic supplements may be of most use to the military end user, during periods of high military specific stress. Currently, caffeine and L-tyrosine are the leading nootropic supplements candidates within the military context. Future military specific research on nootropics should be of high quality and use externally valid methodologies to maximise the translation of research to practice.

Key Messages:

- Nootropics have recently been highlighted as a medium-term human augmentation technology that could support soldier performance by the UK Ministry of Defence report – 'Human Augmentation – The Dawn of a New Paradigm'.
- Herein we discuss the need for cognitive enhancement; current evidence; additional considerations; and future directions all within the military context of dietary nootropics.
- Should robust evidence demonstrate the utility of dietary nootropics to military operators, then they could provide a cost-effective solution compared with other domains of human augmentation.
- Future dietary nootropics research within the military sphere should ensure high-quality methodologies are employed, with efforts made to maximise external validity wherever possible.

Background

Substantial efforts are made by militaries to ensure combat readiness is maintained [1]. The UK Ministry of Defence report – 'Human Augmentation – The Dawn of a New Paradigm' [2], documents a breath of anticipated human augmentation technologies to support military personnel up to ~2050. Similar approaches to human augmentation through technological, methodological, pharmacological interventions have also been discussed in the peer reviewed literature for athletes, the military and other applications [3]. Human augmentation interventions follow different timescales of realisation and have varying degrees of uncertainty and feasibility. Nootropics are identified in The Dawn of a New Paradigm' report [2] as a technology of medium-term interest in the category of optimisation methods. As with all possible augmentation strategies the efficacy of nootropics needs to be comprehensively evaluated [3].

Nootropics, are defined *as a "heterogeneous group of compounds of diverse chemical composition and biological function that allegedly facilitate learning and memory or overcome natural or induced cognitive impairments"* [4]. The term is commonly interchanged with terms such as 'cognitive enhancers' or 'smart drugs' [5] and includes compounds such as stimulants (e.g., amphetamines), herbal compounds (e.g., caffeine, nicotine, ginkgo biloba), amino acids (e.g., tyrosine) and pharmaceutical drugs [2]. As surmised by Schifano and colleagues [5], numerous classifications of nootropics have been attempted, resulting in some ambiguity as to substances that are classified as a nootropic. Whilst the realisation of nootropics is considered medium term [for the Ministry of Defence] (within next 10 years), pharmaceutical drugs were used for cognitive enhancement by soldiers in World War II [6]. Given the differing ethical, safety, and legal considerations associated with the pharmaceutical subset of nootropics, the present paper will focus on dietary supplementation of nootropics which may support cognitive enhancement within an operational setting. With current interest in holistic soldier

performance, renewed interest in nootropics, and sports specific products containing nootropics (e.g., energy gels) this analysis will cover the need for cognitive enhancement; current evidence; additional considerations; and future directions.

Why the need for cognitive enhancement?

During military training and operations, personnel face numerous external stressors, including extreme physical exertion, high cognitive demands, exposure to austere environments, and restriction of sleep and caloric intake [7]. Technology advancements and compressed time for decision making have further increased cognitive demands [8]. Should military personnel fail to manage these demands it could result in negative outcomes such as suboptimal performance, injuries, or fatalities [9]. For example, attenuations in cognitive performance have been demonstrated because of physical exertion during military load carriage tasks [10] and increased anxiety levels [7]. As a result, when individuals and organisations refer to cognitive enhancement modalities, in most instances 'enhancement' is in fact attempts to mitigate/attenuate the deficits in cognitive performance, with 'true' enhancement (i.e., beyond normative performance or above a biological ceiling) being a rarity [11]. Thus, dietary nootropics, within the military context are likely in fact to optimise up to biological potential or mitigate against under performance, as opposed to enhancing beyond biological potential.

