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Emergence Delirium in U. S. Military Combat Veterans

by

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Abstract

This dissertation study examined the phenomenon of emergence delirium in U. S. military combat veterans. Emergence delirium is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia and is characterized by agitation, confusion, and violent physical and/or verbal behavior. Clinical evidence suggests that emergence delirium is occurring with greater frequency among military personnel returning from conflict in the Middle East. This body of work is a culmination of three distinctive phases and is presented in three individual manuscripts. The first manuscript, *"Risk Factors for Emergence Delirium in U. S. Military Members,"* was published in the Journal of PeriAnesthesia Nursing with the purpose of concept development surrounding the risk factors for emergence delirium. Since this was the first time this phenomenon had been explored, it was important to present it in the form of a literature review. The second manuscript entitled, *"Content Validation of the Pediatric Anesthesia Emergence Delirium Scale for use in Adults: A Survey of Nurse Anesthetists Regarding the Concept of Emergence Delirium"* described the results of a mixed method study conducted to define the concept of emergence delirium in adults, while content validating a pediatric instrument for its use in the adult population. The results suggested that the Pediatric Anesthesia Emergence Delirium Scale was a valid instrument for use in clinical research with adults. Finally, the third manuscript entitled, *"The Incidence of and Risk Factors for Emergence Delirium in U. S. Military Combat Veterans"* was written to present the findings of an observational, prospective, and correlational designed study to discover the incidence of emergence delirium in a sample of 130 combat veterans undergoing surgery at one military treatment facility. The results suggested that anxiety,

depression, and posttraumatic stress disorder are risk factors for emergence delirium; the overall incidence was 20%.

Dedication

This work is dedicated to all U. S. military veterans, both past and in the future. Their unwavering dedication and love for their country is unlike any I have ever known. They sacrifice so much: their health and well-being, time away from family and friends, the hardships of deployment, and sometimes, their lives. Their sense of service inspires me to ask the questions and to find the answers to the problems that affect their health and the health of their loved ones. They deserve this and so much more. Thank you for allowing me to serve by your side. I am eternally grateful for the freedom you provide my family, this wonderful country, and me. Semper Fi, Hooah, Ooh-rah, Hooyah, and Go Navy!

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I would like to acknowledge the entire faculty and staff of the University of San Diego Hahn School of Nursing and Health Science. I am forever grateful for their contribution to my education as a nurse scientist and for the generous financial contribution as part of the 2009 Dean's Scholar Research Award. I will not let you down through my service to our patients and this country.

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Chapter 1: PROBLEM

Significance

Deployment stress and exposure to combat are real-world events that are having a profound effect on our current U.S. military population as they continue to support combat operations in Iraq and Afghanistan. As a result, the incidence of major depression, generalized anxiety, and PTSD range from 11-17% in those that return from combat.[1] More recently, it was shown that 69% of veterans of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) being treated at one Veterans Administration (VA) hospital suffer from severe mental health problems.[2] In many instances the psychological cost is immeasurable since many symptoms of mental health disorders frequently go unrecognized and undiagnosed.

A renewed interest in Emergence Delirium (ED) has developed among military nurses, and anesthesia providers due to its increasing incidence among the U. S. military surgical population. Anecdotally, many combat veterans emerge "combative" from general anesthesia. In fact, the results of a survey of military nurse anesthetists who care for veterans of combat suggest that there may be a relationship between a documented psychiatric history and combative/ disoriented behavior following emergence from general anesthesia (J. M. McGuire, MS, CRNA, unpublished data, August 2009). The disorientation and violent thrashing that accompanies this clinical condition creates a dangerous situation for both patient and health care provider. Potential for injury exists as

patients' extremities thrash about and make contact with hard surfaces (e.g., side rails, operating/recovery room equipment). Venous and arterial catheters may be dislodged, interfering with the ability to provide emergency care. Surgical wound dehiscence and bleeding are potential complications of continued involuntary physical activity. Quality of care is compromised when staff struggle to protect the patient, while risking injury to themselves. Nursing resources are stretched because multiple personnel and additional time are required to mange patient care safely and effectively under these circumstances. From the perspective of the military health professional, ED has become an emerging health concern.

A study by Smith and colleagues[3] identified the psychological indicators of executive functioning and depression as independent risk factors for delirium in the post-operative period. These psychological indicators being predictive of ED specifically, has not been studied. Nocturnal panic attacks serve as borderline cases of delirium seen upon emergence from anesthesia in that they contain many of the same defining attributes of ED. It has been demonstrated that individuals with higher levels of anxiety and depression present with a higher incidence of nocturnal panic upon wakening from normal sleep[4]. In a patient with known PTSD, a case of emergence flashback was observed upon emergence from anesthesia, serving as an additional borderline case of ED[5]. It has become apparent that an investigation should be conducted to discover the relationship anxiety, depression, and PTSD may have with the incidence and severity of ED.

Data has indicated that returning U. S. veterans have a higher rate of anxiety, depression, and PTSD than the "normal" population.[1] Taking this into account, as well as

the seemingly large increase in ED described by clinicians (J. M. McGuire, MS, CRNA, unpublished data, August 2009), it is not difficult to hypothesize that a potential relationship may exist between these factors and ED. Evidence of other types of delirium as predicted by changes in cognitive function and depression adds support to this hypothesis[3].

Purpose and Specific Aims

The purpose of this study was to determine the incidence of ED, and to measure anxiety, depression, and Post Traumatic Stress symptomatology, and to the extent to which these would predict ED in a population of combat exposed U. S. military personnel. Specific aims were to determine the pre-operative level and predictive power of 1) anxiety as measured by the State-Trait Anxiety Inventory (STAI); 2) depression as measured by the Patient Health Questionnaire (PHQ-9); 3) PTSD symptomatology as measured by the Post-traumatic Stress Disorder Checklist – Military (PCL-M); for the incidence of ED in a sample of combat exposed military members at one medium-sized military treatment facility (MTF). The Pediatric Anesthesia Emergence Delirium (PAED) Scale measured the incidence and severity of ED.

Secondary aims were to determine the relationship between demographics, level of pain, type of surgery, length of surgery, and the number of surgeries to the presence of ED in this population. In addition, examination of reliability of the PAED Scale was be conducted through inter-rater reliability testing and an estimation of internal consistency (Cronbach's alpha).

Hypotheses

1. The incidence of ED will be identified in this population of combat veterans, which will be higher than the reported incidence in the general adult population.
2. STAI scores will predict the incidence of ED in this population of combat veterans.
3. PHQ-9 scores will predict the incidence of ED in this population of combat veterans.
4. PCL-M scores will predict the incidence of ED in this population of combat veterans.
5. Demographics such as age, number of deployments and a known history of psychiatric conditions will correlate with the incidence of ED in this population of combat veterans.
6. Increased levels of pain, increased length of surgery, increased number of surgeries, and type of surgery will correlate with the incidence of ED in this population of combat veterans.

Theoretical Perspective

For the purposes of this study, ED was considered a response to a stimuli or stressor that presents immediately upon emergence from general anesthesia. Thus, Emergence Delirium (ED) is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia and is "characterized by agitation,

confusion, and violent physical and verbal behavior in the operating room (OR) or the post-anesthesia care unit (PACU)."[6] In order to guide the study, Nuechteriein and Dawson's Heuristic Vulnerability/Stress Model was used.[7] Nuechteriein and Dawson used this model to study variables that might contribute to the development of acute psychotic episodes in schizophrenics. Their theory indicated that there are many possible individual factors that interact and contribute to the development of psychotic symptoms.[7] As applied to this study, the application of the vulnerability model theory described how the variables of combat zone deployment, anxiety, depression, and PTSD symptomatology are related to ED.

Within this model, ED was considered a multidimensional concept containing physiological, psychological, and behavioral components. The factors that contribute to the individual's overall vulnerability is their past combat zone deployment stress. This has caused some degree of autonomic hypersensitivity. Their available processing capacity has potentially been affected by psychological disorders (anxiety, depression, PTSD). Secondary to these factors, their ability to cope has been altered.

The identified environmental stimuli, or mediating variables, that affect the individual were surgery, trauma, and pain. The extent to which these stimuli affect the individual's enduring vulnerability characteristics is also a function of the extent of supportive care available to the individual. The biologic nature of psychological disorders can often affect the individual's coping behavior directly. All of these factors lye on a continuum, each one interconnected and affecting the other.

Service members that have been exposed to combat deployment stress sometimes require general anesthesia as part an elective or required surgical intervention. The general anesthetic, in combination with the individual's present degree of autonomic hyper arousal and processing capacity, is termed the "transient intermediate" state. These are also referred to as the intervening variables (see Figure 1).

Figure 1.

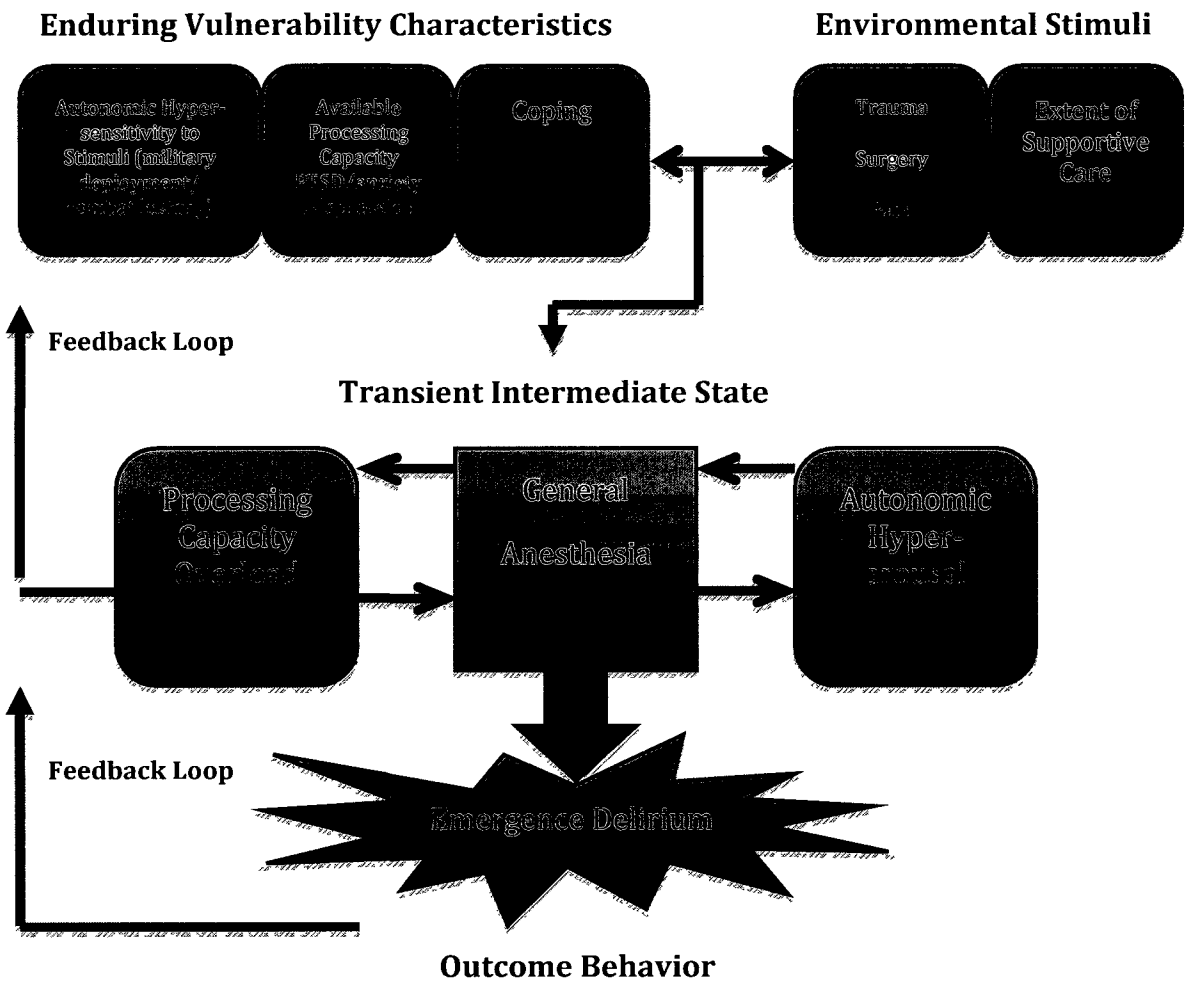


Figure 1. Emergence Delirium Vulnerability Model. Adapted from Nuechterlein, K. H., & Dawson, M. E. (1984). A Heuristic Vulnerability/Stress Model of Schizophrenic Episodes. *Schizophrenia Bulletin, 10*(2), 300-309.

This theoretical perspective, using a vulnerability model, provided a useful way in which to envision the unique characteristics of combat veterans and how they may develop ED. Vulnerability models have been used to describe many different types of stress and how they impact individuals and their susceptibility to mental health problems. Aldwin and Revenson[8] suggested that a vulnerability model closely describes the economic stress imposed on individuals and the extent to which it increases their susceptibility to mental health problems. This in turn produces the reciprocal effect that declining mental health has on continued economic stress.[8] The reciprocal effect in this study is described by the feedback loops presented (see Figure 1). The intervening variables, also known as transient intermediate states, and the outcome of ED have an effect on the individuals enduring vulnerability characteristics.

Nursing has used vulnerability models in the past to describe the impact of stress on vulnerable populations. The model has been used to describe the perinatal and neonatal populations in the context of their vulnerability to illness by the interaction between genetic and environmental stimuli.[9] The extent of how this interaction determines the individual's susceptibility to illness is an adaptation of the model that has been used to describe how clinical interventions, geared toward prevention, can impact vulnerability.[10]

The application of the Heuristic Vulnerability/Stress Model to this study of emergence delirium in the U. S. military population used four classes of variables identified by Nuechteriein and Dawson[7] and are defined in the following manner:

1. Emergence delirium was the outcome behavior measured.
2. The transient intermediate state consists of the intervening variables, events that occurred immediately prior to the outcome behavior of emergence delirium (general anesthesia, autonomic hyper arousal, and processing capacity overload)
3. Environmental stimuli (mediating variables) influenced both the enduring vulnerability characteristics and the transient intermediate states (trauma, surgery, pain). The potential influence of these was also a function of the extent of supportive care.
4. The enduring vulnerability characteristics are the constructs that make up the combat veteran's vulnerability to the development of emergence delirium. They are the variables: history of combat deployment, PTSD, anxiety, and depression.

Chapter 2: REVIEW OF THE LITERATURE

Background

Emergence delirium (ED) is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia in adults and children. It is characterized by agitation, confusion, and violent physical and verbal behavior in the operating room or the post-anesthesia care unit.[6] An historical search reveals that ED, then a condition known as postoperative psychosis, was first termed and documented in 1819.[11] Muncie[11] believed that nearly all operative interventions and medications are probable causes of ED, further implicating opioids, bromides, fever, pain, and mental disorders as the main causes.

Review of 20th century literature reveals ED has been a phenomenon of research concern since 1960.[12] This era brought about new discussion involving other possible etiologies: cyclopropane, ether, sedatives, and anticholinerics.[6] More recently, a renewed interest has developed among military nurses, anesthesia providers, and surgeons in part due to the apparent increase incidence among the combat exposed U.S. military surgical population. Anecdotally, many combat veterans emerge "combative" from general anesthesia. From the perspective of the military health professional, ED has become an emerging health risk.

