

## **US Department of Veterans Affairs: Brain Monitoring Research**

*This research is defining how to monitor and classify the brain dysfunction that occurs in 70 percent of critically ill patients, determining its epidemiology in the aging population at risk for ICU admission, and the role that sedatives and analgesics play in causing these debilitating deficits.*

### **Lead Agency:**

US Department of Veterans Affairs

### **Agency Mission:**

*"To care for him who shall have borne the battle and for his widow and his orphan."*

### **Principal Investigator:**

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### **Partner Agency:**

Alliance for Aging Research (AFAR)  
John A. Hartford Foundation  
National Institutes of Health; National Institute on Aging (NIH/NIA)  
Veterans Health Administration  
Tennessee Valley VA Health Care System

### **General Description:**

This research is the outgrowth of an unmet need in critical care medicine regarding the exceedingly common occurrence of (a) delirium (acute brain dysfunction) among patients, predominantly of advanced age, treated in intensive care units (ICU) and (b) the associated long-term cognitive impairment that occurs in over half of ICU survivors. Every day, over 40,000 ICU patients in the United States alone are suffering from delirium. This problem is getting larger every year due to the aging of the population and the immense growth of critical care beds. Traditionally, ICU delirium was called "ICU Psychosis," and professionals had erroneously not thought it to be clinically significant.

Using clinical tools designed and validated through the VA Geriatric Clinical Research Education Clinical Center (GRECC) and at Vanderbilt University, the *ICU Delirium and Cognitive Impairment Study Group* ([www.icudelirium.org](http://www.icudelirium.org)) has now shown that delirium is associated with a tripling of the risk of death within 6 months of ICU admission. They have further shown that delirium occurs in about 50 to 80 percent of ICU patients. Even considering other factors such as age, severity of illness, duration of coma, and the use of psychoactive medications, every day spent in delirium by ICU patients was associated

with a 10 percent higher risk of death and a 35 percent increased risk of long-term cognitive impairment among survivors. The occurrence of ICU delirium is also associated with dramatically higher hospital costs of over \$25,000 U.S. dollars per patient when comparing those with mild vs. severe courses of delirium, and this doesn't include the added costs and family burden of having patients unable to return home due to the ongoing neuropsychological deficits that we are finding in the majority of younger and especially older survivors. We are only now learning about the relationships between the ICU delirium and the longer-term neuropsychological problems that plague ICU delirium survivors.

Awareness of these issues is reaching a tipping point among the medical and lay community. Thousands of ICUs around the world are now implementing routine bedside monitoring of all ICU patients for arousal levels and delirium based on the above mentioned facts. In addition, there is growing interest in post-ICU specialty clinics to help patients and families deal with the unique constellation of acquired problems involved in returning to a functional and whole human being. The tools available from this research (e.g., a sedation scale called the Richmond Agitation-Sedation Scale (RASS) and a well-validated and easy to conduct delirium instrument called the Confusion Assessment Method-ICU (CAM-ICU), as well as a new "wake up and breathe ABC sedation protocol" that is proven to save 1 life for every 7 patients so treated) have been translated into over 14 languages and international guidelines have recommended delirium monitoring as standard of care. Ongoing clinical trials are now exploring the safest and most effective ways to prevent and treat ICU delirium in hopes that treatment will not only reduce delirium but also the high morbidity and mortality associated with it.

***Excellence:                   What makes this project exceptional?***

Every day, 30,000 to 40,000 people in ICUs are suffering from delirium with potential devastating, long-lasting effects on how their brain will work and a higher chance of death. Once doctors and nurses in the ICU are aware of this problem, they can look out for it, perform simple bedside tests and take steps to reduce or maybe prevent it. The longer a person is delirious, the more likely they are to die.

***Significance:                   How is this research relevant to older persons, populations and/or an aging society?***

Critical Care Medicine is a young field of Medicine, with early ICUs in this country appearing in the 1960s and not routinely being available in most hospitals until the 1970s. Survival rates for many critically ill conditions have shown striking increases, even without evidence of clinical trials of specific therapies showing objective benefits. Many more critically ill patients are now surviving and, in the last decade, it has become clear that these survivors of critical illness have a burden of illness that was previously unrecognized. This was first demonstrated by studies of the self-assessed quality of life in ICU survivors. Initially this finding was puzzling as the function of the failing organ resulting in critical illness often (usually) returned to normal or near-normal. This has been best studied in patients with acute lung injury (often only the most prominent and most severe clinical manifestation of multiple organ failure) where lung function returns

to normal or near normal within 6 months whereas significant decrements in health-related quality of life persisted for years.

Subsequent work has demonstrated that the most severe abnormalities in these critical illness survivors are in three related areas: neurocognitive deficits; psychological disorders (depression, post-traumatic stress disorder and other anxiety conditions); and neuromuscular abnormalities. We call this the post-ICU syndrome. Again, in the case of acute lung injury patients, a careful study showed that the majority of patients at one year following ICU discharge had neuropsychological abnormalities and 100 percent had significant neuromuscular complaints accompanied by objective findings. It would be difficult to over-exaggerate the magnitude of this problem; it is clearly one of public health importance. One of the major issues is that no medical discipline has owned this problem and taken responsible action on it. Although it came to light largely through the efforts of critical care investigators, critical care physicians rarely follow these patients once they leave the ICU. Primary care physicians, who will be following the great majority of these victims, are almost completely unaware of these abnormalities and they usually go unrecognized. Finally, rehabilitation specialists and psychiatrists have not been aware of these morbidities nor involved in their evaluation or management in any meaningful and organized way.

***Effectiveness:                   What is the impact and/or application of this research to older persons?***

This work will define the approach over the next 30 to 40 years to preserving the minds of the millions of older patients who plan to live productive and functional lives well into their 80s and 90s but who, along the way, will have to sustain care in an ICU for some length of time as they overcome an unexpected critical illness.

***Innovativeness:               Why is this research exciting or newsworthy?***

In summary, the problem of post-ICU syndrome is one of public health proportions, has enormous clinical, economic and societal consequences, and yet the problem is largely unrecognized or is being ignored by the medical community. This is a problem which is ripe for attention and intervention, and yet interventions are not going to be funded through the NIH RO1 mechanism. The science of each of the components of the morbidity is not mature, an intervention would by necessity be complex, and preliminary data regarding interventions are lacking; combined, these result in a kiss of death for conventional NIH funding mechanisms, ensuring that the problem will continue over decades. A fresh, innovative, necessarily “high-risk” approach is required to jump start therapeutic solutions to this immense health problem.