

DSO
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Enhancing Human Performance

What do we ask of the average soldier? The commitment is to go into combat to defend the United States during periods of conflict. In the course of carrying out this activity the average 18 to 24 year old is asked to be mentally alert, physically fit and highly trained to use a variety of sophisticated pieces of equipment in life threatening and stressful situations and to perform at a level that maintains the lives of each member of the unit. Physically we ask them to carry 85 to 110 pounds of equipment for extended periods of time over extended distances, on unfamiliar and difficult terrain, while exposed to the environmental extremes of temperature, humidity and altitude. We ask them to have rapid recall of all training and objectives associated with mission success and the use of their equipment. We ask them to perform these tasks under life threatening conditions for periods of three to five days with or without adequate periods of rest or sleep. We ask them to eat on the run and to carry those foodstuffs with them; and if injured to provide some degree of medical aid limited by the available supplies and to continue with the mission objectives.

Can science and technology provide the competitive edge to the "Objective Force Warrior" that will assure mission success and reduce combat fatalities? This is both a serious question and a serious challenge. In Afghanistan, we saw U.S. troops with a significant advantage from a single physiologic enhancement - the ability to perform in darkness. Night vision goggles expand the sensitivity of the retina to provide a degree of visual acuity in low levels of light that allows a level of troop movement and operations in near total darkness. The opponent did not have the same advantage; the end result being mission success with few fatalities. Every enhancement has a single goal: to increase the warfighters' ability to survive and fight in high intensity warfare.

So if we ask what other physical and physiologic limitations need to be overcome to provide for survival under adverse conditions and to meet mission needs under autonomous operations what would we enhance?

What are the physical limits of the human body? What are the physiologic barriers that need to be overcome to produce a superior fighting force? And what are the ethical limitations of such augmentations? Can an ideal physiologic state be achieved that is rapidly induced? Reversible without consequence? Applicable and acceptable to the average military recruit? Increases confidence? And improves the potential for mission success?

The body is constrained by a number of simple physiologic needs. These needs are those activities that we do daily to sustain life, such as sleeping, eating and health maintenance. They are cyclic in our daily lives; they are renewing and rejuvenating. In reality and more importantly they are the limiting factors for optimized performance. Is the body an input / output system with predetermined requirements for maintenance? Does the body need to be rebooted each morning after sleep with fresh sources of nutrients to meet the energy requirements of the system? Does the body require time to heal following minor injury? Can healing times be shortened? Can pain be controlled without a reduction in performance? How far can we enhance physical performance in the area of strength and endurance beyond the level of training? Can energy sources for metabolism be switched to provide extended periods of physical exertion without periodic episodes of hypoglycemia? Can the need for sleep be removed from the picture without a concurrent reduction in decision-making ability, cognitive capabilities or physical performance? Can response times be enhanced for short periods? Can we control cellular metabolism and physical performance under environmental extremes? Can we produce new products needed for treating traumatic injury that defeat the logistics constraints of the battlefield? Can we reduce metabolic requirements within the body following injury in a reversible manner that allows us to transport and triage the injured without time constraints?

If you ask a simple set of questions about the limitations of the soldier in the field you can start to define the areas where significant advantage can be gained. If you ask what factors result in poor or unfocused decision making and contribute to mortality you find areas needing additional investigation and potential solutions to the problem.

Have you ever stayed awake for 24 hours? For 48 hours? For 72 hours? Or longer? How did you feel as time progressed? How well did you function? How was your performance at both the physical and mental level? Did you make good decisions? Could you make good decisions? Could you perform intense physical activity? Could you maintain focus and respond to the world around you? What did you want to do more than anything else in the world? Sleep.

Can we remove the need sleep for periods of up to one week without a reduction in our ability to process sensory input, make decisions and respond to the external environment with focus and intention?

John Carney's Continuous Assisted Performance (CAP) is a DSO program looking at just that. The vision some of you may have at this moment is that of the "Eveready Bunny that just keeps going and going and going" but what we want is

that rabbit to know where it is going, when to go there, how to get there, what to do when it arrives, and then to do it exceptionally well.

Most of us will agree that the warfighter is significantly and continuously stressed during operations, which minimizes their ability to sleep adequately. The concept of a good night's sleep is neither realistic nor practical. If we remove sleep as a performance factor for the warfighter, continuous operations are possible and the tempo for those operations is accelerated. The need for sleep is a significant limiting factor, by removing it an immediate advantage is gained in the form of a force multiplier. While the thought of working three eight-hour shifts for several days does not appeal to most of us; it is the pace required to gain a significant advantage.