Delirium is a disturbance of consciousness involving a cognitive deficit that cannot be explained by a preexisting dementia or mental disorder.[13] According to the *DSM-IV TR*, emergence delirium falls under the subtype of "Delirium Not Otherwise Specified" due to the lack of a clear understanding of its etiology.[13] Wilson and Graves[14] defined ED as "a mental disturbance during the recovery from general anesthesia consisting of hallucinations, delusions and confusion manifested by moaning, restlessness, involuntary physical activity, and thrashing about in bed." Olympio[15] referred to ED as a dissociated state of consciousness where the patient presents as irritable, incoherent, uncooperative, and inconsolable. There are numerous other definitions of ED and these, in combination with definitions of similar but perhaps distinctly different phenomena, lead to confusion as to the etiology of ED, how to recognize it, and how to prevent or treat its occurrence.

Emergence delirium is a phenomenon of great concern to military health care providers working in the peri-anesthesia environment. To understand this one must look at the environmental context in which it occurs. The disorientation and violent thrashing that accompanies this clinical condition creates a dangerous situation for both the patient and the health care provider.[16] The risk of injury greatly increases if ED occurs outside the hospital setting, in austere environments where many military nurses and physicians find themselves caring for post-surgical patients. Even a single episode of delirium can contribute to an overall decline in cognitive function and may increase mortality rate.[17,18] Decreased quality of care is a concern as nurses struggle to protect the patient, all while risking injury to self. Nursing resources are compromised, as it requires multiple

personnel and additional time to mange patient care safely and effectively under these circumstances.

Emergence Delirium in Children

Although there is minimal research of ED in the adult population, there is a myriad of literature that pertains to the pediatric population. The salient literature uses pediatric patients as the study population because the incidence appears to be greater in children (12-13%)[6] as compared to adults (4.7-5.3%).[12,16] The frailty and vulnerability of the pediatric population also gives good cause for this focus. Although there is no single cause for ED, there have been many social, psychological, and biological factors suggested.[19]

Social risk factors have been described as a potential etiology of ED in children.[19] The social interaction between the parent and child is predictive of child behavior, especially surrounding a major event such as surgery and anesthesia. Parental anxiety is a major contributing factor in transference of negative anxious energy to the child,[20] and 90% of parents report being anxious surrounding their child's operative experience.[21]

Anxiety is part of the normal human body's stress reaction and elicits a neuroendocrine response through the central nervous system (CNS). This results in the stimulation of the sympathetic nervous system (SNS) and can contribute to the undesired behaviors representative of ED. It has been suggested that the presence of a calm parent can reduce a child's anxiety level prior to induction of anesthesia.[22] However, their

presence during a child's emergence from anesthesia has not been studied. Parental or caregiver anxiety as a social risk factor for ED in children needs further examination.

Preoperative anxiety is a psychological risk factor linked to ED in children. The assumption here is that the body's normal or pathological stress response, manifesting as preoperative anxiety, translates into an exaggerated stress response immediately following surgery. A history of previously stressful medical encounters can increase a child's anxiety prior to surgery, and further contribute to serious postoperative anxiety, which can manifest as ED.[23] Kain, Caldwell-Andrews, and Maranets[24] discussed a possible link between preoperative anxiety and ED. Preoperative anxiety is a psychological risk factor that may also be of biologic concern. Extreme anxiety that results in an inappropriate stress response clearly has a neuroendocrine component.[25]

Temperament has also been identified as a possible psychological risk factor for ED in children. Although temperament in a child can appear to have some learned social component, those in the field of child psychology believe that it arises from an innate genetic basis.[26] Kain et al.[24] and Voepel-Lewis et al.[27] both conclude that the more excitable, impulsive, and emotional the child, the greater the risk for ED.

Many biological and chemical risk factors have been suggested as possible causes of ED in the pediatric population. The most prominent, and frequently studied, is the rapid emergence from general anesthesia secondary to the volatile inhalation anesthetic used. The speed at which a patient emerges from anesthesia is directly related to the solubility of the anesthetic. If the solubility of the inhalation anesthetic is low, less is absorbed in the tissue, which leads to a faster emergence from the anesthetic. Although

all volatile anesthetics have been implicated as contributing factors to ED, it has been determined that the frequency of its incidence occurs in this order: sevoflurane≈desflurane>isoflurane>halothane. Sevoflurane and desflurane, the most insoluble of all volatile anesthetics, have been implicated as a major causative factor for the incidence of ED in children.[28] Specifically, sevoflurane exhibits CNS stimulating side effects[29] which could lead to post-operative excitement and the development of ED. When compared to propofol, an intravenous general anesthetic, sevoflurane has been shown to have a higher incidence of ED in children.[30-33]

Adjunctive medications used in anesthesia practice are another biological risk factor that have been hypothesized to contribute to the incidence of ED. Anticholinergics, barbiturates, benzodiazepines, droperidol, and metoclopramide can all have direct effects on post-operative behavioral changes and have been associated with emergence delirium in the pediatric population.[34] Individually, none of these medications have been implicated as a singular cause for ED. However, because they have the ability to cause excitement of the CNS, the possibility of their use being a contributing factor cannot be ruled out. For example, midazolam, a common benzodiazepine used peri-opertively in adults and children as a sedative agent, has been associated with severe paradoxical excitement that can result in "restlessness and thrashing about."[35] Further research is required before conclusions can be drawn that adjunctive medications used in anesthesia are causative agents of ED.

Age is hypothesized as a biological risk factor for ED. Martini[36] suggested that the developing child's brain lacks the quantity of neurotransmitters necessary to maintain emotional and neurological equilibrium. This may contribute to their susceptibility to

delirium. A greater incidence of ED has been documented among preschool aged boys under sevoflurane anesthesia.[37] However, as the child ages, the incidence of ED appears to decrease.

Another biological risk factor that has been implicated in the development of ED in children is the type of surgery performed. Surgical procedures in the field of otorhinolaryngology (ENT) have been identified as being an independent risk factor for higher incidences of ED in children.[6,27] However, the past fifty years of scientific inquiry have not been able to explain the relationship between ED and type of surgical procedure performed on a child. Differing surgical procedures are associated with different types of pain experienced by pediatric patients, leading to varying degrees of CNS stimulation and potentially increasing their risk for ED.

Finally, pain is a biological risk factor for ED that has been discussed in the literature. A child in pain emerging from general anesthesia can present as inconsolable, moaning, restless, having involuntary physical activity, and thrashing about in bed, which can confuse the care provider. The presenting symptoms of pain and ED can look strikingly similar. Research suggests that giving preemptive analgesia to pediatric patients greatly decreases the incidence of ED.[38] Giving intranasal an opioid analgesic (fentanyl) has been found to reduce the incidence of ED in children.[39] Alpha-2 receptor agonists (e.g. clonidine and dexmedetomidine), providing both sedative and analgesic properties, have been shown to decrease ED.[40] These studies suggest that there is a relationship between pain and ED. Children's inability to articulate their complaints of pain adds to the difficulty in differentiating their reactions from ED.

Posttraumatic Stress Disorder

The relationship between PTSD and episodes of delirium is recognized in the psychiatric community. PTSD has been both the result and the precursor to delirious episodes.[41,42] Specifically, PTSD as a result of these conflicts maybe directly attributed to the poor physical health of the veterans it affects.[43] There is recent evidence to suggest that the symtomatology of the disorder can be persistent decades after the initial stressful combat event.[44] PTSD is a major health concern not only for the current active duty population, but also for the millions who have served in past U.S. conflicts.

Pediatric Anesthesia Emergence Delirium (PAED) Scale

Sikich and Lerman[45] developed and evaluated the Pediatric Anesthesia Emergence Delirium (PAED) Scale in response to their claim that no reliable and valid rating scale existed to measure ED in children. Their study was divided into two parts, the scale development phase and the scale evaluation phase. In the scale development phase, the investigators collated a list of behavioral descriptions of children thought to have ED through a series of literature reviews on the subject as well as an interview process with clinicians in the fields of nursing, anesthesia, and psychiatry. This resulted in the description of six categories of ED behaviors: cognitive behavior, behavior response to environmental stimuli, behavior threatening patient safety, motor behavior, affective behavior, and vocal behavior.[45] A panel of seven experts preliminarily evaluated 100 participants between the ages of 18 months and 6 years of age in order to test 27 behavioral descriptions. The experts arrived at 21 behaviors that were deemed content

valid. After eliminating statistically invalid items, the authors arrived at five behavioral profiles that comprised the PAED scale. The five behavioral description were: 1) the child makes eye contact with the caregiver, 2) the child's actions are purposeful, 3) the child is aware of his/her surroundings, 4) the child is restless, and 5) the child is inconsolable.[45] This scale was then evaluated on 50 children emerging from anesthesia; testing five hypotheses to determine construct validity. Three of the five hypotheses correlated with the scores obtained on the PAED Scale, representing some validity. The internal consistency and inter-rater reliability was reported at 0.89 and 0.84, respectively, lending reliability to this instrument.

The authors claim that the observed behaviors in the PAED Scale were well developed and added to the content validity because they were constructed from a variety of sources.[45] The 21 behavioral descriptions were obtained through clinician interviews. The content and the philosophical assumptions that guided these interviews were not described, creating a potential source of bias. To determine the validity of the 21 behavioral descriptions, steps should have been taken to describe this aspect of the qualitative study so that it could be effectively reproduced. If an interpretive approach to the study of this phenomenon was utilized, it is not so stated. Since the study was performed from an empirical stance, the reader has to assume that the interview aspect was approached in the same manner. Lack of method description puts the validity of this scale in question.

Previous Research – Validation of the PAED Scale

Before a study examining the prevalence of ED among military members, it was first recognized that one must describe whether or not the phenomenon is of interest to those who care for these patients in the operative environment. In the summer of 2009, a survey-designed study of ED entitled "*Scale Development Survey – Emergence Delirium in Adults*" was conducted with 36 military expert nurse anesthetists that were in attendance at an annual professional meeting. Results indicated that ED occurred in these nurse anesthetists' adult practices among patients with a known history of a psychological disorders and/or combat stress (24%). Additionally, ED was identified as an important phenomenon of interest among this group of participants (100% of sample) (J. M. McGuire, MS, CRNA, unpublished data, August 2009). These nurse anesthesia providers not only witnessed ED in their adult practices, they also reported that they would find an instrument to evaluate ED in this population very helpful (94% of sample) (J. M. McGuire, MS, CRNA, unpublished data, August 2009).

Sikich and Lerman[45] isolated 21 behavioral descriptions of ED in the pediatric population that were deemed valid by a panel of seven experts. For this dissertation research, it was recognized that in order to use the 5-item PAED Scale to assess ED in an entirely different military population, additional content validation would be required (see Manuscript II). Throughout this dissertation, a philosophical perspective was adopted that ED consists of the same behavioral descriptions, regardless of whether in presents in adults or children. After consulting with Dr. Jerrold Lerman (author of the PAED Scale), a study was conducted that included the 21 behavioral responses from Sikich and Lerman's study, using the adult population as the focal point. Findings

showed that the PAED Scale was deemed content relevant for the purpose of identifying ED in clinical research with adults (J. M. McGuire, MS, CRNA, unpublished data, August 2009).

Chapter 3: METHODOLOGY

Design

An observational, descriptive, correlational design served as the method in which to discover the incidence of ED and the relationship between anxiety, depression, and PTSD with ED.

Sample and Sample Size Calculation

A purposive sample consisted of active, reserve, and separated military members with a self-reported history of deployment to a combat zone in support OIF/OEF since the beginning of operations in 2001, and who required surgery in the main operating room at Naval Hospital Camp Pendleton (NHCP). Inclusion criteria included males and females age 18 to 35 years, were able to read and speak English, and who required general anesthesia for surgery. Demographic data was collected on age, ethnicity, marital/relationship status, education, military rank, deployment experience (number of deployments, dates), medications, and self-reported history of psychological disorders (see Appendix).

Based on the purpose of this study, which was to describe the incidence of ED in this population and to identify possible predictive factors (anxiety, depression, PTSD) while adjusting for the potential influence of confounding variables (demographics), multiple

linear regression was used to analyze the data. There is no consensus on the approach to compute the power and sample size with regression modeling; although as pointed out by Katz[46], ten outcomes for each independent variable is appropriate. In linear regression, some assumptions are made about the dependent variable (ED), the relationship is linear, and is normally distributed.[47] Some authors use the likelihood ratio test; some use the test on proportions; some suggest various approximations to handle the multivariate case. Some advocate the use of the Wald test since the Z-score is routinely used for statistical significance testing of regression coefficients.[48] Since this was a descriptive study, the Stepwise Backward Linear Regression, which includes significance defined by $p<0.05$, where p is from the Wald test for Confidence Interval for the Odds Ratio and overall statistical significance was tested by the likelihood ratio test $p<0.1$, was used to demonstrate linear regression model fit.

No previously published studies have been conducted that focus on the incidence of ED in the military member with a history of deployment to a combat zone. The sample size for this study was based on the estimation that the incidence of ED occurs at a rate of 27% in adult anesthesia practice among patients with a known history of psychological disorders and/or combat stress (J. M. McGuire, MS, CRNA, unpublished data, August 2009). Utilizing Katz's[46] guideline of ten outcomes per independent variable, 30 outcomes of ED were required. Taking in consideration that the estimated incidence of ED in this study population is 27%, the estimated sample size for this investigation was 111 subjects. Accounting for an estimated 20% attrition rate (incomplete data collected in phase II), 135 subjects were recruited to participate.

Setting

The setting for this research was in the pre-operative anesthesia clinic, the main operating room, and the post-anesthesia care unit at Naval Hospital Camp Pendleton (NHCP). NHCP is a medium-size Naval medical treatment facility (MTF) in the western United States. The main operating room performs approximately 5,000 surgical cases per year, which includes veterans returning from the U. S. involved conflicts in Iraq and Afghanistan. In fact, approximately 70% of the surgical population is active-duty U. S. Marines, many with a history of combat zone deployment.

Instrumentation

Measure of Emergence Delirium

Sikich and Lerman[45] developed and evaluated the Pediatric Anesthesia Emergence Delirium (PAED) Scale in response to their claim that no reliable and valid rating scale existed to measure ED in children. Their study was divided into two parts, the scale development phase and the scale evaluation phase. In the scale development phase, the investigators collated a list of behavioral descriptions of children thought to have ED through a series of literature reviews on the subject as well as an interview process with clinicians in the fields of nursing, anesthesia, and psychiatry. This resulted in the description of six categories of ED behaviors: cognitive behavior, behavior response to environmental stimuli, behavior threatening patient safety, motor behavior, affective behavior, and vocal behavior.[45] A panel of seven experts preliminarily evaluated 100 participants between the ages of 18 months and 6 years of age in order to test 27

behavioral descriptions. The experts arrived at 21 behaviors that were deemed content valid. After eliminating statistically invalid items, the authors arrived at five behavioral profiles that comprised the PAED scale: the child makes eye contact with the caregiver, the child's actions are purposeful, the child is aware of his/her surroundings, the child is restless and the child is inconsolable. Each of the five behavioral descriptions was measured on a scale of zero to four, 0=none, 4=most. The scores were then summed and this represented the total PAED scale score. The instrument was evaluated on 50 children emerging from anesthesia; testing five hypotheses to determine construct validity.

