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Enhancing Human Performance in Combat

What do we ask of 18-to-24-year-old warfighters going into combat to defend the United States? We ask them to be mentally alert, physically fit, highly trained in the use of 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. We ask them to carry 85 to 140 pounds of equipment for extended periods over extended distances on unfamiliar and difficult terrain while exposed to 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 3 to 5 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 with limited available supplies and then to continue with the mission objectives.

Imagine if science and technology could provide the competitive edge to the Objective Force Warrior that would ensure mission success and reduce combat fatalities. By asking a simple set of questions about the limitations of the warfighter in the field, we can begin to define the areas where significant advantage can be gained.

If we ask what factors result in poor or unfocused decisions and contribute to mortality, we find several areas needing additional investigation:

- Need for sleep
- Effects of sleep deprivation
- Need for additional calories as food
- Traumatic injury in the field

Today, I am going to describe four program areas in DSO aimed at enhancing human performance in combat. They are:

- Continuous Assisted Performance (or CAP)
- Metabolic Dominance
- Persistence in Combat (or PIC)
- Metabolic Engineering for Cellular Stasis (or ME)

Have you ever stayed awake for 24 hours?

Even longer?

How did you feel as time progressed?

How well did you function?

How was your performance at both the physical and mental levels?

Did you make good decisions?

Studies have shown that sleep deprivation results in poor judgment and lowers physical performance. The ability to maintain focus and respond to the world around you is lessened, and these are precisely the attributes that a warfighter needs most. The need for sleep is a significant limiting factor for the warfighter, and, by removing it, an immediate advantage is gained in the form of a force multiplier. Continuous operations are possible, and the tempo for those operations is accelerated.

Imagine if we could remove the need to sleep for periods 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.

You might be envisioning the Energizer Bunny that just "keeps going and going and going." But what we want is for the 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.

CAP has four major research efforts underway to reduce the need for sleep and, more importantly, to increase cognitive performance during periods of sleep deprivation. The CAP Program focuses on:

- Preventing changes seen in the brain that are caused by sleep deprivation;
- Expanding or optimizing available memory space within the brain to extend performance;
- Rapidly reversing adverse changes in the brain caused by sleep deprivation; and
- Developing 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. The CAP Program will focus on maintaining the interconnections of neurons within the hippocampus and increasing long-term potentiation. Because the hippocampus is the memory center of the brain, one goal of this work is to enhance short-term memory.

Selectively stimulating the production of receptors that improve recall and controlling receptor distribution will augment cognitive ability. The process includes identifying physical and pharmacological agents that can improve learning and recall. Additionally, we will identify endogenous factors that allow some people to function on very little sleep, while others require a standard 8 hours.

If we look to the world of biology, what types of models exist for answering the question: Why do we need sleep?

We can start with looking at circadian cycles. Circadian cycles are what tell us we should be awake during the day and asleep at night. Are circadian cycles obligatory?

The recently developed ENU mouse, born without a circadian clock, suggests they might not be. These mice sleep randomly, yet still function normally.

Another area of interest is type of sleep. Is REM sleep required for normal functioning and memory? Recent work in marine mammals indicates that they lack REM sleep, yet have high cognitive abilities. Marine mammals, in particular whales and dolphins, demonstrate hemispheric sleep. They sleep on half the brain and then switch to the other half at intervalsa, critical behavior when you are an air-breathing mammal sleeping in water.

If we lose synapses is it bad for memory? If you recall, a few minutes ago, I explained that synapses are the interconnections between neurons that are thought to aid in maintaining short-term memory. The hibernating arctic ground squirrel loses about one-third of its synapses during the winter every year, but on awakening, rapidly regrow them without cognitive losses.

How do scientists measure ground squirrel cognitive ability? I think they use the ground squirrel's ability to complete the New York Times crossword puzzle. Imagine if humans could function without a circadian cycle, sleep on only half our brains, and rapidly produce additional neural synapses.

The rapid expansion of our fundamental knowledge in neuroscience and molecular biology affords an opportunity for developing new interventions 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 that are associated with the need for sleep. By using innovative approaches that integrate animal models, technology and neuroscience, we hope to remove sleep as a limiting factor in wartime performance.

While every college student and medical resident in the country will appreciate the outputs of the CAP Program, the focus of this project remains the warfighter. If kept awake and alert for a week, the 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 3 to 5 days with a minimal intake of food without experiencing intermittent bouts of hypoglycemia? The consequences of hypoglycemia—loss of muscle strength, a potential for cramping and as, it worsens, a loss of mental focus and a general feeling of hopelessness—can be catastrophic on the battlefield.

DSO recently funded a seedling effort known as Metabolic Dominance to investigate new methods for rapidly and selectively switching cellular energy sources from carbohydrate to lipids. It asks fundamental questions about nutrition and energy metabolism.

A primary area of interest for this project is mitochondria. Mitochondria are prokaryotes. Like bacteria, they have formed an interactive relationship with the nucleated cells in our body and have assumed the function of generating high-energy phosphates in the form of ATP, which we use as an energy source.

As with other programs, we once again look to what we know to occur in living organisms. The data show that endurance athletes have greater numbers of mitochondria per slow twitch muscle fiber and the athletes' mitochondria metabolize carbohydrates and lipids more effectively than the mitochondria of the average "couch potato."

We also know that the number of mitochondria in our cells decrease during certain common infections, but increase in number once the infection is gone.

The key to enhanced utilization of mitochondria as an energy source relies upon our ability to manipulate mitochondrial function.