CAP has four major research thrusts to reduce the need for sleep and more importantly to increase cognitive performance. They focus on: preventing changes seen in the brain that are caused by sleep deprivation; methods to expand or optimize available memory space within the brain to extend performance; methods to reverse changes in the brain caused by sleep deprivation; and methods to train problem solving circuits within the brain that are sleep resistant. Neuroscience has gotten to a place where we can examine these needs in terms of real solutions based on the underlying mechanisms within the brain.

How can we maintain the interconnections of neurons and increase long-term potentiation within the hippocampus to enhance short-term memory? Can we target receptor distribution and stimulate selectively the production of receptors that improve recall? Can we identify physical and pharmacologic agents that enhance learning and recall by selectively enhancing limited growth of critical neurons? Can we identify those endogenous factors that allow some of us to exist on very little sleep while everyone else requires a standard eight hours of sleep?

If we look to the world of biology what types of models exist for answering these questions? Are circadian cycles obligatory? The recently developed ENU mouse, born without a clock, suggests that they might not be; so why do we get jet lag. Is REM sleep required for normal functioning and memory? Recent work in marine mammals indicates that they lack REM yet have high cognitive abilities. Marine mammals, in particular the whales and dolphins demonstrate hemispheric sleep. They sleep on half the brain and then switch to the other half at intervals. We can all recognize the number of cetaceans that would drown if they fell asleep while swimming. If we lose synapses is it bad for memory? The hibernating arctic ground squirrel loses about one third of their synapses during the winter period but on awakening rapidly grows them without cognitive losses. Can these evolved adaptive mechanisms be incorporated into the human body when needed?

The rapid expansion of fundamental knowledge in neurosciences and molecular biology affords an opportunity for developing new pharmaceuticals and nutraceuticals for dealing with sleep and cognition. New noninvasive techniques for functional visualization and evaluation of the brain has given us a new set of maps for looking at critical areas in the brain associated with the need for sleep. While every college student and medical resident in the country would appreciate the outputs of the CAP program the end user remains the warfighter.

Coupled to this DSO has also recognized the need for changing concepts of energy utilization by the body. If we can keep you awake and alert for a week, your body will need to adapt to a new set of nutritional requirements based on the extended period of physical activity. How do you provide the warfighter with the capability to do continuous aerobic activity for three to five days with a minimal intake of food without experiencing intermittent bouts of hypoglycemia. The consequences of hypoglycemia can be catastrophic on the battlefield at environmental extremes. Hypoglycemia results as glycogen stores become depleted from muscle after about three hours of continuous aerobic activity. Runners refer to it as "hitting the wall" cyclists call it "bonking" regardless of its name it results in loss of muscle strength, a potential for cramping, and as it worsens a loss of mental focus and a general feeling of hopelessness. This seedling known as "Muscle and Mitochondria" is looking for methods to rapidly and selectively switch cellular energy sources from carbohydrate to lipids. It asks some fundamental questions about slow twitch muscle fibers and their resident mitochondria. Since mitochondria are prokaryotes, bacteria that moved into a nucleated cell, and are the major source for generating high energy phosphates in the form of ATP; can the cytosol of the cell be treated as enriched bacterial culture media and can we get the mitochondria to increase in number and efficiency? Can we change what mitochondria metabolize and affect their efficiency to use the more abundant fat stores in our body? We know that endurance athletes have greater numbers of mitochondria per cell. We know that these mitochondria metabolize carbohydrates and lipids more effectively than the standard couch potato. We also know that mitochondrial numbers go down during certain common infections and then recover. So how do we transition the average soldier into an Olympic level endurance athlete on demand? We will probably measure program success by a total ban of the method by the International Olympic Committee. By coupling cellular energetics to continuous performance we provide a more complete system for providing the 24/7 soldier.

A third area of interest focuses on changing the way we perceive and provide medical care on the battlefield. If the description of the "objective force warrior" is accurate; we will see small autonomous units far forward in the field of conflict without any proximity to sophisticated medical care. Secondly, smaller units will become dysfunctional if they lose even a small number of their

compliment. So the question is simple how do you provide the potential for self-aid in the field and at the same time allow that far-forward soldier to continue fighting to achieve mission success?

Can we picture the self-healing warfighter and meet their needs in the field? Kurt Henry's program, "Persistence in Combat" (PIC) intends to do just that. The first questions that need to be answered are what types of injury or circumstances remove the soldier from battle. Obviously, fatal and serious wounds, but what keeps the soldier who is not critically injured from continuing. The two most frequent causes of incapacitation are acute hemorrhage and acute intractable pain. If the injury is not life threatening can the soldier when injured self-administer and care for their wounds. To achieve this PIC has asked some basic questions on controlling hemorrhage and shock. Are there mechanisms other than compression for controlling bleeding? There is evidence that certain neural mechanism may contribute to the clotting cascade that may be rapidly inducible and effective in non-compressible hemorrhage. Are there other methods for controlling bleeding that are quick and portable?