Three of their five hypotheses correlated with the scores obtained on the PAED Scale, representing some validity. The authors claim that the observed behaviors of the PAED Scale were well developed and added to the content validity because they were constructed from a variety of sources.[45] The 5-item PAED Scale was obtained by clinician interviews manifested from the 21 behavioral descriptions. The internal consistency and inter-rater reliability was reported at 0.89 and 0.84 respectfully, lending reliability to this tool.

Since there is no valid and reliable instrument to measure ED in the adult population, this author recognized that the modification of the PAED scale was the most appropriate action for measurement of ED in the military population. Considering the limitations of dissertation research (cost and time), a full-scale development and psychometric testing of an entirely new instrument for the military population was not be feasible. In addition, utilization of instruments previously used to measure ED in the adult was not appropriate considering none were designed to measure the phenomenon in question rather, they were designed to measure sedation and/or agitation in the ICU.[16] The decision was made,

since the operational definition is the same for ED whether it is observed in adults or in children, that a modification of the PAED scale was most appropriate to measure ED in the military population.

In the summer of 2009, 36 military nurse anesthetists that witness ED in adults were surveyed concerning this phenomenon. The nurse anesthetists rated Sikich and Lerman's 21 behavioral items in regard to the relevance of each item as it pertained to ED in their adult patients. The PAED scale items were confirmed as relevant in describing ED in adults (J. M. McGuire, MS, CRNA, unpublished data, August 2009). This served as support to use the PAED Scale as a basis for a modified instrument with adults.[49]

The modified scale, the Adult Emergence Delirium Scale (AEDS), consisted of five scale items. The first five items were a replication of the PAED Scale: 1) the patient makes eye contact with the caregiver; 2) the patient's actions are purposeful; 3) the patient is aware of his/her surroundings; 4) the patient is restless; and 5) the patient is inconsolable. Scale items 1-3 were reversed scored as follows: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Scale items 4 and 5 were scored as follows: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely. The last five items (6-10) consisted of behavioral descriptions that were deemed content relevant items from previous research (J. M. McGuire, MS, CRNA, unpublished data, August 2009). They were as follows: 6) the patient behavior threatens his/her safety; 7) the patient has behavior that requires supervision; 8) the patient's behavior is uncontrollable; 9) the patient seems panic stricken; and 10) the patient is hypersensitive to tactile stimulation. These scale items were scored as follows: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely (see Appendix). These items were

tested in the sample population but were ultimately found to be irrelevant and not included in the analysis.

The AEDS was a pencil-and-paper instrument that resulted in a scaled score from "0 to 20." Totaling all individual scale item scores (1-5) provided the AEDS score. A score of 10 or greater was defined as a true positive score for ED as described by Sikich and Lerman.[45] Scores ≥15 on the scale represent a greater severity of ED. The score of ≥15 was adopted as the cut off for ED in this study. Scores ≤5 identified the patient as presenting with less of the behavioral indicators for ED. Minimal training was required for the experienced clinician to complete this instrument for the study. The tool was completed in less than a minute by most providers and provided an easy-to-use instrument for the evaluation of ED.

Measure of Anxiety

Anxiety was measured using the State-Trait Anxiety Inventory (STAI). The STAI is the definitive instrument to measure the specific domain of anxiety in the adult. It is the most widely used instrument for the assessment of anxiety.[50] The purpose of the instrument was to not only measure anxiety, but also to distinguish between state anxiety (temporary, surrounding the surgical experience) and trait anxiety (permanent characteristic).[51] It was particularly valid for this study population because it had been normed for the 19-39 year-old age group. Further validating the STAI, it is positively correlated with the Anxiety Sensitivity Index[52], as well as the Anxiety Scale Questionnaire and the Manifest Anxiety Scales.[53] It is both a reliable and valid instrument for the measure of anxiety (see Table 1).

The STAI is a 40-question pencil-and-paper instrument. Each question is centered on the emotions or feelings of the participant. Items are scored on a 1-4 scale: 1 being not at all relevant, 4 being very much relevant. Total scores range from 20 (low anxiety) to 80 (high anxiety) on both the state-anxiety and trait-anxiety portions of the exam. Approximately 10 minutes were required for the participant to complete the entire STAI. The STAI is inexpensive and was readily available for purchase and licensing through Mind Garden Publishing.

Measure of Depression

Depression was assessed using the Patient Health Questionnaire (PHQ-9). The PHQ-9 is a simple 9-item instrument used to assist clinicians in identifying depression. The items were derived directly from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) signs and symptoms of major depression.[13] It is a pencil-and-paper examination that centers on those symptoms and how they have "bothered" the patient over the previous two weeks on scale from zero to three (0=not at all, 3=nearly every day).[54] Scores were added resulting in a number between one and twenty-seven, 1-4 revealing minimal depression and 20-27 representing severe depression. The assessment was delivered to the subject, which took approximately 2 minutes to complete.

The PHQ-9 is a valid and reliable measure of depression in the adult population. There is a positive correlation between the results of the PHQ-9 and those of the Medical Outcomes Study Short Form (SF-20), also another valid and reliable measure of depression.[55] A strong positive correlation with the Beck Depression Inventory (BDI) has been identified.[56] Internal reliability was excellent across two studies with a Cronbach's

alpha of >.86.[57,58] Considering individuals with neurological trauma, such as individuals with TBI, the PHQ-9 is a valid and reliable instrument for the identification of depression.[59] This instrument was available free of charge via download from Pfizer Incorporated.

Measure of PTSD Symptomotology

PTSD symtomotology was assessed using the PTSD Checklist – Military (PCL-M). It is the original PCL version, designed to measure 17 symptoms of PTSD from the DSM-IV.[13] Questions are centered on the participant's response to "stressful military experiences" ranging from 1 (not at all) to 5 (extremely).[60] It is a brief self-report instrument that has a long history of use among veterans with a history of physical and psychological injury.

The PCL-M correlates strongly with the Clinician-Administered PTSD Scale (CAPS) (0.929), which is used to diagnose PTSD, and presents with an internal consistency of 0.94 (Cronbach's alpha).[61] Test-retest reliability has been reported as 0.88 and 0.96.[61,62] It has also been proven to be both sensitive and specific for measuring PTSD across several different populations[63,64] (see table 1). The PCL-M is not a diagnostic tool; however, it does indicate a probable diagnosis. Possible scores range from 17-85, with scores greater than 50 indicating a high likelihood of combat-related PTSD.[60] The participant was be able to complete the assessment in about 3 minutes. Permission was received from the National Center for PTSD, the publisher of the instrument, and was available free of charge.

Table 1.

Instrumentation for ED Study

Instrument	Reliability and Validity	References
STAI	Internal consistency (alpha) >0 90 for S-anxiety and T-anxiety Test-retest 0 75 for T-anxiety Correlates with ASI, ASQ and MAS	52 53 65
PHQ-9	Correlates with the BDI and SF-20 for depression Internal consistency (alpha) >0 86	55 58
PCL-M	Cronbach's alpha 0 94 Test-retest 0 88 and 0 96 Valid measure for combat-related PTSD according to multiple studies	60-64 66 67
PAED Scale	Internal consistency (alpha) 0 89 IRR 0 84 Sensitivity 0 64-0 85 Construct validity determined through hypothesis testing	45 68 69
AEDS	Content validity supported, modified from PAED Scale	(J M McGuire, MS, CRNA, unpublished data, August 2009)

Data Collection Protocol

1. All patients scheduled for elective surgery at NHCP normally report to the anesthesia pre-operative clinic prior to the date of scheduled surgery (1-14 days) to complete a pre-operative anesthesia questionnaire. Nursing, medical assistant, and anesthesia staff were briefed on the study and the process of participant recruitment through the anesthesia pre-operative clinic. As part of the check in procedure, the clinic staff asked the patient about a history of combat operations/deployment to a combat zone in support OIF/OEF since the beginning of operations in 2001 and their willingness to participate in the study entitled *"Emergence Delirium in the U S. Military "* If the

patient was scheduled for surgery, reported a deployment history to a combat zone, and expressed interest in the study as a participant, the clinic staff contacted the primary investigator (PI) by pager about the potential for recruitment into the study. The PI was present on the medical center grounds during normal working hours (0700-1600) Monday through Friday during the data collection period. The PI approached the patient about their potential enrollment in the ED study if their prescribed surgical procedure required general anesthesia. If the inclusion criterion was met and they agreed to participate, the patient was told that they may refuse to participate at any time and may withdrawal without any retribution.

2. After informed consent was obtained, baseline demographic data was collected and the STAI, PHQ-9, and the PCL-M was be delivered and collected. This data collection period (Phase I) took no longer than 30 minutes to complete (See Figure 2 for estimated times).
3. Phase II of the data collection period occurred on the day of the participant's scheduled surgery. Upon arrival to the surgical staging area, the participant was reminded of the previously obtained informed consent and their ability to refuse participation in the study at any time.
    a. **Baseline pre-surgical data**. Information regarding type of surgical procedure, site and laterality of surgical procedure, current medications and baseline self-report of pain (VRNS) was obtained from the patient and documented.
    b. **Intra-operative data.** Information on type and duration of the general anesthetic used was obtained and documented either from the anesthesia record or the responsible anesthesia provider. In addition, the amount and type

of adjunct medications used (e.g., opioids, sedatives) were obtained and documented.

c. **Post-operative Data.**

i. ***Operating room.*** Utilizing the AEDS, any combination of two providers (PI, operating room nurse, anesthesia provider) completed the instrument according to the patient's behavioral response during the emergence from the administered general anesthetic.

ii. ***Post-anesthesia care unit.*** Utilizing the AEDS, the PACU nurse completed the instrument according to the patient's behavioral response during the patients' recovery from general anesthesia.

iii. ***Additional Data.*** Following discharge from the PACU, information regarding the type and amount of medication administered in the PACU was obtained and documented either from the PACU record or the responsible PACU nurse.

4. Phase III of the data collection period occurred one week following the surgical procedure via a telephone call placed by the investigator. At this time, the participant was informed of any untoward instances or information in regard to participant's involvement in the study. The participant was notified of suspected episodes of ED and any results of psychological testing that lead to a suspect of a psychiatric disorder. The patient was given a consultation for psychiatric services through the Mental Health Department or Deployment Health at NHCP if it warranted and desired by participant. All necessary information was documented and this completed data collection period.

5. The investigator scored and interpreted all psychological tests according to the specific instrument's manual. All other raw data from demographics, pre-, intra-, and post-operative data was analyzed and compiled. A clinical psychologist was available for consultation during the analysis of all the psychological measures.
6. All data was coded with a subject number. All patient health information was removed per HIPAA regulations. The investigator secured informed consent forms in a locked file. Copies were provided to the participant and to the participant's medical record.
7. Figure 2 is a flow chart of the data collection protocol that was provided to all the healthcare providers involved in the patients care, to include: pre-operative nurses, operating room nurses, anesthesia providers and PACU nurses. Estimated times are listed. Please note the protocol was developed to minimize interference with the acute patient care involved in the immediate post-operative period. Figure 3 displays the algorithm for the data analysis plan.

Figure 2.

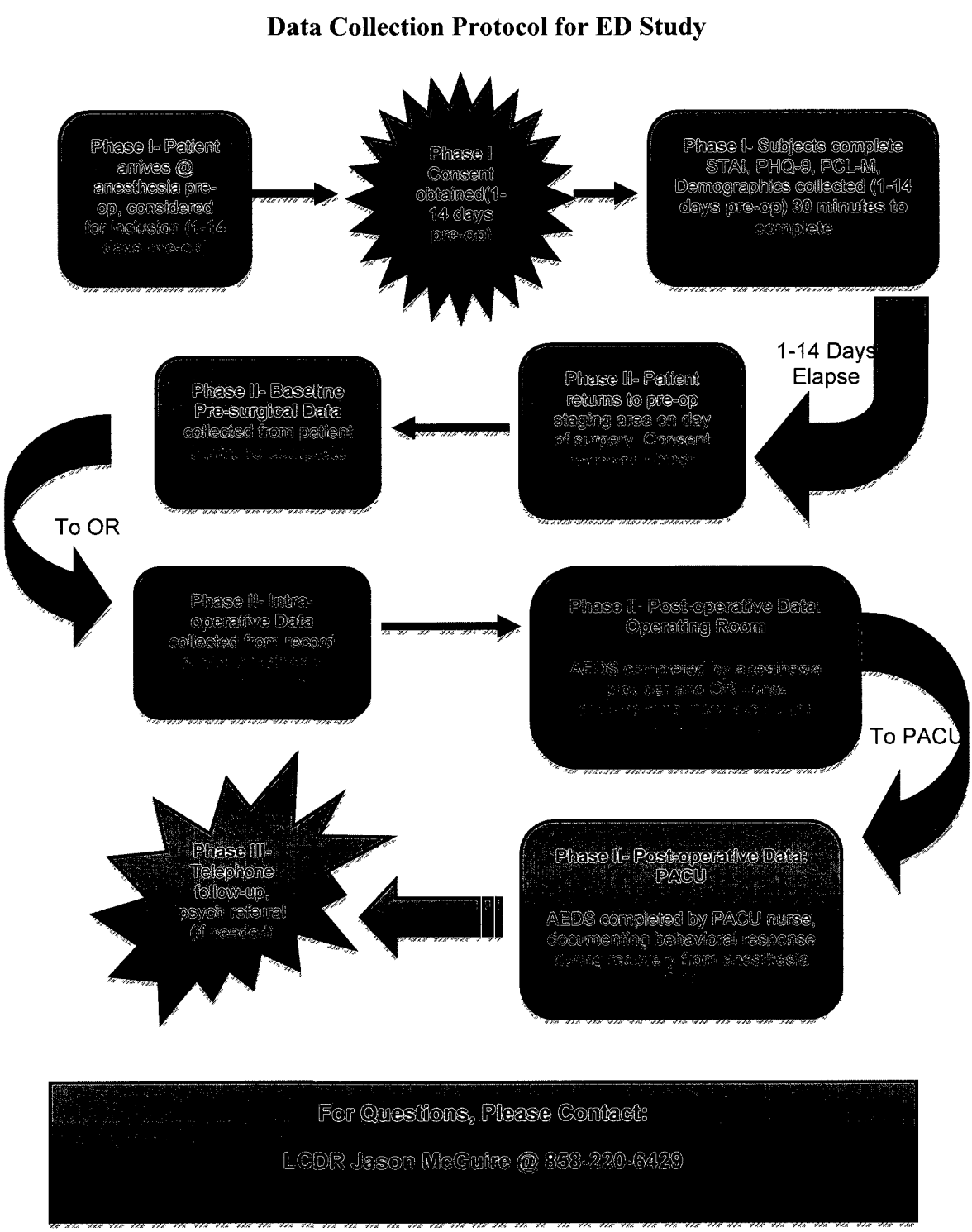
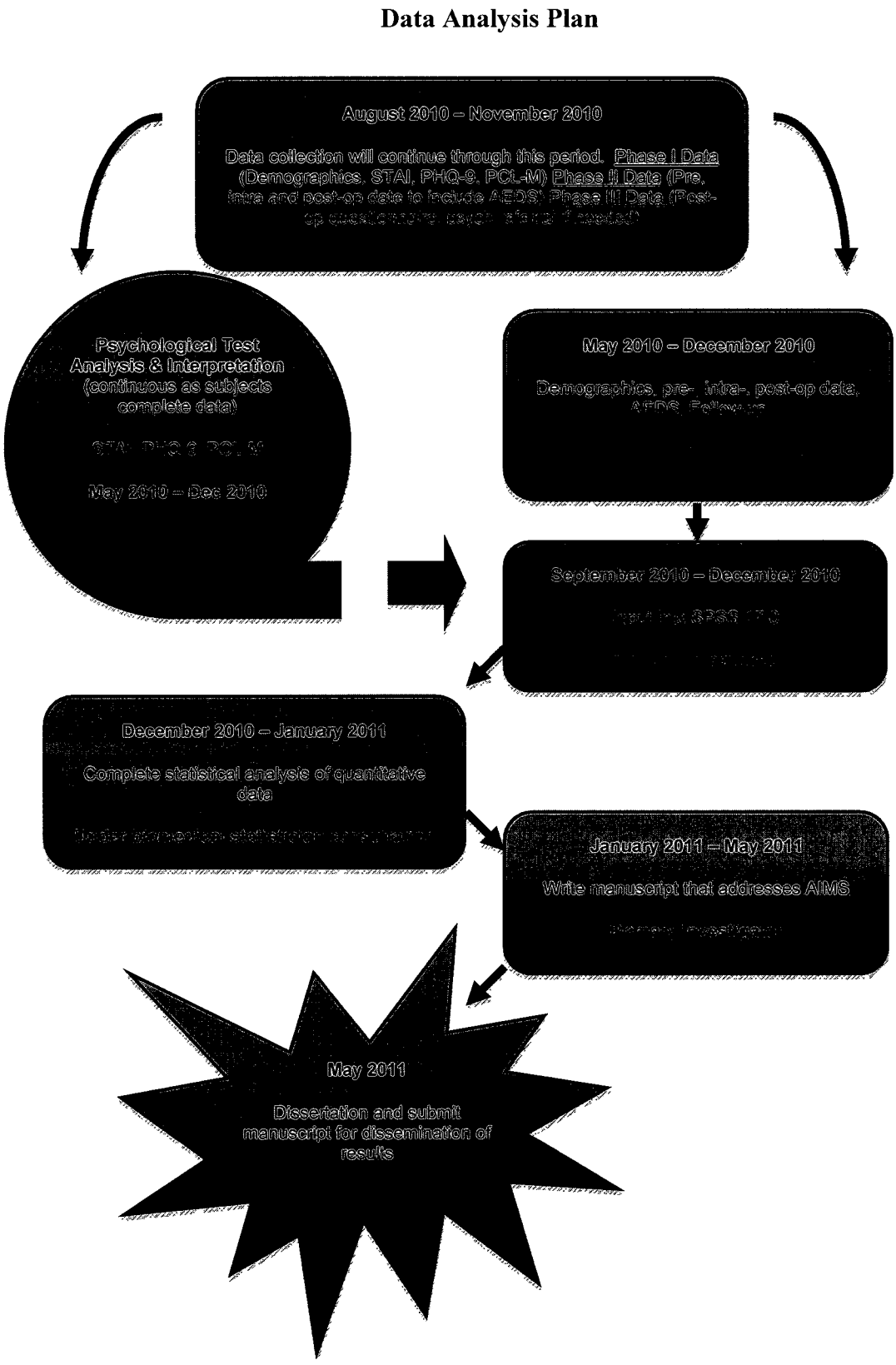

