The Importance of the Study of Cognitive Performance Enhancement for U.S. National Security

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INTRODUCTION: The American military is embarking on the 'Third Offset'—a strategy designed to produce seismic shifts in the future of warfare. Central to the approach is the conjoining of humans, technology, and machines to deliver a decisive advantage on the battlefield. Because technology will spread rapidly and globally, tactical overmatch will occur when American operators possess a competitive edge in cognition. Investigation of cognitive enhancing therapeutics is not widely articulated as an adjunct to the Third Offset, yet failure to study promising agents could represent a strategic vulnerability. Because of its legacy of research into therapeutic agents to enhance human-machine interplay, the aerospace medical community represents a front-running candidate to perform this work. Notably, there are strong signals emanating from gambling, academic, and video-gaming enterprises that already-developed stimulants and other agents provide cognitive benefits. These agents should be studied not only for reasons of national security, but also because cognitive enhancement may be a necessary step in the evolution of humankind. To illustrate these points, this article will assert that: 1) the need to preserve and enhance physical and cognitive health will become more and more important over the next century; 2) aeromedical specialists are in a position to take the lead in the endeavor to enhance cognition; 3) signals of enhancement of the type useful to both military and medical efforts exist aplenty in today's society; and 4) the aeromedical community should approach human enhancement research deliberately but carefully.

KEYWORDS: performance enhancement, performance optimization, cognitive enhancement, Third Offset.

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The U.S. Department of Defense's (DOD's) "Third Offset' strategy is not routinely discussed in medical circles, but it would be wise for military health strategists to consider the strategy's implications for medical research in cognitive enhancement. This article will assert that changing patterns of disease will elevate cognitive enhancement research in importance over the upcoming decades. It will then demonstrate that the Third Offset provides an impetus to launch this effort now. Before describing pitfalls to avoid, the article will make a case that the aeromedical community is positioned to lead in this new paradigm.

The Emerging Medical Third Offset

In 1900, life expectancy in the United States was 47 yr. The top three causes of death were pneumonia/influenza, tuberculosis, and gastrointestinal infections.¹⁶ In the American population at large, such demise was neither heartbreaking nor unnatural, but the expected order of things. 'Normal aging' was characterized by different morbidities than today. Fortunately, because of the 'offset' advantage of antibiotics, it is now possible to consider this early $20^{\rm th}$ century lifespan as tragically short.

The term 'offset' was coined by the U.S. defense establishment to define national strategies that deliberately pursue innovation as a method to overcome the threat of enemies who would otherwise overpower America in numbers, capabilities, or both. The term is also appropriate for the historical impact of antibiotics because, like military revolutions, their discovery produced quantum change and a major reorganization of accepted order. In a hundred years, our descendants will be able to view our present attitudes about health and disease as a snapshot in time similar to the way we now consider those of

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1900. Will what we consider 'natural' death today be regarded as easily preventable in the future?

Such a scenario is likely, but recent history suggests that offsets will occur predominantly in an incremental and multifactorial fashion instead of as the result of single, earth-shattering discovery. For example, evidence suggests that we are in the midst of a second and prolonged offset to substantially reduce the burden of atherosclerotic disease (the current leading cause of death in the United States).¹⁶ Thanks to the progression of scientific meticulousness in research and the growth of large networks of coordinated specialists, medical discovery in cardiovascular medicine is accelerating. Rigorously conducted trials now routinely produce survival-prolonging cardiovascular interventions. Indeed, the miracle statin drugs have been shown to produce regression of atherosclerotic disease.²⁴ Statins are now used on a massive scale to prevent atherosclerotic disease before any sign of heart disease (or traditional risk factor) is present.²⁶ It is interesting to think of America as a place in which death due to atherosclerosis will be a threat similar in scale to that of infectious disease. But if declines in U.S. heart and stroke mortality rates continue at their current pace (as they have since their peak in the early 1960s), atherosclerotic death will reach that mark by 2060. With the atherosclerotic pathology rate contained, humanity will begin to consider ways to ignite a third medical 'offset.'

Assuming the absence of novel medical threats, the target of a third medical offset will, by default, be the eradication of nonatherosclerotic metabolic derangements. Efforts to attack cancer, the prototype of metabolism gone awry, will redouble. Cognitive decline may replace atherosclerosis as the most menacing medical threat on the epidemic scale. Science will be enlisted to address causes of mental and physical frailty such that disability does not poison the extra years of late life granted by medical advancement in cardiovascular medicine. Researchers will seek public health mechanisms to defeat decay of the mind and body. Synonymous with preserving youth in the present paradigm, the forestallment of mental and physical deterioration will mark the next step of an evolution of what is perceived as illness. With luck, our children's grandchildren may view our current ideas of 'normal' aging in the same way we now view antibiotic-curable infectious disease and will eventually view atherosclerosis: as disease isolated to those unfortunate enough not to have access to preventative elements delivered through public health efforts.