Current Evidence

Pomeroy et al. [12] have presented the most recent and comprehensive evidence for the effect of dietary supplements on cognitive performance in military personnel (and young adults). The review reported findings from investigations on the supplementation of carbohydrate, amino acids (L-tyrosine and beta-alanine), omega-3, nitrates, prebiotics, B- and multi-vitamins, and herb/plant-based supplements (caffeine, guarana, flavonoids, ginseng, and gingko biloba). The authors concluded that for most supplements the evidence base was

inconsistent between studies, and although positive effects were observed for a range of supplements, these were not typically observed across all cognitive domains or all metrics of a particular cognitive domain. The authors only concluded that L-tyrosine and caffeine could be used under certain situations to enhance cognitive performance. However, most worryingly when compared to the SIGN50 guidelines, only 73% of the research within this area, and included within the review, was recorded as being low quality. Critically, a large portion of the studies in the review involved no stressors experienced in military work and training (e.g., sleep restriction/deprivation, high cognitive or physical load), with only two papers investigating combined stressors. This is despite the external validity of employing a military stressor within the study methodology. Thompson and colleagues [13] investigated nitrate consumption on concomitant exercise and fatiguing cognitive assessments, whilst Hoffman and colleagues [14] investigated beta-alanine supplementation during 28 days of fatiguing military training. Along with research quality and the external validity of methodologies employed, supplement dosage likely plays a significant role in the results observed to date. For example, Lieberman et al. [15] investigated caffeine dosage on U.S. Navy S.E.A.L trainees; with results indicating an optimum dosage of 200 mg caffeine to improve cognitive function which had been degraded by operational stressors (including sleep deprivation). Similarly, recent evidence has suggested that genetic phenotypes may influence the physiological responses observed following supplementation (e.g., caffeine; [16]). Bioavailability of the nootropic supplements may also contribute to the variation in results observed, as this can be affected by factors including the consumption matrix and the nootropic source [17]. Notably, measuring the bioavailability of certain nootropics can be particularly difficult due to their mechanism of effect being within the brain.

Critically, there were also a range of dietary supplements that were not covered in the review by Pomeroy et al. [12] that purportedly have nootropic properties. For example,

McMorris et al. [18] demonstrated a 7-day loading of creatine monohydrate attenuated decrements in prefrontal cortex performance and mood associated with 24-h sleep deprivation. Waldman and colleagues [19] demonstrated that a ketone monoester consumed with carbohydrate increased psychomotor vigilance test response time and incongruent flanker response time, reciprocal reaction time, and responses correct per second following exercise (30-minute ramp and 10 km time trial) compared with a carbohydrate control. Despite the different supplements investigated in these two examples, similar mechanism regarding brain energetics are likely at play; highlighting the importance of utilising methodologies that reflect military environments where stressors may alter brain energetics. For example, during field exercises or deployments where energy expenditure exceeds energy intake, during sleep deprivation, or when processing information from multiple sources over a prolonged period.

In the recent review by Brunyé et al., [11], nutritional and dietary interventions were considered a method of indirect cognitive enhancement, compared with other direct cognitive enhancement methods such as 'Noninvasive Brain Stimulation' or 'Reality Augmentation'. Arguably however there is a continuum of effector pathways for nutritional supplements, with some having more of a direct effect on brain function compared with others. For example, creatine, and ketone monoesters may influence cognitive performance by way of altering brain energetics. In contrast, a recent systematic review by Cooke at al. [20] concluded that modulation of gut microbiota provided a promising strategy for cognitive enhancement, despite the research limitations. There may also be nutritional strategies which have even more indirect effects and may improve cognitive performance via second order effects. For example, during load carriage, ratings of mental effort, thermal comfort, and ratings of perceived exertion have been demonstrated to increase [21]. Should nutritional supplements be able to positively alter perceptions (e.g., thermal comfort; [22]), then the unfavourable use of working memory capacity by internal distractors (e.g., increasing thermal discomfort) could be prevented. This

could plausibly mitigate against this decrease in cognitive processing efficiency and subsequent impacts on performance effectiveness [22].