Data Collection Protocol for ED Study
Phase I- Patient arrives @ anesthesia pre-op, considered for inclusion (1-14 days pre-op)
Phase I Consent obtained(1-14 days pre-op)
Phase I- Subjects complete STAI, PHQ-9, PCL-M, Demographics collected (1-14 days pre-op) 30 minutes to complete
1-14 Days Elapse
Phase II- Patient returns to pre-op staging area on day of surgery. Consent
Phase II- Baseline Pre-surgical Data collected from patient
To OR
Phase II- Intra-operative Data collected from record
Phase II- Post-operative Data: Operating Room
To PACU
Phase II- Post-operative Data: PACU
AEDS completed by PACU nurse, documenting behavioral response
Phase III- Telephone follow-up, psych referral (if needed)
For Questions, Please Contact:
LCDR Jason McGuire @ 858-220-6429

Figure 3.


Data Analysis Plan
August 2010 – November 2010
Data collection will continue through this period. Phase I Data (Demographics, STAI, PHQ-9, PCL-M) Phase II Data (Pre, intra and post-op data to include AEDS) Phase III Data (Post-
Psychological Test Analysis & Interpretation (continuous as subjects complete data)
May 2010 – Dec 2010
May 2010 – December 2010
Demographics, pre-, intra-, post-op data, AEDS, Follow-up
September 2010 – December 2010
December 2010 – January 2011
Complete statistical analysis of quantitative data
January 2011 – May 2011
Write manuscript that addresses AIMS
May 2011
Dissertation and submit manuscript for dissemination of results

Statistical Analysis

Descriptive statistics (e.g., means and standard deviations for continuous variables, frequencies and percentages for categorical variables) were computed for each variable as appropriate.

For Hypothesis 1 – The incidence of ED is represented as a percentage of total subjects enrolled in the study. For this analysis, ED is considered a dichotomous variable with only two possible outcomes: the highest PAED score ≥ 15 is positive for ED and the highest PAED score <15 represent no ED.

For Hypotheses 2, 3, and 4 – Initially, bivariate correlation was conducted using Pearson's Product Moment Correlation in order to investigate whether the independent variables of anxiety, depression, and PTSD, considered separately, was related the incidence of ED (dependent variable). This analysis provided information on collinearity that could possibly affect the use of these variables in a regression model. The independent or predictor variables (anxiety, depression, PTSD) were considered continuous in the backward linear regression model. Linear regression was conducted to examine the relationship between the independent variables and emergence delirium. In backward linear regression, three models were represented. The first model included all predictor variables considered. The second model included all the predictor variables, minus the variable that had the least change in the unstandardized coefficient (B). Finally, the third model included the variables from model 2, minus the variable that had the least change in the unstandardized coefficient (B). A p-value of 0.05 was used for significance testing.

For Hypotheses 5 and 6 – Descriptive statistics were calculated for demographic/ background variables such as age, gender, marital/relationship status, medications, deployment history (number of deployments, location, combat zone v. combatant), and history of known psychiatric disorders. Descriptive statistics were also calculated in regard to pain, type of surgery, length of surgery, and number of surgeries. Differences between ED positive and negative participants (those deemed to experience ED and those that did not) on demographic variables were analyzed using t-tests (if continuous) or chi-square tests (if categorical). In addition, descriptive analyses were performed with demographics and ED as a continuous variable.

Compliance Plans

The primary investigator (PI) was present in the main operating room/anesthesia pre-op areas at NHCP during the months of data collection. However, if the PI was unable to be present secondary to other commitments, the nursing staff in pre-op was responsible for asking inclusion questions to incoming patients and obtaining contact information from interested patients. Those potential subjects were then contacted at the earliest convenient time in which an appointment was arranged to obtain Phase I data. Additionally, explicit instructions about the protocol were given to the all subjects and staff regarding data collection. Furthermore, to ensure maximal patient enrollment and to minimize missing data during Phase II data collection on already enrolled patients, the co-investigator on the study was available on the days the PI was unable to be present. The investigator(s) were present at all data collection times. Subjects and staff were given copies of Figure 2 for reference.

Statement of Assumptions/Limitations and Protection of Human Subjects

Previous studies involving similar procedures (clinical psychological testing) have never reported significant injury to a subject. The collection of psychometric data involved a minimal risk to subjects. "Minimal risk" was defined as risks no greater than those experienced in everyday life. Included in that risk was the experience of unpleasant emotions such as fear, anxiety and sadness. If the subject experienced any negative emotions, he or she was immediately offered psychiatric counseling services at NHCP. This occurred with two subjects during data collection. Both subjects experienced interest in psychiatric services and requested that the PI arrange the consultation for them under the condition that the request was a self-referral. These and all subjects were reminded that their participation was completely voluntary and that they were able to cease participation at any time. If the subjects refused services, they were provided contact information for the mental health resources available to them. In addition, they were given the number to San Diego County Mental Health Hotline, 1-800-479-3339; in the case they experienced negative emotions at home as a result to their participation in the study.

An additional minimal risk to subjects was fatigue. In Phase I of the data collection period, the subject was asked to complete a battery of clinical psychological tests (STAI, PHQ-9, PCL-M) and a questionnaire. This involved sitting and required their cognitive attention to the paper-and-pencil tasks for approximately 30 minutes or less. If fatigue occurred, the subject was able terminate the completion of the instruments and no longer participate in the study. This did not occur during the data collection period of this study.

The principal investigator was a Naval Officer and many of the participants were enlisted members. To minimize the risk of coercion, the principal investigator asked inclusion questions, provided study briefings, and obtained consents out of military uniform. The subjects were vocally instructed that their participation or lack of participation had no bearing on the healthcare they received and it did not affect their military service in any way, thereby confirming the wording of the consent. If subjects had questions or concerns they were able to speak with the investigator at any time before or after the informed consent. Subjects were informed at consent and throughout the study that they could withdrawal at any time from the study without retribution. To ensure confidentiality all data was labeled with a unique subject identifier that linked the subject with the data, and only the investigators involved in the study had access to this link. No personal health information was attached to the psychometric instruments, and all electronic data was stored on a password-protected computer. Staff at NHCP was unaware of the subject's results from any of the data collected in Phase I. These measures ensured compliance with HIPAA standards.

There was the possibility during the course of this study that the investigator could uncover subjects who were at significant risk for psychological disorders such as anxiety, depression and PTSD based on the data collected. This could of created an ethical issue because the investigators could of felt, based on the findings, that the subject should be referred for mental health counseling. At the same time, there was the need to protect the subject's confidentiality and to ensure that the research findings did not impact their military careers. The psychometric tools used in this study have been found to be reliable and valid measures in past research, and have been used to aid in the diagnosis of

psychological disorders. However, the combination of these instruments with the potentiality of discovering the incidence of ED had not been studied in this population, hence the purpose of the study. Furthermore, informing subjects that they may be referred for mental health evaluation if their psychometric scores indicated a potential disorder may have biased the sample to only those subjects who are low risk for psychological disorders, therefore limiting the generalizability of the findings.

Based on the risk of breach of confidentiality, this investigator believed data collected during this study should be protected and not shared with personnel or providers outside of the study. However, the investigator did personally inform individual subjects of findings from the study that indicated the subject was at significant risk for a diagnosed psychological disorder. At such a time, subjects were given information on how to contact the mental health clinic at NHCP. This plan was consistent with steps military researchers have used in past research protocols involving military personnel. In no way was the data collected in this study used to influence the subject's careers.

Safety Precautions and Emergency Procedures

This study involved risks that were minimal to the subject as previously described. All routine and emergency medical care was provided in a usual manner associated with peri-operative care by the surgical team. The ED study did not interfere with this care in any way. The use of standard Navy medical procedures was deemed sufficient to deal with any untoward events and/or injuries. This study was conducted at a medium-sized Naval MTF. At no time during the in-hospital collection of data was the subject left

unattended by a medical professional. The principal investigator was a nurse anesthetist and qualified to delivery advanced cardiac life support. Members of the surgical team were qualified to provide any emergency care needed.

Description of the System for Maintenance of Records

Sources of data for this study included the STAI, PHQ-9, PCL-M, and the PAED Scale. All these instruments were coded using each subject's assigned number. The master-coding list was kept in a locked file in an assigned office in the anesthesia department at NHCP and only the investigators involved in the study had access to this data. Data was entered into a password-protected computer. The only link to the subject's identity was the unique subject identification number. No protected health information was on any of the data collection forms or computer files.

The principal investigator kept the research protocols and consent forms in a locked file in an assigned research office. Completed protocols and consent forms were stored in compliance with SECNAVINST 3900.39C and BUMEDINST 3900.6B. Only the investigators had access to the consent forms and the master list. No protected health information was placed on any of the psychometric instruments. These measures ensured compliance with HIPAA standards and those of the Clinical Investigations Department (CID) at the Naval Medical Center San Diego.

Limitations

A limitation to this study is the small sample size of combat veterans enrolled from one military hospital. This limits the generalizability of the findings; therefore it is difficult oversimplify these results and apply them to all combat veteran populations at other healthcare facilities. The majority of the sample included active duty members of the U. S. Marine Corps. This branch of service often carries the stigma of anxiety, PTSD, and depression that may potentially affect the way in which one completes self-report measures aimed at identifying these psychological disorders. Although great care was taken during the consent process to ensure that the veteran understood how these measures would be used, Marines are often concerned with how these conditions might negatively effect how they are perceived as a "warrior." This may have resulted in an inaccurate assessment of anxiety, PTSD, and depression. This could explain the stronger relationship between those previously diagnosed with a psychological disorder and the higher incidence of ED. A previous diagnosis may bring about a certain amount of acceptance in the veteran concerning their condition, therefore, removing this as a barrier to accurate assessment. If this study was somehow carried out in a non-military environment with non-military investigators as members of the research team, this could limit potential error in psychological measurement.

Furthermore, future research warrants a calculation of power in order to determine the sample size necessary to detect smaller differences among study variables. To my knowledge, this was the first time ED was studied in the combat veteran population, making it difficult to predict adequate sample size. Based on the results of this study and the future researcher's plans for statistical analysis, an effect size can be calculated in

order to more accurately detect differences and generalize findings to the larger combat veteran population.

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Chapter 4: MANUSCRIPTS

Manuscript I

UNIVERSITY OF SAN DIEGO

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Risk Factors for Emergence Delirium in U. S. Military Members

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Abstract

Emergence delirium (ED) is a postanesthesia phenomenon occurring in both adults and children during recovery from general anesthesia. Although the pediatric population has been an ongoing focus of research and publications regarding ED, a renewed interest in ED has developed among military nurses and anesthesia providers because of its increasing incidence among the U. S. military surgical population. The purpose of this article is to identify potential risk factors for emergence delirium in the U.S. military population. Possible relationships between the physiological and psychological changes in U. S. military veterans and the surgical experience are explored. A review of ED as it occurs among the pediatric, adult, and elderly populations is also provided to support potential etiologies for the occurrence of ED in the military population. Pain and physical and psychological trauma as a result of military duty are identified and linked to ED as potential risk factors. Identification of these risk factors may provide guidance for scientific inquiry into this phenomenon in the military population. Implications for future study are also explored.

Keywords: emergence delirium, military population, anesthesia, post-anesthesia care, military nursing care.