Prevention of decay can be restated as an effort to maintain health at an optimal level as age increases or as physiology worsens. This formulation allows the term 'prevention' to be synonymous with performance enhancement 'relative' to the aging cohort. As an example, a golfer on the senior tour who has maintained the abilities of his 20-yr-old-self (through medical intervention) would be considered to be performanceenhanced compared to his competitors. Work on an Alzheimer's vaccine is now underway.²² This vaccine may prove to be an agent of both prevention and relative enhancement. The aerospace medical community stands out as a specialty that routinely studies relative enhancement. It has discovered effective therapeutics to maintain optimal performance in healthy pilots in degraded states of physiology. In this case, relative performance enhancement as a form of prevention is a practical matter.

Nonmedical communities likely do not equate enhancement with prevention. Traditional ideas of performance enhancement emphasize 'absolute' enrichment of natural physiology. The goal is not preservation of an optimal level of health, but the achievement of a level of function better than merely healthy. Prevention and absolute performance enhancement, however, are not mutually exclusive. Assuming that enhancement improves baseline physiological function, it would be logical to suppose that it could contribute to our evolution into fortified pathology-resistant beings.

Caffeine offers a case study of an agent capable of both absolute enhancement and mortality prevention. Caffeine has clear and quantified evidence of absolute performance-enhancing effects.^{12,19,20} These results are important but not surprising. What has been unexpected, however, are revelations that caffeine, at least when combined with the other ingredients in coffee, prevents mortality.¹⁰ Put another way, coffee has accomplished the health-preserving goal that every marketed vitamin has sought, but has never proven it could achieve. Furthermore, it establishes that absolute enhancement and primary mortality prevention can occur synonymously. Ultimately, the predicted battle to defeat current mechanisms of aging will represent a merging of the disease-based approaches (statins for cardiovascular disease, for example) and enrichment of metabolic function (as illustrated by the effects of caffeine and coffee).

The example of coffee and caffeine provides plausibility that prevention of death and decay may accompany absolute performance enhancement. What has been lacking is rigorous scientific study (safety and dose ranging trials, for example) of similar effects in emerging potential performance enhancers. Such research should not be avoided.

The Emerging U.S. Military Third Offset

The strategic environment within the United States is ripe for an accelerative burst toward a third medical offset.² This opportunity exists because the U.S. national defense establishment is now pursuing its own 'Third Offset.^{9,21} In the same way that globally beneficial vaccines were developed by military researchers in order for American soldiers to operate in foreign environments, the needs of the military may again provide the motivation for revolutionary medical growth.

Unlike in health and disease, in which the term is used nontraditionally and retrospectively, the word 'offset' is used deliberately by strategic leaders seeking to achieve a revolution in military affairs. The first named military offset was the development of nuclear weapons. The second was the development of precision-guided munitions. The Third Offset strategy is difficult to summarize as succinctly as the first two, but envisions a highly technological future—one in which warriors will be deeply interconnected with computers, networks, automation, and machines. In the seminal 2015 description of the Third Offset, Bob Work, the U.S. Deputy Secretary of Defense, used an allegorical anecdote to illustrate the fundamental tenant of the third offset strategy: "Tyler Cowen wrote a book called 'Average is Over'. He's an avid chess player. What he said was, 'It used to be a matter of faith that a machine would never beat a human,'...Now machines consistently beat grandmasters. And what he found out in a thing called three-play chess is the combination of a man and a machine always beats the machine and always beats the man. I believe that what the Third Offset Strategy will revolve around will be threeplay combat."²⁹

In a later speech, Work added some detail to the proposed Third Offset, identifying its six areas of interest: autonomous 'Deep Learning' machines, human-machine collaboration, assisted-human operations, enhanced-human operations, advanced human-machine teaming, and semiautonomous weapons.²¹ The Third Offset will be pursued through the Defense Innovation Initiative (DII), which defines two of its three main thrusts as achieving superiority in technology and attracting the talent needed to optimally engage in three-play combat.²¹

The U.S. military's pivot toward emerging technology is visible everywhere. In 2016, U.S. Secretary of Defense Ash Carter proposed that \$72 billion dollars of the DOD budget be dedicated to research and development alone.⁶ To speed defenserelated technology discovery, Carter erected the Defense Innovation Unit-Experimental, a new DOD 'outpost' in Silicon Valley designed to help connect the DOD with "leading-edge technologies and the entrepreneurs behind them."⁶ One need only follow one of the DOD's social media outlets to be constantly reminded of similar examples of the Department's commitment to emerging technology.