Additional Considerations

In some instances, nootropic supplements may be highly advantageous to military operators beyond just improving cognitive performance. For example, creatine and omega-3 fatty acids may have a neuroprotective effect against symptoms of traumatic brain injuries and concussion [23] and beetroot juice improves athletic performance/endurance [24]. However, the converse may also be the case for some nootropic supplements, with negative implications associated with their use. For example, caffeine gum may enhance acute cognitive performance during a night operation, however it could also reduce subsequent sleep quality or quantity [25] leading to a larger cognitive decrement on subsequent days.

Contamination of dietary supplements with banned substances also presents a risk for military personnel [12]. Crawford and colleagues [26] identified 650 dietary supplement products marketed for brain health and cognitive performance, content analysis from the subset of twelve products selected demonstrated that 67% did not contain a listed ingredient, whilst 83% contained a non-listed ingredient. A prudent step would be to suggest that all nootropic supplements used with military personal should be batch tested.

The nutritional intake of soldiers should be considered when assessing the likely efficacy of dietary nootropic supplements. A recent study of British Army standard-entry infantry trainees, identified their nutritional knowledge compared with civilians was significantly worse [27]. Whilst dietary intake was not reported, it likely infers that their diet would be suboptimal when choice was involved. Given that some dietary nootropic supplements are highly prevalent within some diets/populations, this could also impact the efficacy of a particular nootropic. For example, Knapik and colleagues [28] reported higher caffeine consumption within military

personnel (n = 26,680), compared to National Health and Nutrition Examination Survey data. The placebo/nocebo effect on a supplement's efficacy should also be considered. A recent systematic review has suggested a small to medium effect (d = 0.35) on sports performance can be induced though placebo and nocebo effects of nutritional ergogenic aids [29]; with dramatically larger effects evident following the use of pre-conditioning procedures. There are likely a range of other factors that need to be considered prior to implementing a nootropic intervention within military populations.

Future Directions

Existing research on the impact of dietary supplements on cognitive performance in military personnel (and healthy young adults) is generally poor quality [12]. Military focused dietary nootropics research should utilise high-quality research approaches, with externally valid methodologies to ensure the translation potential of the research outcomes. Identifying exact user cases (e.g., tier 1 operators on sequential night operations), where cognitive enhancement would be beneficial, would support the down selection of candidate supplements and the external validity of the research methods employed. Interdisciplinary research which seeks to combine nootropic supplementation with other cognitive enhancement methods may also be an avenue of future interest. Equally, establishing the smallest effect size of interest is essential to correctly power the investigation, but also for the interpretation and translation of research findings. As noted by Burke [30], there are several questions surrounding supplement usage within the athlete population which would be equally relevant to military operators and their potential use of dietary nootropics. Firstly, what are the effects of co-ingesting dietary supplements each with proven benefits (e.g., a hypothetical supplement which contain both caffeine and L-tyrosine) and secondly, the influence of repeated supplement uses within a short time frame (half-life, desensitisation). Co-ingestion may be of particular interest with respect to military use of nootropics; should research suggest that different substances can affect

different domains of cognitive function. Similarly, repeated supplement use may be of particular interest given that military operations are frequently longer than sporting events and may last upwards of 24 hours. Both areas present significant research opportunities, which would provide important outcomes to the military end user. Given these future directions, and the relatively more complex operational environments of the military compared with sporting contexts, the formulation of evidence-based guidelines which can support military personnel may be prudent. A valuable first step would be developing a comprehensive framework for supplement characterisation (e.g. proven vs potential/promising vs unlikely).

Conclusions

Dietary nootropics continue to be a growing area of interest within the sports and occupational research spheres. This may be a result of their lesser ethical, safety, and legal considerations when compared with the pharmaceutical subset. Should research on dietary based nootropics demonstrate benefits to military operators, then they could provide a cost-effective enhancement compared with other domains of human augmentation. Dietary nootropics will likely only provide performance optimisation up to and not beyond biological potential. Future military focused dietary nootropics research should ensure high-quality methodologies and attempt to maximise external validity wherever possible. Selection of nootropics, should consider the individual characteristics of the military end-user (e.g., habitual consumption, baseline diet etc.) and external stressors they are exposed to in their training and work environment.

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