Emergence Delirium (ED) is a postanesthesia phenomenon that occurs in both adults and children during recovery from general anesthesia. It is characterized by transient agitation, confusion, and violent physical and verbal behavior in the OR or the PACU.[1,2] Known originally as postoperative psychosis, ED was first documented in 1819.[3] From a historical perspective, Muncie[3] reported that nearly all operative interventions and medications are probable causes of ED, particularly implicating opioids, bromides, fever, pain, and mental disorders. Research conducted in the early 1960s revealed other possible causes including cyclopropane, ether, sedatives, and anticholinerics.[1]

The pediatric population has been an ongoing focus of inquiry because of the increased incidence when compared to adults. More recently, however, a renewed interest in ED has developed among military nurses and anesthesia providers because of its increasing incidence among the U. S. military surgical population. Case reports have shown that both combat and noncombat veterans emerge ''combative'' or disoriented from general anesthesia.[4,5] The disorientation and violent thrashing that accompanies this clinical condition creates a dangerous situation for both patient and health care provider.[6] Potential for injury exists as patients' extremities thrash about and make contact with hard surfaces (e.g., side rails, OR/PACU equipment). Venous and arterial catheters may be dislodged, interfering with the ability to provide emergency care. Surgical wound dehiscence and bleeding are also potential complications of continued involuntary physical activity. Quality of care is compromised when staff struggle to protect the patient while risking injury to themselves. Nursing resources are stretched because of the multiple personnel and additional time required to manage patient care safely and

effectively under these circumstances.[7] From the perspective of the military health professional, ED has become an emerging health concern.

Delirium is a disturbance of consciousness involving a cognitive deficit that cannot be explained by a preexisting dementia or mental disorder.[8] According to the DSM-IV-TR, emergence delirium falls under the subtype of ''Delirium Not Otherwise Specified'' because of the lack of a clear understanding of its etiology.[8] Although ED has been used interchangeably with the term emergence agitation, it is important to recognize the distinction. Agitation does not necessarily reflect a change in the patient's postanesthetic behavior.[9] ED is defined as a postoperative event immediately after the emergence from general anesthesia, where the patient presents with marked disorientation, nonpurposeful movement, restlessness, incoherence, agitation, or unresponsiveness.[10] Wilson and Graves[2] defined ED as a mental disturbance after general anesthesia consisting of hallucinations, delusions, and confusion as evidenced by moaning, restlessness, involuntary physical activity, and thrashing about in bed. Olympio[7] referred to ED as a dissociated state of consciousness in which the patient presents as irritable, incoherent, uncooperative, and inconsolable. These, in combination with other definitions of the same phenomenon, lead to confusion as to the etiology of ED, how to recognize it, and how to prevent or treat its occurrence.

The purpose of this article is to identify and discuss possible risk factors for ED among the U. S. military population. Exploration of the risk factors for ED previously identified in children and adults aids in the discussion when hypothesizing the relationship between the combat/deployment experience, posttraumatic stress disorder (PTSD), multiple surgeries, and pain, and how these may relate to the incidence of

emergence delirium in the military population. Relationships are proposed among the physiological and psychological changes occurring in the combat injured veteran, surgery, and the incidence of ED. Implications for future research are also explored.

ED in the Pediatric Population

Emergence delirium first appeared in modern literature during the early 1960s.[1,11] More recently, Vlajkovic and Sindjelic[12] explored many of the previously identified risk factors for ED, including volatile anesthetics, adjunctive medications, pain, surgery type, age, anxiety, and temperament. The literature addresses pediatric patients as the study population because the incidence of ED appears to be greater in children (18%-57%)[10,13] than in adults (4.7%).[14] Although there is no single cause of ED, many contributing environmental, social, biological, and psychological factors have been suggested.[15] For the purpose of this article, the probable risk factors for ED in children are divided into four groups: environmental, social, biological, and psychological etiologies.

Environmental Risk Factors

Emergence delirium is an excitatory neurological phenomenon; therefore, environmental factors such as noise, light, and temperature may cause or exacerbate its occurrence. Excessive noise and bright lights, experienced while waking from general anesthesia, overstimulate the central nervous system (CNS). This can lead to confusion and agitation; however, no scientific evidence exists that suggests that these are contributing factors for ED. No study to date has examined levels of light and noise as independent risk factors for ED. Removing extraneous noise from the OR environment

could potentially reduce the risk of ED by lowering CNS activity. This is supported by lower bispectral index (BIS) measurements (lessened CNS activity) in operative environments where noise was reduced.[16]

Thermoregulation is under the physiologic control of the CNS. Room temperature is often decreased in the operative environment. Researchers have demonstrated that the role of the hypothalamus in the regulation of body temperature is suppressed in children under general anesthesia.[17] Immediately upon emergence from anesthesia, intense afferent signaling of thermal information is relayed to the brain and spinal cord, resulting in sympathetic nervous system (SNS) stimulation, which may trigger ED.[18] Therefore, it is considered necessary to maintain normothermia in this population.

Social Risk Factors

Social risk factors have also been described as contributors to ED in children.[15] Social interaction between parent and child is predictive of child behavior, especially surrounding a major event such as surgery. Parental anxiety is a major contributing factor in transference of negative anxious energy to the child,[19] and 90% of parents report being anxious about their child's operative experiences.[20] Anxiety, as a part of the normal human stress reaction, elicits a neuroendocrine response through the CNS. This response stimulates the SNS and can contribute to the undesired behaviors exhibited in ED. It has been suggested that the presence of a calm parent can reduce a child's anxiety level before induction of anesthesia.[21] However, research has shown that parental presence during a child's emergence from anesthesia has no effect on the degree of agitation.[13] Caregiver anxiety as a risk factor for ED in children needs further

examination.

Biological Risk Factors

Many biological and chemical risk factors have been suggested as possible causes of ED in the pediatric population. The most prominent and frequently studied is the rapid emergence from general anesthesia secondary to the type of volatile anesthetic used. The speed at which a patient emerges from anesthesia is directly related to the solubility of the anesthetic. If the solubility of the inhalation anesthetic is low, less is absorbed into the tissue, which leads to faster emergence from the anesthetic. Although all volatile anesthetics have been implicated as contributing factors in ED, sevoflurane and desflurane, the most insoluble of volatile anesthetics, have been implicated as major causative factors in the incidence of ED in children.[22] Specifically, sevoflurane exhibits CNSstimulating side effects,[23] which could lead to postoperative excitement and the development of ED. When compared with propofol, an intravenous general anesthetic, administration of sevoflurane has been associated with a higher incidence of ED in children.[24-27]

Adjunctive medications are other biological risk factors that may contribute to the incidence of ED. Anticholinergics, barbiturates, benzodiazepines, droperidol, and metoclopramide can all have direct effects on postoperative behavior and have been associated with ED in the pediatric population.[28] None of these medications has been implicated as a singular cause for this phenomenon. Midazolam has been associated with severe paradoxical excitement that can result in ''restlessness and thrashing about.''[29] Often used in clinical practice for the treatment of ED, scientific evidence supports that

midazolam may not decrease excited emergence behavior postoperatively.[30]

Age is also hypothesized as a risk factor for ED. Martini[31] suggested that the developing child's brain lacks the number of neurotransmitters necessary to maintain emotional and neurological equilibrium. This may contribute to his or her susceptibility to delirium. A greater incidence of ED has been documented among preschool-aged boys under sevoflurane anesthesia.[32] However, as the child ages, the incidence of ED appears to decrease.

Another factor implicated in the development of ED in children is the type of surgery performed. Otorhinolaryngologic (ear-nose-throat) procedures have been identified as being an independent risk factor for a higher incidence of ED in children.[1,10] However, scientific investigation has not been able to explain the relationship between ED and other types of surgical procedures performed on children.

Pain is both a biological and psychological risk factor for ED and has been extensively studied. A child in pain emerging from general anesthesia can present as inconsolable and restless, exhibiting involuntary physical activity and thrashing about in bed. The presenting symptoms of pain and ED can look strikingly similar. Administration of an intranasal opioid analgesic (fentanyl) has been found to reduce the incidence of emergence agitation in children from 21% to 7%.[33] Alpha-2 receptor agonists (e.g., clonidine and dexmedetomidine), which provide both sedative and analgesic properties, have been shown to decrease ED. Findings from one study indicated that the incidence of agitation in children was decreased from 39% to zero when caudal clonidine was administered.[34] These studies suggest that there is a relationship between pain and ED. A child's inability to articulate his or her complaints adds to the difficulty in differentiating

ED from behavioral reactions to pain. The question remains: Is pain a cause of ED, or does superimposed pain confuse assessment and recognition of ED? The cause of ED is most likely multifactorial; some studies conducted on nonsurgical patients have shown that the incidence of postoperative agitation in pediatric patients can be independent of pain.[27,35] Pain also has a psychological impact on children that can cause postoperative behavioral changes independent of ED.

Psychological Risk Factors

Preoperative anxiety is a psychological risk factor linked to ED in children. The body's normal stress response, manifesting as preoperative anxiety, can potentially transform into an exaggerated stress response immediately after surgery. A history of previously stressful medical encounters can increase a child's anxiety before surgery. This further contributes to more serious postoperative anxiety, manifesting as ED.[36] Kain et al.[37] recently identified a positive correlation between preoperative anxiety and ED. In addition, extreme anxiety that results in an inappropriate stress response has a neuroendocrine component.[38]

The final psychological risk factor for ED is the child's basic temperament. Although temperament can have some learned social components, experts in the field of child psychology believe that it has an innate genetic basis.[39] Kain et al.[37] and Voepel-Lewis et al.[10] concluded that the more excitable, impulsive, and emotional the child, the greater the risk for ED. The extent to which the results of these investigations among the pediatric population can be applied to the adult members of the US military is not known.

ED in the Adult and Elderly Populations

The phenomenon of ED has not been adequately studied in adults. In fact, only one prospective study has been conducted to date. Lepouse et al.[14] studied 1,359 patients ages 15 to 99 and reported an incidence of ED of 4.7%. They found that breast and abdominal surgery, long duration of surgery, and the preoperative use of benzodiazepines were associated risk factors.[14] ED, however, was measured using the Riker sedation-agitation scale, an instrument only shown to be reliable and valid for measuring sedation and agitation in the critically ill adult intensive care unit (ICU) patient.[40]

Confusion exists as to whether emergence delirium has been studied at all in the elderly population. A study of postoperative delirium in the elderly demonstrated an incidence of 44%,[41] but the delirium was determined via a daily ICU assessment, not associated with the PACU. A more recent study found the incidence of postoperative delirium to be 13.2%, with probable risk factors including increased age, cognitive impairment, and psychopathology.[42] There have been no studies to date linking cognitive impairment in the elderly specifically to ED.

Postoperative delirium among the elderly has been well described in the literature; however, the operational definition of this phenomenon is clearly different from that of emergence delirium. ED, defined as occurring immediately after emergence from general anesthesia, has been inadequately studied in the geriatric population. Delirium immediately upon emergence from general anesthesia in the elderly is difficult to identify because it is often characterized as a global disorder related to attention and cognitive deficits that increase with age. Many studies have identified a relationship between delirium and cognitive decline among the elderly.[42,43] Metabolic derangements, infectious

processes, and disturbed sleep-wake cycles have also been implicated as possible causes.[44] The extent to which the results of these investigations among the adult and elderly populations apply to adult members of the U. S. military is uncertain.

Differential Diagnosis

Before considering the possible etiologies for ED in the US military population, it is important to recognize that there are other borderline or related cases that mimic the presentation of ED that should be considered as part of a complete differential diagnosis. Numerous anesthetic medications have been implicated in the development of a rare transient neurological disorder known as central anticholinergic syndrome (CAS). CAS is characterized by symptoms of CNS excitation or depression that can include disorientation, restlessness, memory dysfunction, and delirium.[45] Common classes of medications associated with an episode of CAS include but are not limited to anticholinergics, antispasmodics, antidopaminergics, benzodiazepines, phenothiazines, opioids, selective serotonin reuptake inhibitors, and tricyclic antidepressants.[46]

The patient's respiratory function should be assessed for signs of hypoxia and hypercapnia secondary to any physiologic, pathologic, or mechanical abnormality. Metabolic disorders such as acute electrolyte imbalance and hyper/hypoglycemia should be considered as root causes because often times these patients can present with neurologic and behavioral dysfunction. Neurologic incidences such as an embolus, seizure, or other events that could result in brain injury should not be discounted when caring for the agitated patient. Underlying psychological disorders such as panic disorder, anxiety, and PTSD should be considered when a patient emerges from anesthesia

combative and disoriented. Intraoperative use of medications such as ketamine should also be ruled out because hallucinations are common. Finally, the postanesthesia provider should evaluate the patient for other common etiologies of restlessness such as bladder distention and pain.

Identifying ED Risk Factors Among U. S. Military Members

Anecdotally, many military nurses, physicians, and technicians caring for patients with a history of deployment/combat exposure describe the occurrence of ED in the perianesthesia arena as common. A recent survey of Certified Registered Nurse Anesthetists (CRNAs) caring for patients with a history of combat exposure and/or known psychological disorders report the incidence of ED symptoms at 24% (McGuire JM, unpublished data, August 2009). Emergence behavior of military members with a deployment/combat history shows they often emerge from general anesthesia agitated, restless, confused, and combative (McGuire JM, unpublished data, August 2009).

Military perianesthesia nurses often prepare during the surgical procedure for what they ''know'' will soon occur: the violently combative emergence of the soldier, sailor, airman, or marine. Colloquial phrases like ''anesthesia rodeo,'' ''wild wake-up,'' and ''post-anesthetic wind-up'' have all been used to describe ED as it occurs in some military members. Recently injured combat veterans returning for their third, fourth, or even fifth surgeries sometimes prepare their perianesthesia team stating, ''Watch out, I've been told I wake up swinging.'' Perioperative nurses dim the lights and minimize excessive noise in the OR in an effort to decrease sensory stimuli. Anesthesia providers may give additional benzodiazepine and opioids in an effort to ''smooth out''

the emergence. However, all available personnel are present to ensure the protection and safety of the patient and staff. If the characteristics of ED continue into the PACU, the standard of care is continued administration of benzodiazepine and opioid treatment.

Considering the ongoing combat operations in Iraq and Afghanistan, it is important to investigate the phenomenon of ED as it occurs among members of the military. We must begin by defining the possible risk factor profile for ED in the adult military population. It is no longer difficult to infer what we know of the risk factors for ED in children, adults, and elderly populations and begin to hypothesize how these findings may relate to the military population. Based on the personal clinical experience among military perianesthesia providers, ED appears to occur with greater incidence among combat veterans compared with the general military population of the same age (McGuire JM, unpublished data, August 2009). Here lies the hypothesis: there is a relationship between deployment/combat exposure and the occurrence of ED in veterans. For the purpose of this discussion, risk factors for ED in the military population are categorized in five main areas: (1) medication, (2) physical trauma requiring surgical intervention, (3) pain, (4) traumatic brain injury, and (5) psychological trauma (Table 1).

Table 1. Potential Risk Factors for Emergence Delirium

	Environmental	Social	Biological	Psychological
Pediatric Population	-Light -Noise -Temperature	-Care giver anxiety	-Rapid emergence -Medication -Age -Type of surgery -Pain	-Anxiety -Temperment -Pain
Adult/Elderly Population			-Type of surgery -Medication	
Adult U. S. Military Population*	-Light -Noise	-Lack of social support	-Physical trauma requiring surgery -Traumatic brain injury -Medication -Type/duration of surgery -Pain	-Pain -PTSD -Anxiety -Depression

PTSD, posttraumatic stress disorder.