In spite of this commitment, it is accepted that advantages in technological sophistication will be fleeting due to the speed of the current information age. The mitigation factor embraced to defeat this inevitability is to have superior operators. When premiering the DII in 2014, then U.S. Secretary of Defense Chuck Hagel emphasized this point in his very brief overview of the program, stating, "[The DII] will focus on our most important asset—our people."14 Details were left unexplored in the speech, but DOD Strategic Capabilities Office Chief William Roper expanded on the concept in 2016, stating, "If both sides are pointing at each other with the same kind of equipment...it's going to boil down to people. ... You're going to see a higher level of proficiency required for operators, who are going to have to quarterback these machines."9 In 2015, Work emphasized the necessity to ensure that American Forces were always in a position of tactical superiority:

"...our technological superiority is slipping. ...But please do not think that my time and attention on technology in any way, shape, or form keeps me not focused on making sure we retain the best people that we can possibly get. The fact is that we want to achieve an over-match over any adversary from the operational theater level, all the way down to the fighter plane, Navy ship, or infantry squad. As General Dempsey has often said, we never, ever want to send our troops into a fair fight.²²⁹

A focus on human performance at the tactical level, with the 'playing-field' leveled by common access to similar technologies, provides a framework for the nexus of military and medical offsets and distinguishes the Third Offset from the previous two.

For as much evidence that exists demonstrating the U.S. military's commitment to the technology thrust of the DII, there is a relative paucity of information indicating how the Department will achieve the advertised tactical-level superiority in combat performance. To date, the U.S. military in general, and the Army in particular, has labored to achieve a competitive health advantage over adversaries. Through its 'Performance Triad' of sleep, activity, and nutrition, the U.S. Army has sought to invigorate a healthy and ready military force.¹⁵ The Third Offset, with its emphasis on 'human-machine symbiosis,' encourages the study of enhanced cognition. To this end, the military is considering "brain training" and "cognitive gyms."²³ While traditional opportunities to identify safe improvements in physical strength and cognitive processing should not be ignored, they are not likely of 'offset' caliber.

The prevailing context in which absolute performance enhancement is discussed in society at large is the imbalanced advantage therapeutics provide to individuals and teams in competitive endeavors. The unfair 'edge' characterized by such scenarios harmonizes precisely with the message of DOD leaders, yet discussion of performance enhancement drugs is just beginning to enter into concepts of military doctrine. Even though buried in an appendix, its inclusion in the Army's 2014 'Human Dimension Concept' pamphlet is noteworthy. In this document, the Army acknowledges that medications will have a role in human performance enhancement "in the near future."7 Less trepidation is needed. As discussed in a recent Nature commentary, drugs (and other interventions) "should be viewed in the same general category as education, good health habits, and information technology-ways that our uniquely innovative species tries to improve itself."13 To not rigorously explore this area would be incongruent with the contemporary entrepreneurial approach of the DOD.

The Convergence of Offset Strategies

There currently exists an unsophisticated paradigm of the warfare imagined in the future. The competitive video-gaming industry sponsors professional sporting events in which fiveman infantry squads battle each other in virtual combat. The software ensures a level playing field, isolating the skill set of the individuals as the independent variable that determines success or failure. The nature of the physical gaming environment would not be unfamiliar to aeromedical specialists who have studied the health and performance of air traffic controllers. And while it may be absurd to suggest that video games have any significant connection to actual combat, they may not be a far cry from three-play combat in the future. The Defense Advanced Research Projects Agency's 'Squad X' initiative, for example, seeks to incorporate the situational awareness available in video games into heads-up displays worn by soldiers engaged in combat, creating an "augmented reality."^{3,11} Unmanned aircraft systems operators are already engaging in warfare from behind computer monitors.