A second area of interest looks at how we currently treat hemorrhagic and septic shock. Is Lactated Ringer's Solution the best product we have for fluid replacement? It is tried and true and every medical student knows its benefit and how to use it. After 100 years of service it still works. But just when was the last improvement in fluids made and submitted for to the FDA for approval? With new advances in understanding the cellular and molecular mechanisms associated with shock is there anything better? A number of studies are anticipated to evaluate alternative energy sources during shock that should provide greater protection to an injured soldier against multiple organ failure.

Pain is the other area that needs significant attention. Morphine works well to control acute pain but in non life threatening injuries it may remove the soldier from continuing in combat by reducing alertness and coordination. Are there other long acting pharmaceutical or physical methods for controlling pain? Are methods such as acupuncture adaptable to the warfighter's needs? Are there methods for pretreating for pain that do not reduce mobility, cognition and attention that can be used prior to entering into combat?

PIC is asking serious questions about healing and how to accelerate that process. The program is focusing initially on reversing the adverse effects of laser on the retina and reducing both the immediate and long-term consequences to pilots. There are a growing number of laboratories that are evaluating light sources as a way to enhance healing. Such a portable system could be applied immediately in the field to reduce convalescence and maintain far forward troops in an optimal state

of physical readiness. Enhanced healing, stabilization prior to the onset of shock, pain control and rapidly controlling hemorrhage are key areas of the program.

The Metabolic Engineering for Cellular Stasis Program (ME) is the last program that looks at enhancing human performance. Its focus is to reduce the logistics burden associated with providing stable blood and blood products to the battlefield. Currently by the time we can move 1000 units of blood the need is gone. We cannot move platelets at all because of the stability of the product so we do without. ME explores naturally occurring models of cell survival under adverse conditions, especially desiccation. To date we have successfully stored platelets in a desiccated state for about a year with outstanding in vitro responses. Animal studies are underway at this time and hopefully the in vivo results will be comparable. Studies looking at RBCs have just started and we are looking at storing nucleated cells using similar methods. At present the two most promising technologies for desiccation of cells involves the incorporation of the disaccharide, trehalose into the cell. This was accomplished by identifying the membrane phase transition points and incubating the cells with trehalose at this temperature. At the membrane phase transition temperature the membrane becomes semipermeable to small molecules as the lipid bilayer goes from a crystalline to gel phase. The second successful method has been to place cells in a glycan which appears to stabilize the membrane during desiccation. I am hopeful that by the end of the program, platelets will be at FDA; RBCs will be in animal trials and nucleated cells will be close to complete.

This program is also looking at animal models that show survival in the extremes; and are able to enter hypometabolic states for extended periods without consequence. Deep diving marine mammals demonstrate the diving reflex which lowers heart rate, regionalizes blood flow and allows the animal to be without oxygen for about thirty minutes. This response is seen in children who fall into cold water and even after 20 or 30 minutes are revived without long-term consequence after becoming hypoxic. Can we induce this response in injured soldiers or expand our ability to survive without oxygen for short periods. It is also looking at hibernation models and trying to identify functional protein products that seem to protect hibernators during cold exposure and reduced nutrient availability. Can these methods be used to induce a state of suspended animation in the injured warfighter and allow transportation and triage to occur after the area is determined to be safe?

The last goal of the program is to look at the regulation of adult stem cells and determine if they can be called into play when needed. The question is fairly simple can we make an injured adult heal like a two year old? The difference between the two ages is the number of mesenchymal stem cells found in the bone marrow. Can you regulate these numbers when needed to facilitate healing?

One clear example of a new technology application that has come out of ME is the development of a non contact electrode that is capable of detecting bioelectrical potentials at a distance of several centimeters. This device lets you look at heart rate and an electrocardiogram without having an electrode or ground attached to the patient. It can be incorporated into vests, litters, blankets or whatever surface you have. It will work if the patient is wet or dry, burned, traumatized or completely healthy. Enhancing performance includes monitoring the benefits of the enhancement.

The concept of enhancing human performance obviously has benefit to both the warfighter and the mission. The ability to provide a force multiplier, increase the tempo of operations, incorporate self aid and think about suspended animation for improving survival of the seriously injured provides the military with a unique set of advantages. Perhaps the slogan "be all that you cab be" should be enhanced with the phrase "and a lot more."

DARPA Tech 2002

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