What we would like to know is if the cytosol of the cells can be treated as enriched bacterial culture media enabling us to increase the number and efficiency of mitochondria per cell? Can we change what mitochondria metabolize and affect their efficiency to use the more abundant fat stores in our body?

By engaging cellular energetics during continuous performance, we may be able to transition the average warfighter into an Olympic-level endurance athlete during periods of intense combat.

So far, we've discussed projects addressing problems associated with disruptions in sleep patterns and the resulting changes in nutritional requirements. However, during battle, physical injury is always a potential problem.

A major area of interest for the military 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 proximity to sophisticated medical care. We know these smaller units rapidly become dysfunctional if they lose even a small number of their complement. So, we must address the problem of how we can keep these warfighters functional until replacements can be recruited.

What factors keep the warfighter who is not critically injured from continuing in combat? The two most frequent causes of incapacitation are acute hemorrhage and acute intractable pain.

If we can enable an injured warfighter in a far-forward unit to provide self-aid in the field that will allow them to continue fighting until help can be recruited, we may be able to minimize overall casualties. Kurt Henry's program, Persistence in Combat (PIC), intends to address several issues pertaining to field injuries.

Determining techniques that can enhance healing, control hemorrhage, stabilize the warfighter before the onset of shock, and control pain will empower warfighters in the field to address critical medical needs without the need for a medic. PIC is asking serious questions about healing and how to accelerate that process.

The program is focusing initially on reversing the adverse effects of lasers on the retina and reducing both the immediate and long-term consequences to pilots. The program will be expanding, however, to investigate new methods for increasing survivability and effectiveness by treating injuries with a minimum of external care. A growing number of laboratories 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.

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, after 100 years of service, it still works. But just when was the last improvement in fluids made and submitted to the FDA for approval?

Are there mechanisms other than compression for controlling bleeding? There is evidence that certain neural mechanisms might contribute to the clotting cascade that could be rapidly inducible and effective in noncompressible hemorrhage. Imagine the increase in activity and ability if other methods for controlling bleeding that are quick and portable are used.

With new advances in understanding the cellular and molecular mechanisms associated with shock, is there anything better than the current treatment of rapid expansion of the interavascular fluid volume, steroids and antibiotics? A number of studies are anticipated that will evaluate alternative sources of energy that can be utilized during shock and provide greater protection to an injured warfighter 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 might remove the warfighter 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?

Could we pretreat for pain before entering into combat so mobility, cognition, and attention will not be reduced if injury occurs?

There are many issues yet to be addressed in the field of combat medicine. We hope that by improving existing technology, we can provide warfighters new options for addressing injuries that occur during combat.

The last program I want to discuss today is Metabolic Engineering for Cellular Stasis (ME). This program focuses on:

- Improving our ability to transport blood products into combat situations;
- Selectively moderating our body's oxygen utilization;
- Understanding the physiology of hypo-metabolic states; and

- Developing methods for enhancing healing.

Currently, the logistics burden associated with providing stable blood products to the battlefield is overwhelming. By the time we can move 1,000 units of blood, the need is gone. Red blood cells must be kept frozen and transported with their liquid component, making them very heavy and impractical in the combat environment. Under ideal circumstances, platelets last only about 5 days; thus, due to their instability, we do not transport them into combat at all.

To address these problems, ME is exploring 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 and, hopefully, the in vivo results will be comparable. Studies looking at desiccating red blood cells have just started, and we are looking at storing other nucleated cells using similar methods.

At present, we have two promising technologies for desiccation of cells. The first involves the incorporation of the disaccharide trehalose into the cell. The second successful method has been to place cells in a glycan that appears to stabilize the membrane during desiccation.

I am hopeful that by the end of the program, desiccated platelets will be passing regulatory review at FDA, desiccated RBCs will be in animal trials, and the desiccation process for other nucleated cells will be close to complete. Imagine lightweight, easily stored, and transported blood as well as other cells that can be carried with personal gear and reconstituted when needed by personnel in combat situations.

Another goal of the ME program is to enhance our ability to utilize hypometabolic states. Utilizing animal models, we are studying how some animals routinely enter hypometabolic states to enhance their survival under extreme environmental conditions. Deep-diving marine mammals demonstrate a diving reflex that lowers heart rate, regionalizes blood flow, and allows the animal to be without oxygen for about 30 minutes.

A similar response is also seen in children who fall into cold water and are hypoxic for 20 or 30 minutes. These children have been revived without long-term consequence.

Can we induce this response in injured warfighters or expand our ability to survive without oxygen for short periods? We are also looking at various animal hibernation models and trying to identify functional protein products that seem to protect these hibernating animals 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 2-year-old? The difference between the two ages is the number of mesenchymal stem cells found in the bone marrow. Imagine if we could upregulate these cells needed to facilitate healing.

One example of a new technology application that has already come out of the ME program is the development of a noncontact electrode that is capable of detecting bioelectrical potentials at a distance of several centimeters. This device lets us 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 we have. It will work if the patient is wet or dry, burned, traumatized, or completely healthy. Imagine a stethescope-like device that lets the physician to listen to the heart and see the EKG simultaneously.

Future endeavors should focus on methods and technologies to train a person to regulate his or her own immune system when injured or challenged. Such an approach would incorporate multiple DSO programs for the ultimate benefit of the warfighter—self-enhancing, self-healing, and adaptable to any environment.

The concept of enhancing human performance obviously has benefit to both the warfighter and the mission. Imagine the combat advantage we could achieve if we can provide a force multiplier, increase the tempo of operations, enable warfighters to provide self-aid, and utilize hypometabolic states to improve survival of the seriously injured.

Perhaps the slogan "be all that you can be" should be enhanced with the phrase "and a lot more."