What is notable about the video-gaming example is that the Electronic Sports League (one of the major gaming organizing bodies) recently identified stimulant abuse as a problem in its competitors.²⁸ Kory Friesen, a player on the Counter Strike Cloud9 team stated, "We were all on Adderall...tons of people do it."28 This comment provides evidence of a perception (apparently shared by many professionals) that the stimulant provides a competitive edge in three-play contexts. Similarly, a 2015 international survey of poker players found that 80% admitted to using "drugs and other substances to enhance their performance."25 College students are also increasingly turning to stimulants and other substances to help with examination preparation. The signs emanating from current competitive environments should unleash a flood of research hypotheses and proposals from military scientists. Seizing the opportunity to learn about the short- and long-term effects of these drugs would be more than a military imperative. It would accelerate the larger medical offset and begin its convergence with that envisioned by the U.S. military.

Stimulants are merely one of many avenues that should be studied as the military and medical offsets align. The list of candidate drugs is large and growing. Furthermore, medications represent the tip of the human-performance iceberg. Transcranial stimulation is showing promise in the realm of cognitive enhancement. Nontherapeutic interventions in the domains of nanotechnology, biotechnology, and information technology are 'converging' for the sake of national security.³⁰ The ways in which such technologies may be employed remains wide open. Interventions may be used, for example, to accelerate learning, to heighten vigilance, and/or to prolong endurance either in combat or in preparation for it.

The Future of U.S. Military Medical Research

The U.S. military's Third Offset is something new. Unlike the previous two, its technological reach is beyond weapons or sensors, but extends to humans themselves: their intellect, speed-of-thought, and accessible memory. This paper argues that the study of performance enhancement for the purposes of the military Third Offset can benefit an emerging third medical offset—if done properly. Even so, to suggest that the convergence would occur easily would be inaccurate. In fact, the future is far from determined and many hazards exist. To facilitate the convergence, it would be beneficial to explore four potential pitfalls.

1. The U.S. military medical community does not recognize the military's Third Offset as worthy of an 'all-in' commitment. One might think that the field of performance enhancement is widely studied, but, in fact, it is weak and fractured. A meta-analysis in the medical literature could find "only a few" studies on the topic of stimulant efficacy in normals.¹⁸ In 2008, military researchers scanned the global body of literature for conclusive data in the field. The term used to describe the quantity found was "surprisingly little."¹⁷

If the military medical research community does not recognize the Third Offset as a 'call-to-arms,' it may remain reactive to changes in the field as opposed to driving the field toward new discovery. Indeed, if the pursuit of discovery is left in its current state, there is potential for our enemies to seize the very advantage articulated as fundamental to the U.S. offset strategy. The Pentagon commissioned the MITRE Corporation to study such a scenario in 2008. In its report, the authors found that:

"There is the distinct promise for new drugs that improve alertness and learning with fewer side effects than previous stimulants. These drugs have demonstrated effectiveness in remediating cognitive losses, and will certainly be tested and evaluated for cognitive enhancement. Threat potential could arise from adversarial use of such drugs to mitigate the effects of sleep deprivation, or in enhancing specialized training."²⁷

This vulnerability is not isolated to the military. The following commentary in the journal *Nature* reflects the possible societal and business impacts:

"The new methods of cognitive enhancement are 'disruptive technologies' that could have a profound effect on human life in the twenty-first century. A laissez-faire approach to those methods will leave us at the mercy of powerful market forces that are bound to be unleashed by the promise of increased productivity and competitive advantage."¹³

Some thought leaders argue that the DOD should be a 'rapid adapter,' meaning that it should adopt any technology relevant to its missions developed in private industry. There is a role for industrial surveillance in medical fields. Even so, U.S. military laboratories exist to study those areas that are meaningful to the armed forces, but not incentivized by the demand from the public at large. The MITRE report states: "Extrapolation of civilian research to military scenarios cannot be relied upon to yield useful conclusions."²⁷ The fact of the matter is that a military medical effort must be pursued aggressively in human enhancement research. The effort must remain vigilant to nongovernment work, but it must also direct research in areas crucial to national security in which barriers to entry are too high for profit-incentivized private industry.

2. The U.S. military medical community recognizes the importance of its involvement in the strategy, but approaches it without organization and efficiency. The current portfolio of U.S. military medical research is broad. Of the U.S. Army's six specialized medical laboratories, many address aspects of human performance. The same is true of nonmedical U.S. military laboratories such as the Army Research Laboratory's Human Research and Engineering Directorate and the Defense Advanced Research Projects Agency. The U.S. Air Force and Navy likewise study areas of human performance pertinent to their specific fields of endeavor. Federally Funded Research and Development Centers are sponsored to study areas within the field. Finally, grants are proffered by the DOD to nongovernment agencies to pursue specific research questions. What is missing in this large and dynamic community is the coordination needed to make true synergy possible. While research in all of the laboratories may be progressing, it does so without clear guidance to unify its movement in the same direction.