*Hypothesized risk factors.

Medication

Mefloquine hydrochloride has been used as antimalarial prophylaxis for military personnel deployed overseas for Operations Enduring Freedom (OEF) and Iraqi Freedom (OIF). Neuropsychiatric reactions have been reported by patients receiving mefloquine, with anxiety, depression, and sleep disturbances listed as common side effects.[47] Several cases of ED have been reported in US military members receiving mefloquine.[5] Further investigation is required before we can ascertain the contribution of mefloquine treatment to the incidence of ED in this population.

Physical Trauma Requiring Surgical Intervention

Physical trauma sustained as a result of combat often requires surgical intervention. This results in a physiologic change that may present as a behavioral response in the form of postoperative ED. Between October 2001 and July 2010, an estimated 38,655 American service members have been wounded in Iraq, Afghanistan, and the surrounding areas.[48] Their injuries are the result of motor vehicle accidents, gunshot wounds, and explosive injury from improvised explosive devices (IEDs). Victims of explosion often have penetrating fragmentation wounds, contusive organ injury, fractures, traumatic amputations, soft tissue injuries, and burns. Nearly all of these injuries require immediate damage control surgical intervention in the field, as well as multiple subsequent surgeries when staged surgical treatment is required.

After trauma, hemorrhage, and multiple surgeries, a chronic inflammatory response causes drastic physiologic changes. The stress response is continually engaged, causing overstimulation of the SNS; this response occurs to a greater extent in surgery resulting from trauma than in elective surgery.[49] Multiple surgeries result in a highly elevated neuroendocrine response that may take hours to several weeks to resolve.[50] Circulating catecholamine and other toxic mediators (e.g., cytokines) continue the cascade of the inflammatory response and contribute to immune suppression.[51] The victim of severe physical trauma continues to suffer from these physiologic changes, caused not only by the initial trauma, but also by multiple surgeries. Multiple surgeries and their relationship to ED have not been studied. The physiologic component of the stress response to trauma and multiple surgeries may present in the form of a behavioral response, manifesting itself as ED.

Pain

Research suggests that pain-related stress, as well as the negative emotional state produced by pain, may affect the cognitive ability of chronic pain patients.[52] If pain is presumed to affect the cognitive ability of individuals, it is possible that this could result in an adverse behavioral response when emerging from anesthesia. Soldiers, sailors, airmen, and marines often experience a great deal of pain as a result of combat injury. A patient inadequately treated for pain during emergence from general anesthesia appears much like the patient experiencing an ED crisis. Confusion, restlessness, and violent physical movements are shared presentations. Because of the similarities, it is clear why many anesthetists and PACU nurses intervene with opioid therapy. Opioid treatment has been shown to decrease the incidence of ED in children.[33] Inadequate pain relief has also been correlated with the onset of chronic pain syndrome (CPS) and PTSD.[53] Both CPS and PTSD result in abnormal behavioral responses, which could continue into the anesthesia recovery period. Chronic pain patients often form maladaptive behavioral responses as a result of SNS activity and the overall neuroendocrine response.[54] Untreated pain in the immediate postoperative period may cloud the diagnosis of ED, or it may be a direct cause.

Traumatic Brain Injury

Traumatic brain injury (TBI) is another physiologic change that may produce a postoperative behavioral response in the form of ED. TBI is an insult to the brain caused by an external force, leading to permanent or temporary impairment of cognitive, physical, or psychosocial function.[55] It is often associated with an altered state of

consciousness. Since the beginning of the actions in Iraq and Afghanistan, it has been difficult to estimate the extent to which this injury occurs. Because of the high rate of explosions in the current conflicts, TBI is estimated to affect between 10% and 20% of the combat-exposed population.[55]

TBI is frequently undiagnosed because the majority of TBI is closed, also referred to as a concussion or mild TBI. In addition, combat-exposed personnel are less likely to report mild concussive injury. The effect general anesthesia has on military members diagnosed with mild TBI has not been studied; however, these patients appear to wake up slower than similar patients without TBI. They have a higher rate of confusion in the PACU, resulting in a greater acuity level. Although they are less likely to emerge combative, there seems to be a longer time until their baseline level of consciousness (LOC) returns. Whether this change in LOC is a manifestation of ED or a separate behavioral response related to TBI is unknown. Further study is required to discover a link between the high rate of TBI among the combat population and the apparent increase in the incidence of ED.

Psychological Trauma

Mental health disorders are a potential psychological cause for ED. Deployment and combat stress are directly related to the combat veteran's risk of developing a myriad of mental health disorders.[56-58] Depression, substance abuse, social and behavioral dysfunction, and PTSD have all been reported as outcomes of combat exposure.[57] According to the National Center for PTSD, nearly 20% of returning combat veterans develop PTSD, and the prevalence is even higher among injured veterans.[56] In fact, 23%

of trauma survivors present with symptoms of PTSD one year after injury.[58] A heightened stress response is the hallmark of PTSD. Many individuals with PTSD complain of feeling irritable, overreacting when startled, and experiencing angry outbursts. Again, many patients who experience symptoms of PTSD do not report them when questioned on postdeployment assessments. The reasons vary from a lack of trust in health care providers to fear that acknowledging their symptoms could put their careers at risk.[56] The lack of self-report of PTSD by service members makes it difficult to examine in this population.

Upon emergence from general anesthesia, a combat veteran who is already hyper-aroused could easily startle from many external and internal stimuli. A recent case study reported an episode of emergence flashback after general anesthesia in a patient with a known diagnosis of PTSD and depression.[59] Rapid emergence from unconsciousness to consciousness, pain, light, noise, and temperature are all examples of stimuli that may elicit an episode of ED in the patient with PTSD. Whether diagnosed or undiagnosed, PTSD is an emerging risk factor for ED in the combat-exposed veteran.

The psychological resilience and social support systems of returning veterans are protective mechanisms against the harmful effects of traumatic stress and depression.[60] Veterans without adequate social support may be at higher risk for the development of psychological problems after deployment. Given the long separations from families and the fact that the majority of the fighting force is single or divorced, it is not surprising that postdeployment veterans often report inadequate military unit and family support.[56,60] Poor psychological resilience and insufficient social support systems as they relate to emergence delirium are unknown.

Implications for Future Study

We are just beginning to discover possible risk factors for the development of ED among the military population. Exploring what we know of ED in the pediatric population is necessary because this is where the state of the science emerges. Understanding the individual physiological and psychological changes that have occurred in the combat veteran helps one understand the context in which ED is occurring. Constructing a list of potential risk factors for ED in the military veteran helps guide scientific inquiry into this fascinating phenomenon. Potential areas of research that have implications for contemporary nursing practice are presented next.

A survey-designed study of ED was conducted among 72 military and nonmilitary expert nurse anesthetists, and the results indicated that ED is a phenomenon of interest as it occurs in their adult anesthesia practice (McGuire JM, unpublished data, August 2009). Using a questionnaire to discover how other perianesthesia providers (e.g., PACU and OR nurses) experience ED in their practices will bring forth additional perspectives and shed more light on this observable fact. An investigation such as this will provide additional insight on how to more clearly define and assess ED in the military veteran population.

Scientific inquiry should also focus on the construction of an instrument to identify ED in adults. To date, there is no instrument for the assessment of ED in the adult population. Of the many instruments used to identify ED in the pediatric population, only one has been psychometrically validated.[61] Sikich and Lerman's Pediatric Anesthesia Emergence Delirium (PAED) Scale[61] can be appropriately modified to assess ED in the adult. This becomes imperative because previously

conducted research regarding ED has lacked methodological rigor because of the failure to use a validated tool for its assessment.

Formulating a useful and content-validated instrument to be used among adults will assist in empirically identifying the true incidence of ED in the military population. A study should be conducted at a medical center that cares for military members and veterans of military service. It is here where the surgical population will likely present with many of the proposed risk factors described (e.g., PTSD, anxiety, depression). Discovering the incidence of ED and its contributing factors will guide further research and lead to studies directed toward prevention and treatment. The goal of an ED program of research in the adult population is to identify outcomes that will lead to a change in current perianesthesia clinical practice.

Conclusion

Emergence delirium is a postoperative complication that has become a phenomenon of interest to those who care for members of the US military and veterans of military service. Its incidence appears to be on the rise since the beginning of combat operations in the Middle East in 2001. A review of the ED literature allows one to hypothesize about the potential relationship between ED and the many physiological and psychological conditions that may be present among military members. This discussion brings to light the combat/ deployment experience, PTSD, multiple surgeries, pain, and how these may relate to the incidence of ED. ED, and the context in which it occurs in the military veteran, must be readily identifiable to the perianesthesia care team to ensure a safe surgical experience for the patient. Further scientific research should work to

discover the true incidence of ED and its associated risk factors in the U. S. military population. The continued search for improved interventions and preventive treatment is the goal. Creating a safer and healthier perianesthesia environment for our military patients gives importance to this work.

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Manuscript II

UNIVERSITY OF SAN DIEGO

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Content Validation of the Pediatric Anesthesia Emergence Delirium Scale for use in Adults: A Survey of Nurse Anesthetists Regarding the Concept of Emergence Delirium

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Abstract

Anecdotal evidence suggests that the phenomenon of emergence delirium (ED), a complication following the delivery of general anesthesia, is occurring with greater incidence among members of the U. S. military than in the general adult population. To determine the true incidence of ED among military members, it is important to utilize an instrument that accurately measures this post anesthetic complication in adults. Thirty-six expert nurse anesthetists that care for combat veterans were surveyed and asked to further define the concept of ED in adults. In addition, they were asked questions in regard to the scale items of the Pediatric Emergence Delirium (PAED) Scale in an effort to content validate its use in adults. The findings suggest that ED is a phenomenon of interest to nurse anesthetists caring for combat veterans and that the items of the PAED Scale are appropriate for use in future research with adults.

Keywords: U. S. military, emergence delirium, general anesthesia, postoperative complications, PAED Scale

Introduction

Emergence delirium (ED) is a post-anesthesia complication occurring upon emergence from general anesthesia in the operating room (OR) or post-anesthesia care unit (PACU). It is described as confusion, restlessness, and possibly combative behavior following surgery. Few studies have examined the incidence of this phenomenon in the adult population and those that have failed to use an instrument that specifically measures ED. The concept of ED and its risk factors are well established in the perioperative community when it occurs in children.[1,2] Anecdotally, the incidence of restless and combative adult patients following general anesthesia appears to be on the rise among active duty military personnel. It is only recently that risk factors for ED in the adult military population have been hypothesized.[3]

As United States military operations continue in the Middle East, the number of combat veterans steadily rises. Symptoms of depression, anxiety, and post-traumatic stress disorder (PTSD) are common among returning combat veterans when compared to the general adult population.[4] As the population of combat veterans increases, along with the associated symptoms of post-traumatic stress disorder (PTSD), anxiety, and depression, so does the apparent incidence of ED. Emergence delirium, as it occurs in combat veterans, is an unexplored phenomenon. In pediatric patients, research has described a relationship between anxiety disorders and ED.[5,6] The mental health of members of the armed services should be aggressively studied in order to provide optimal care in the acute perioperative setting.

To date, only one reliable and valid instrument exists to measure ED, the Pediatric Anesthesia Emergence Delirium (PAED) Scale.[7] The purpose of this study was to further define the concept of ED in adults, while validating the content of the PAED for use with adults. The authors argue that validating an existing instrument for use in the adult was most appropriate since the observed manifestations of ED are similar, whether it presents in children or adults. Previous studies of ED in adults used instruments that were not designed for use in the OR or PACU immediately following general anesthesia, rather, they were designed to assess for levels of sedation and agitation in the intensive care unit (ICU).[8,9]

The PAED Scale

Sikich and Lerman developed and evaluated the Pediatric Anesthesia Emergence Delirium (PAED) Scale in response to their claim that no reliable and valid rating scale existed to measure ED in children.[7] Their study was divided into two parts, the scale development phase and the scale evaluation phase. In the scale development phase the investigators collated a list of behavioral descriptors of children thought to have ED through a series of literature reviews on the subject as well as an interview process with clinicians in the fields of nursing, anesthesia, and psychiatry. This resulted in the development of six categories of ED behaviors: 1) cognitive behavior (e.g., making eye contact); 2) behavioral response to environmental stimuli (e.g. agitated when touched); (3) behavior threatening patient safety (e.g., pulling at IV); 4) motor behavior (e.g.

hyperactivity); 5) affective behavior arising from emotions (e.g., inconsolability); and 6) vocal behavior (e.g. yelling).[7]

A list of preliminary scale items to describe emergence behavior was generated, based on these six behavioral categories. Seven experts rated the relevance of each preliminary scale item and determined which of the six behavioral categories each item best represented. Items that were considered content-valid were pretested and resulted in a final list of 21 preliminary scale items (Table 1). These scale items were analyzed using statistical item analysis and the items found to have a good statistical profile were chosen to comprise the five items of the PAED Scale. The five behavioral descriptions of the scale are: 1) the child makes eye contact with the caregiver, 2) the child's actions are purposeful, 3) the child is aware of his/her surroundings, 4) the child is restless, and 5) the child is inconsolable.[7]

Table 1. Preliminary Scale Items Identified by Sikich and Lerman[7]

Patient can focus attention on caregiver	Patient is restless*
Patient pulls at monitoring equipment or IV	Patient behavior makes postoperative care difficult
Patient behavior threatens his/her safety	Patient is aware of his/her surroundings*
Patient movements are disruptive	Patient is distressed by the monitoring equip.
Patient mood is irritable	connected
Patient makes eye contact with caregiver*	Patient is inconsolable*
Patient has hyperactive motor behavior	Patient's behavior is uncontrollable
Patient actions are purposeful*	Patient seems panic stricken
Patient is agitated when touched by caregiver	Patient interacts purposefully with caregiver
Patient has behavior that requires supervision	Patient is hypersensitive to tactile stimuli
Patient is combative toward caregiver that tries to comfort	Patient is attentive to his/her surroundings

* Items that comprise the PAED Scale

The PAED Scale then entered the scale evaluation phase. It was evaluated on 50 children emerging from anesthesia; testing five hypotheses to determine construct validity. Three of the five hypotheses correlated with the scores obtained on the PAED Scale, representing some validity. The internal consistency and inter-rater reliability were reported at 0.89 and 0.84, respectively, suggesting an acceptable level of reliability for this instrument.

Sikich and Lerman claimed that the observed behaviors of the PAED Scale were well developed and added to the content validity because they were constructed from a variety of sources.[7] The 21 behavioral descriptors were obtained through clinician interviews. The content and the philosophical assumptions that guided these interviews were not described, creating a potential source of bias. In determining the validity of the 21 behavioral descriptions, steps should have been taken to describe this aspect of the qualitative study so that it could be effectively reproduced. Despite these limitations, we agree that the PAED Scale is a valid and reliable instrument.