A solution is offered by that of the government's aerospace medicine laboratories. Such teams, independently of an authoritative charter, have, for years, united together for an annual 'Aerospace Medicine Research Alignment and Collaboration' working group. This group includes senior scientists from the aerospace medicine laboratories of the U.S. Army, U.S. Navy, U.S. Air Force, Federal Aviation Administration, and NASA. The conference's goal is to ensure that the collective research of the laboratories represents a logical, nonredundant, and complete portfolio. It provides a stewardship function to confirm that the consortium addresses the most relevant medical problems afflicting aviation as a whole.

The ongoing collaboration in aeromedical work is mentioned as a model, but it would make sense for the aerospace medicine community to actually assume the mission of research in the human-machine dyad. The community has decades of experience in testing stimulants and other agents in human subjects in flight simulations.^{4,5,8} Extending such methodologies to other machine and computer interfaces would be intuitive. Indeed, the aviation community has already moved into this space. As an example, the Air Force created the 711th Human Performance Wing in 2008.³¹ Furthermore, the Aerospace Medical Association changed its scientific journal's name from 'Aviation, Space, and Environmental Medicine' to 'Aerospace Medicine and Human Performance' in 2015, reflecting a burgeoning commitment.¹ While the sports medicine community is well postured for research in physical enhancement, the aviation medicine community is best positioned to lead cognitive efforts.

3. The U.S. military medical community allows the potential for ethical concerns to stall or prevent the initiation of research in human performance. This article has presented an argument that cognitive enhancement research plausibly holds keys to mortality prevention. But opposite philosophies exist. The risks of cognitive enhancement came sharply into focus in 2003 when pilots taking 'Go Pills' committed fratricide. Beyond highlighting aerospace medicine's current presence in the field of human cognitive enhancement, the event introduces a counterpoint to the argument of potential benefits to its study. Efforts at cognitive enhancement may prove harmful in some contexts. If research does not provide thoughtful regulatory practices, therapeutic agents may create addiction, produce serious side effects, psychologically harm combatants, and/or create unwanted outcomes. Debate must occur and research must bridge gaps in knowledge. Philosophical differences are not inherently dangerous. They should be welcomed and explored to help inform the movement. What is dangerous, however, is that the topic of human enhancement becomes such an ethical and political 'third rail' that scientists avoid human cognitive enhancement research altogether, allowing a 'blind spot' to exist in our medical and military research programs.

4. The U.S. military medical community conducts adequate human performance research, but fails to properly inform strategic leaders on the implementation of solutions. The MITRE Report identified a need for the military to develop a corps of subject matter experts "capable of evaluating technical developments in human performance modification. These analysts should be trained in assessing the meaning of statistical metrics, and also in assessing the experimental methods and results of the original literature on which claims are based."27 The placement of study results in the proper statistical context is no small matter. As an example, the DOD spent billions of dollars on suicide prevention measures, even when none of the purchased solutions offered any evidence of efficacy. The results have not significantly changed suicide rates in spite of enormous expenses.³² Epidemiology experts, social scientists, and experienced clinical trialists could have predicted this outcome-an outcome familiar to medical researchers who often see 'plausible' therapies fail to produce results when exposed to the countless variables present in the in vivo environment. While efforts had to be made to reverse suicide trends, it would have been wise for decision makers to proceed cautiously where scientific evidence was low.

Communicating complex science (especially statistical analysis and epidemiology) to senior nonmedical decision makers is a competency not yet highly valued by the military medical research community. Yet it is crucial. Plausibility can generate much enthusiasm for new solutions and products. Even so, the road to effective therapeutics (or nonmedical solutions) is littered with failed competitors. Clear and accurate communication of the presence, scale, and significance of efficacy must be relayed to acquisition leaders. Such communication implies a new approach. Achievement of the Third Offset cannot reach its full potential without proactive and deep involvement from the medical community. It must envision itself as 'in the game' rather than 'on the bench.'

Military medicine has a great legacy of contributions to medicine and humanity. The development of vaccines and major advancements in trauma care are just two examples of countless innovations and convergences. The DOD's Third Offset strategy has opened a window of opportunity for military medicine researchers (and aerospace medicine specialists in particular) to once again propel forward a field that will help humankind if studied properly. The key tasks may not be yet articulated, but the intent is clear. We must secure the support of our military and governmental leadership and embark on the convergence of offsets.

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