Validation of the PAED Scale for Use in Adults

We hypothesized that the PAED Scale would be a useful instrument to measure ED in adults. The theoretical approach to the content validation of the PAED Scale for use in adults lies in the examination of the 21 preliminary scale items by another population of experts with experience in ED in the adult population. These experts were asked to rate the relevance of each item as it related to their experiences in ED in adults. In addition, the experts also categorized each item in relation to one of the six behavioral categories previously discussed. Both were considered equally important. Content validation was considered by examining the results of not only the item relevance, but also in combination with how each item was categorized by type of behavior. In order to maintain the integrity of the instrument, strong evidence must exist in order to justify the replacement of one of the PAED Scale items with another item from the preliminary list

of items. The use of the PAED Scale with adults is predicated on the combination between the relevance and the assigned behavioral category.

Materials and Methods

Using practicing Certified Registered Nurse Anesthetists (CRNAs) providing anesthesia to combat veterans as content experts, a mixed-method survey was administered at a national nurse anesthesia conference. The aims of the survey were to: 1) identify defining characteristics/attributes of ED; 2) examine contextual variables that may further describe ED from the perspective of the CRNA; 3) describe relevance and the labeling of behavioral category responses of an expert sample to the scale items identified by Sikich and Lerman[7] for the content validity of the PAED Scale for use in adults.

The study protocol was IRB approved and the American Association of Nurse Anesthetists (AANA) granted permission for the researchers to collect data during its annual meeting. Data was obtained using an author-constructed instrument, the *"Scale Development Survey – Emergence Delirium in Adults."* Thirty-six military and prior military CRNAs were surveyed at the annual meeting of the AANA in San Diego, CA. Participants were recruited by means of a booth in the exhibition hall. Inclusion criteria for the stratified, purposive sample were practicing military or prior military CRNAs with greater than 5 years anesthesia practice experience, who self-reported witnessing confused, restless, or combative behavior in adult combat veterans following the delivery of general anesthesia.

Participants were given the following definition of ED: "Emergence delirium (ED) is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia in adults and children; it is characterized by agitation, confusion, and violent physical or verbal behavior in the operating room or the post-anesthesia care unit." Participants were then presented with a model case of an adult for whom ED was a suspected diagnosis. They were given 18 descriptive words and phrases used to describe cases of ED in the literature and were asked to rate each item on a 1-7 Likert-type scale, with 1 indicating "not at all descriptive of ED" and 7 indicating "extremely descriptive of ED." Participants were then asked to provide qualitative data in the form of additional comments or descriptions used to describe their experience with ED in their practice. In addition, the participants were asked to estimate the incidence of ED in their patients that present with a history of combat exposure.

The 21 preliminary scale items identified by Sikich and Lerman to describe the behavioral presentation of patients experiencing a delirious emergence from general anesthesia were listed. Participants were asked to rate the relevance of each scale item as a general descriptor for ED in adults on a 1-7 Likert-type scale, with 1 indicating "not at all relevant" and 7 indicating "extremely relevant." Additionally, CRNA participants were asked to categorize each scale item into one of the six behavioral categories of ED.

Participants were asked if, when ED was observed, they pharmacologically treated the symptoms. If participants did treat the symptoms, they were then asked to identify what agents they used to treat ED. Finally, CRNAs were asked if they believed that ED in the adult population was a concern in their practice and if so, would they find an instrument to assist in assessment of ED to be useful.

The Statistical Package for the Social Sciences (SPSS©/17.0) was used to analyze the data. Descriptive statistics were used to summarize variables and to identify central tendency, variability, and percentages of key variables. Scale items were deemed to display content validity if participants rated the item as 4 or higher on the seven-point scale and if it represented one of the six ED behavioral categories. Inferential statistical analyses were performed to examine relationships between and among study variables. Open-ended responses on the *"Scale Development Survey – Emergence Delirium in Adults"* were examined for thematic repetition.

Results

A purposive sample of 36 participants was enrolled. The sample consisted of 19 men and 17 women, ranging in age from 33 to 66 years (x= 46.1, ± SD 8.0). Active-duty military nurse anesthetists comprised 75% of the sample while 25% were prior active-duty military nurse anesthetists. Members from the U. S. Navy, Army, and Air Force were represented. Anesthesia experience ranged from 5 to 38 years (x= 13.4, ± SD 8.2). All of the participants reported caring for combat veterans in an anesthesia context.

The CRNA experts selected the following items as being *very descriptive* (>80% of respondents scoring ≥4 on Likert-type scale) of adult ED: "restlessness," "thrashing about," "confusion," "agitation," "lack of cooperation," "yelling," "violence" and "combativeness." The following items were reported as being *moderately descriptive* (>70% of respondents scoring ≥4 on Likert-type scale): "hallucinations," "delusions," "angry," "frightened," and "verbally abusive." The following items were reported as

being *not descriptive* (<50% of respondents scoring ≥4 on Likert-type scale): "moaning," "involuntary physical activity," "crying," "incoherent speech," and "weeping." The participants offered no additional qualitative data used to describe ED behavior.

CRNAs caring for patients with a history of combat exposure estimated that they observed ED symptoms in 24% of the combat veteran population they treated. The entire sample believed that ED is a phenomenon of interest. Ninety-four percent said they would find an instrument to measure ED helpful.

When ED occurs in the practice of those CRNAs sampled, 71% pharmacologically treat the symptoms. Eighty percent of those individuals utilize benzodiazepine, while 9% choose opioids as the primary pharmacologic treatment. Three individuals offered additional qualitative data. Two of the individuals reported using clonidine as a preventive treatment for ED in patients identified as combat veterans prior to surgery. One individual described his use of an intraoperative dexmedetomidine infusion for the prevention of ED in the combat veteran population.

The corresponding percentages of sample agreement (≥4 on a 1-7 Likert Scale) to each item of the PAED Scale are as follows: (1) the patient is inconsolable – 94%, (2) the patient is restless – 78%, (3) the patient's actions are purposeful – 69%, (4) the patient is aware of his/her surroundings – 64%, and (5) the patient makes eye contact with the caregiver – 64%. The remainder preliminary scale items and the corresponding percentages of sample agreement are described in Table 2. Participants categorized each of the preliminary scale items into one of the six behavioral categories of ED. The highest rate of response for category selection is described in Table 2.

Table 2. Preliminary Scale Items: Percentage of Sample Agreement and Behavioral Category

	Relevance	Behav. Cat. (% sample agreement)
Patient makes eye contact with caregiver*	64%	Cognitive (89%)
Patient actions are purposeful*	69%	Cognitive (78%)
Patient is aware of his/her surroundings*	64%	Cognitive (100%)
Patient is restless*	78%	Resp. to stim./Affect. (42/31%)
Patient is inconsolable*	94%	Affective (81%)
Patient can focus attention on caregiver	67%	Cognitive (92%)
Patient pulls at monitoring equipment or IV	92%	Response to stim./Pt. safety (42/42%)
Patient behavior threatens his/her safety	94%	Patient safety (72%)
Patient movements are disruptive	89%	Motor (50%)
Patient mood is irritable	84%	Affective (78%)
Patient has hyperactive motor behavior	81%	Motor (67%)
Patient is agitated when touched by caregiver	92%	Response to stimuli (69%)
Patient has behavior that requires supervision	94%	Patient safety (50%)
Patient is combative toward caregiver that tries to comfort	94%	Affective/Pt. Safety (36/36%)
Patient behavior makes postoperative care difficult	97%	Patient safety (47%)
Patient is distressed by the monitoring equip. connected	92%	Response to stimuli (75%)
Patient's behavior is uncontrollable	100%	Patient safety (47%)
Patient seems panic stricken	97%	Affective (61%)
Patient interacts purposefully with caregiver	61%	Cognitive (94%)
Patient is hypersensitive to tactile stimuli	97%	Response to stimuli (83%)
Patient is attentive to his/her surroundings	58%	Cognitive (83%)

* Items that comprise the PAED Scale

Discussion

This study confirms that emergence delirium is a phenomenon of interest to CRNAs caring for combat veterans. In fact, a large majority of CRNAs in this sample indicated that an instrument to identify ED in the adult population would be useful in practice. Many of the descriptive words and phrases used to define ED in the pediatric literature were also used by CRNAs that witness ED in adults.

The first aim of this study was to identify defining characteristics of ED in adults. Literature review resulted in a litany of descriptive words and phrases that have been used to describe this post-operative complication dating as far back at 1960. Historically, clinical investigations have focused on ED in children because of the increased incidence when compared to adults.[3] The results of this study suggest that regardless of whether the condition manifests in children or adults, the behavioral descriptions used by clinicians are similar: restlessness, confusion, agitation, inconsolability, thrashing about, anger, yelling, violence, and combativeness.

The second aim of this study was to examine some contextual variables that further describe ED from the perspective of the CRNA. One of those variables was whether or not clinicians pharmacologically treat ED symptoms. CRNAs in this sample largely treated restless behavior in the post-operative period with a benzodiazepine. Midazolam, a common perianesthesia benzodiazepine, has been reported to successfully treat ED in children and is often used to treat other types of delirium.[2,10] The use of midazolam, however, can be accompanied by a paradoxical reaction manifesting as restlessness and

agitation.[11] Treatment of restless behavior in the post-operative period with a benzodiazepine is common clinical practice, as this study suggests.

The literature has also suggested that opioid use is a common first line preventive and post-operative treatment for ED.[12,13] Although used less frequently as a first line treatment when compared to midazolam, some respondents treated delirious emergence with an opioid. Further research is required to determine whether benzodiazepine or opioid therapy is a more effective for the treatment of ED in the adult population.

Individuals in this sample indicated using alpha-2 adrenergic agonist therapy (e. g. clonidine, dexmedetomidine) for the prevention of ED among combat veterans. A literature search revealed that dexmedetomidine has recently been studied for the treatment of emergence behavior of children as well as postoperative delirium in adult cardiac patients.[14,15] Dexmedetomidine has similar sedative properties when compared to midazolam and has been associated with less delirium.[10] There are no absolute contraindications to the use of dexmedetomidine. The use of alpha-agonists in the prevention of ED in combat veterans deserves further study.

The sample reported a perception that 24% of the combat veteran population emerged from general anesthesia with symptoms of ED. This should not be construed as a true incidence of ED among combat veterans, but it does raise concern. The reported incidence of ED in children is 18-57%.[2,16] Research in the general adult population reports an incidence of 4.7%.[8] A recent study reported an incidence of 5%, but excluded individuals with a past medical history of psychiatric illness.[9] Combat veterans present with a higher incidence of depression, anxiety, and PTSD (11.2-17.1%).[4] Future research

should be conducted that describes the incidence of ED in the combat veteran population and that explores depression, anxiety, and PTSD as possible predictors of ED.

The third aim of this study was to describe the relevance of the PAED Scale items as they pertain to the adult population. In addition, the sample of CRNAs were asked to categorize each scale item from one of the behavioral categories in order to assist in the determination of the instrument's use in the adult population. The relevance percentages of each of the preliminary scale items are described (Table 2). Participants scored less than <80% relevance on four of the five PAED Scale items. These results do not appear to be consistent with the prior work by Sikich and Lerman.[7] These four scale items would seem not to be indicative of ED. However, the request was made to the participant to rate the relevance of each scale item that they believed best-described ED behavior *in general*. At that point, the participants were not asked to consider the six behavioral categories associated with the items. For example, it seems logical that the patient's ability to maintain eye contact with the provider would not seem to describe ED in general, but the participants largely agreed that this scale item was descriptive of a cognitive behavior. A change in cognition is an essential feature when evaluating a patient for delirium.[17] The PAED Scale seems to reflect this, based on the fact that three of the five scale items were assigned to the cognitive behavior category.

The majority of the preliminary scale items, that were ultimately not included in the final PAED Scale, scored relatively highly (>80%) when considering the item as being descriptive of ED behavior *in general*. However, very few of these items represented the hallmark feature of ED, cognitive dysfunction. Again, these results do not appear to be consistent with the prior work by Sikich and Lerman.[7] The disparity between the results

of this study and that of Sikich and Lerman is most likely due to the confusion and misinterpretation of the sample because of the author's lack of clarity when constructing the *"Scale Development Survey – Emergence Delirium in Adults."* The composition of the PAED Scale was decided following statistical item analysis following its pre-testing on a sample of 100 children.[7] The results of this study show the percent agreement of experts when describing ED *in general* and are not based on a true analysis of the items when pre-testing them on a sample of patients experiencing ED, as was done by Sikich and Lerman. Modifying the PAED Scale by replacing scale items with those that may have scored higher in regard to relevance, would compromise the scale's overall ability to classify delirium appropriately. Recent literature suggests that an accurate description of cognition is necessary to the classification of delirium.[18,19]

When evaluated collectively, the items of the PAED Scale appear to be the best representation of the previously identified behavioral categories of ED when considering the adult population. The scale item *patient is restless* describes behavior that crosses several of the behavioral categories: response to environmental stimuli, affective, and motor. This item's ability to combine the evaluative process across three differenet behavioral categories adds to the ease-of-use as a bedside instrument. The scale item *patient is inconsolable* is largely a descriptor of the patient's affect, which can refer to a change in the individual's emotion. This item scored the highest percentile among the affective behavioral category items, justifying it as a critical component of the PAED Scale.

The PAED Scale is a short, easy-to-use, valid, and reliable instrument to measure ED.[7,15,20] These attributes, along with the content validation presented in this article,

suggest it would be appropriate for future research when evaluating ED in the adult population. After initial use in research with the combat veteran population, its validity and reliability can be corroborated or rejected for this proposed use.

Both in past research and in clinical application, there are numerous instruments that are effective at recognizing delirium. A recent study systematically reviewed these instruments and concluded that they all have the utility of identifying a patient with delirium, with time available being the only limiting factor.[19] The one thing that all these instrument have in common is that none of them were designed and content validated for use in the adult patient emerging from general anesthesia. The context in which emergence delirium occurs is different than that of other types of delirium (e. g. postoperative delirium).[3] The PAED Scale was developed for use in the OR or PACU. As stated at the beginning of this article, the authors believe that validating this instrument for use in the adult population was most appropriate.

Overall, and when considering the arguments in this discussion, the PAED Scale would be an appropriate instrument for measuring emergence delirium in future research with adults. Until this research is conducted, clinicians in a practice setting should not utilize the PAED Scale. A recommendation for further research is to identify the true incidence of ED in the combat veteran population while simultaneously performing psychometric evaluation of the PAED Scale for this use. Completion of this research is required before the PAED Scale is used in the clinical setting to aid in the assessment of ED for the adult population.

Instrument development in health science research is a complex and lengthy process by which one commits to discovering the best way to measure health-related conditions, often concerning a phenomenon that can appear very subjective. Results of this study can be considered as an early step in a multistage effort to validate the use of this instrument in the adult population. Clinicians and researchers can test the use of existing scales in differing populations, if they appear to have face validity, and if they appear to measure the same concept.[21] These results should be corroborated in other studies with CRNAs, especially those who treat non-military and/or non-combat patients.

Emergence delirium is a known postoperative complication in the adult population, specifically in the combat veteran where the incidence appears to be higher than among the general population. However, the true incidence remains undiscovered in this population, primarily because there has not been an instrument available to accurately identify the behavioral symptoms of ED. As the population of combat veterans continues to increase in the United States, it becomes important for military and civilian health scientists to accurately measure this phenomenon so that potential risk factors can be identified and treatments developed.

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Manuscript III

UNIVERSITY OF SAN DIEGO

Hahn School of Nursing and Health Science

The Incidence of and Risk Factors for Emergence Delirium in U. S. Military Combat Veterans

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Abstract

The purpose of this research was to identify the incidence and potential risk factors for Emergence Delirium (ED) in a U. S. military combat veteran surgical population at Naval Hospital Camp Pendleton (NHCP). ED is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia and is characterized by agitation, confusion, and violent physical and/or verbal behavior. Clinical evidence suggests that ED is increasingly seen among military personnel returning from the wars in Iraq and Afghanistan. Research suggests that the incidence of anxiety, depression, and Posttraumatic Stress Disorder (PTSD) are higher in this population than in non-combat troops and/or non-military populations. This observational, prospective, correlational study measured pre-operative anxiety, depression, and posttraumatic stress symptoms, and determined to what degree these predict the incidence of ED in a sample of 130 post-operative military personnel who had a history of combat exposure. The incidence of ED in this sample was 20% (N=26). Those previously diagnosed with a psychological disorder had a higher rate of ED (50%) than those that did not (17.5%), X^2=5.53, p<.05. There was a positive relationship between ED in veterans who reported greater amounts of anxiety, PTSD symptoms, and depression (state anxiety- $r(128)$=.40, p<.001, trait anxiety- $r(128)$=.40, p<.001, PTSD- $r(128)$=.35, p<.001, depression- $r(128)$=.25, p=.002). This study revealed the incidence of ED and identified anxiety, PTSD, and depression as risk factors. Regression modeling suggested that state-anxiety served as the best predictor. These findings increase clinicians' understanding of ED among combat veterans and give direction to future studies that should focus on preventive treatment.

Keywords: U. S. military, emergence delirium, general anesthesia, postoperative complications, anxiety, depression, PTSD

The 21st century has been marked by the American military involvement in the wars of Iraq and Afghanistan. Thousands of combat veterans continue to serve on active duty; others have made the transition to civilian life. Collectively, all American combat veterans have made an enormous sacrifice through their service. Exposure to combat and other deployment stressors has resulted in a myriad of mental health problems including, generalized anxiety, depression, and post-traumatic stress disorder (PTSD).[1] In order to improve the lives of these American heroes, efforts have begun to research problems that affect veterans in order to optimize the health care they receive.

Emergence delirium (ED) is a post-anesthesia complication that affects adults and children. It is defined by the behavioral symptoms of restlessness, confusion, and possible combativeness upon waking from general anesthesia.[2] Recent anecdotal evidence suggests that the rate of occurrence is increasing among the combat veteran population. CRNA experts caring for this population estimated that they observe ED symptoms 27% of the time.[3] However, research to discover the true incidence among combat veterans has never been conducted. The purpose of this study was to describe the incidence of ED in a sample of combat veterans at one military hospital. In addition, secondary aims were to discover if anxiety, depression, and PTSD are possible predictors of this phenomenon.

Materials and Methods

Following approval by the institutional review board, this prospective, descriptive, correlational design investigation was conducted with a sample of combat

veterans that reported for elective surgery at Naval Hospital Camp Pendleton (NHCP). A purposive sample was sought to consist of active duty or separated military service members with a self-reported history of a combat zone deployment in support of Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) since the beginning of operations in 2001. Inclusion criteria included males and females between the ages of 18-35 years, who were able to read and speak English, and who required general anesthesia for surgery.

All patients scheduled for elective surgery at NHCP reported to the preoperative clinic 1-14 days prior to surgery to complete an anesthesia questionnaire. As part of the check-in procedure, the medical assistant staff at the clinic questioned the patient about whether or not they had a history of participation in combat operations in support of OIF/OEF since 2001. If they screened positive, the medical record was reviewed for further inclusion criteria. If all criteria were met and they expressed interest in participation, they were approached for possible inclusion in the study.

Following informed consent, routine demographic data was collected which included number of deployments, self-reported history of psychological disorders, and medications the subject was currently taking. Subjects then completed three measures: the 1) State-Trait Anxiety Inventory (STAI), 2) PTSD Checklist – Military (PCL-M), and 3) Patient Health Questionnaire (PHQ-9) in a secluded and quiet interview room. Each subject was monitored from outside the room and was asked to seek assistance, if needed, in order to properly complete the instruments. After completion, the subject was sent home until the day of surgery with a brochure that listed available deployment health resources.

On the day of surgery, the subject reported to the surgical staging area and the research team confirmed their agreed participation in the study. Data regarding self-report of pain, type, site, and laterality of surgical procedure were obtained. The subject then proceeded to the operating room for induction of general anesthesia in accordance with routine anesthesia procedures at NHCP.

Following surgery and upon emergence from general anesthesia, the subject was observed for behavioral signs of ED in the operating room. The operating room nurse and the anesthesia provider completed the Pediatric Anesthesia Emergence Delirium (PAED) Scale, without collaboration. The patient was then transferred to the PACU where the subject continued to recover from anesthesia. Referencing the subject's behavioral response during recovery, the recovery room nurse completed a third PAED Scale. Immediately following discharge from the PACU, data were collected on the type and amount of medication administered in the OR and PACU. Total surgical time and post-operative pain scores were also collected.

The Statistical Package for the Social Sciences (SPSS©/17.0) was used to analyze the data. Descriptive statistics were used to summarize the demographics and to identify central tendency, variability, and percentages of key variables. Inferential statistical analyses were performed to examine relationships between and among study variables.

The relationships between the two groups, those that had ED (PAED $\geq$15) and those that did not (PAED <15), were determined using, Student's *t* test, Fisher's exact test, Pearson's χ^2, and the Wilcoxon Rank-Sum test as appropriate. A multivariate analysis was performed using a backward linear regression to determine predictors for

ED. Emergence delirium was the dependent variable and the independent variables were state-anxiety, trait-anxiety, depression, and PTSD. $P < 0.05$ was considered significant.

State-Trait Anxiety Inventory

Anxiety was measured using the State-Trait Anxiety Inventory (STAI). The STAI is the definitive instrument to measure the specific domain of anxiety in the adult. It is the most widely used instrument for the assessment of anxiety.[4] The purpose of this instrument is to not only measure anxiety, but to distinguish between state anxiety (temporary, surrounding the surgical experience) and trait anxiety (permanent characteristic).[5] It is particularly valid and reliable for this study population. It has been validated for the 19-39 year-old age group ($\alpha > .90$ for state and trait anxiety). Further validating the STAI, it is positively correlated with the Anxiety Sensitivity Index,[6] as well as the Anxiety Scale Questionnaire and the Manifest Anxiety Scales.[7]

The STAI is a 40-question pencil-and-paper instrument. It is comprised of the Y1 (state-anxiety measure) and Y2 (trait-anxiety measure). Each question is centered on the emotions or feelings of the participant. Items are scored on a 1-4 scale: 1 being "not at all relevant," 4 being "very much relevant." Total scores range from 20 (low anxiety) to 80 (high anxiety) on both the state-anxiety and trait-anxiety portions of the exam.

Patient Health Questionnaire

Depression was assessed using the Patient Health Questionnaire (PHQ-9). The PHQ-9 is a simple 9-item instrument used to assist clinicians in identifying depression.

The items were derived directly from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) signs and symptoms of major depression.[8] It is a pencil-and-paper examination that centers on those symptoms and how they have "bothered" the patient over the previous two weeks on scale from zero to three (0=not at all, 3=nearly every day).[9] Scores are added resulting in a number between one and twenty-seven, 0-4 revealing no depression, 5-9 representing mild depression, 10-14 representing moderate depression, 15-19 representing moderately severe depression, and 20-27 representing severe depression.

The PHQ-9 is a valid and reliable measure of depression in the adult population. There is a positive correlation between the results of the PHQ-9 and those of the Medical Outcomes Study Short Form (SF-20), also another valid and reliable measure of depression.[10] A strong positive correlation was also identified with the Beck Depression Inventory (BDI).[11] Internal reliability was excellent across two studies with a Cronbach's alpha >.86.[12,13] Considering individuals with neurological trauma, such as individuals with TBI, the PHQ-9 is a valid and reliable instrument for the identification of depression.[14]

Post-traumatic Stress Disorder Checklist – Military

PTSD symtomotology was assessed using the PTSD Checklist – Military (PCL-M). It is the original PCL version, designed to measure 17 symptoms of PTSD from the DSM-IV.[8] Questions are centered on the participant's response to "stressful military experiences" ranging from 1, "not at all" to 5, "extremely."[15] It is a brief self-report

instrument that has a long history of use among veterans with a history of physical and psychological injury.

PCL-M correlates strongly with the Clinician-Administered PTSD Scale and has an internal consistency of 0.94 (Cronbach's alpha).[16] Test-retest reliability has been reported as 0.88 and 0.96.[16,17] The PCL-M is not a diagnostic tool; however, it does indicate a probable diagnosis. Possible scores range from 17-85, with scores greater than 50 indicating the likelihood of combat-related PTSD.[15]

Pediatric Anesthesia Emergence Delirium Scale

Emergence delirium was measured using the Pediatric Anesthesia Emergence Delirium (PAED) Scale.[18] It is a five-item scale used to measure the patient's behavioral response upon emergence from general anesthesia. It is the only valid and reliable instrument designed to measure ED in children; there is no instrument designed to measure ED in adults. Each item is scored on a five-point scale ranging from "not at all" to "extremely," resulting in an aggregate score of 0-20. Construct validity was determined through hypothesis testing; internal consistency and inter-rater reliability has been reported at 0.89 and 0.84 respectfully.[18]

Content validity was performed in order to justify the use of the PAED Scale in adults using a cohort of expert certified registered nurse anesthetists (CRNAs) with experience of caring for combat veterans (McGuire JM, unpublished data, August 2009). Results of this study confirmed that the PAED Scale measured the same behaviors of ED, regardless of whether or not they occurred in children or adults. The decision to proceed

with the use of the PAED Scale for the measurement of ED was predicated on this notion and the fact that previous studies of ED in adults used instruments not designed to measure ED.[2,19]

The PAED is a reliable instrument for detecting symptoms of ED in this population of combat veterans (α=.84, 95% CI=.795 to .882). This was the first time this instrument was utilized to measure ED in a sample of combat veterans. Inter-rater reliability between the two PAED Scale scores recorded in the operating room was in agreement and highly significant 42% (κ=.36, p<.001). The internal consistency for the remainder of instruments is displayed in Table 1.

	Cronbach's Alpha
State-Anxiety Inventory	**.87**
Trait-Anxiety Inventory	**.92**
Posttraumatic Stress Disorder Checklist – Military	**.93**
Patient Health Questionnaire	**.85**
PAED Scale	**.84**

Table 1. Cronbach's Alpha Calculations for Study Sample.

Results

A total of 135 subjects were enrolled in the study. Five subjects were disqualified because they did not receive a general anesthetic on the day of surgery. All subjects were male with one exception (female, N=1). Members of the U. S. Marine Corps made up 92% of the sample (N=119) while members of the U. S. Navy comprised 8%. The entire sample reported at least one deployment to a combat zone while 88% identified

themselves as a combatant. A combatant was defined as an individual who had fired a weapon or taken enemy fire in a combat zone. The number of combat deployments (since 2001) ranged from 1 to 6 (mean 2.23, ± SD 1.22).

Of the 130 subjects included in the analysis, 26 were classified as having ED either in the OR or PACU (20%) according the highest PAED score obtained (positive for ED ≥15). No significant differences were found between those that experienced ED and those that did not when considering age, race, rank, education, marital status, number of deployments, type of surgery, location of surgery, length of surgery, type of anesthetic used, and use of adjunct medications (droperidol, metoclopramide).

Emergence delirium differed significantly between those that reported a history of a psychological disorder. Twenty-eight percent of the combat veterans in this study reported a past diagnosis of a psychological disorder (anxiety, depression, PTSD)(N=36). Those previously diagnosed had a higher rate of ED (46%) than those that did not (13%), X^2=5.53, p=.027. Thirty-nine percent of those with a known psychological disorder reported current pharmacologic treatment.

Demographic Variable	Emergence Delirium *(PAED ≥15)* N=26 (20%)	No Emergence Delirium *(PAED<15)* N=104 (80%)	P-value ED *vs.* No ED
Age [mean and (SD)]	27(5)	26(4)	0.281*
Years of education:			
12 (high school)	20	65	0.167¶
>12	6	39	
Race			
White	15	74	
Latino	9	19	0.383 □
African decent	1	6	
Other	1	5	
Marital status			
Married	18	67	0.818**
Single/Divorced	8	37	
Rank			
Junior (E1-E5 & O1-O3)	20	85	0.584**
Senior (E6-E-7)	6	19	
Number of deployments			
1	10	35	
2	6	34	
3	6	18	0.976§
4	2	13	
5	1	3	
6	1	1	
Type of surgery			
Orthopedics	15	58	0.254¶
Otolaryngology/OMF	9	25	
General/Urology	2	21	
Location of surgery			
Extremity	15	58	0.254¶
Head/neck	9	26	
Chest/back/abd/pelvis	2	20	
Type of volatile anesthetic			
Sevoflurane	16	70	0.645**
Desflurane	10	34	
Use of nitrous oxide			
Yes	19	88	0.248**
No	7	16	
Use of metoclopramide			
Yes	1	11	0.458**
No	25	93	
Use of droperidol			
Yes	1	5	1.000**
No	25	99	
Self-report of psychological disorder (anxiety, depression, or PTSD)			0.027**
Yes	12	24	
No	14	80	

*t Test / **Fisher's Exact Test / §Wilcoxon Rank-Sum Test / ¶ Pearson χ^2 / □ Likelihood Ratio

Table 2. Demographic Variables

The Verbal Numeric Pain Scale (VNRS) is a valid and reliable instrument for the assessment of acute pain.[20] There was no correlation between pre-operative VRNS scores and the highest PAED Score. The correlation between the highest PAED score and post-operative VNRS scores was statistically significant, $r(128)=.21$, $p=.018$. Combat veterans that complained of greater amounts of pain in the PACU experienced greater ED symptoms. The correlation between the highest PAED score and the amount of fentanyl received was also statistically significant, $r(128)=.18$, $p=.038$. Combat veterans that received greater amounts of fentanyl for pain experienced more ED symptoms. There was no significant relationship between use of midazolam and PAED score.

There was a positive relationship between anxiety, PTSD, depression, and ED. Zero-order correlations between state anxiety, trait anxiety, PTSD and ED were all moderate and statistically significant; state anxiety- $r(128)=.40$, $p<.001$, trait anxiety- $r(128)=.40$, $p<.001$, PTSD- $r(128)=.35$, $p<.001$. Twenty-two percent of subjects in our study scored ≥ 50 on the PCL-M, which is indicative of a likely diagnosis of PTSD.[16] Five percent of the sample presented with moderately severe to severe depression (PHQ ≥ 15). The correlation between depression and ED was small but statistically significant, $r(128)=.25$, $p=.002$. Combat veterans who reported a greater amount of anxiety, PTSD symptoms, and depression presented with greater symptoms of ED. Individuals who scored higher on these psychological tests displayed more symptoms of ED and therefore, were more difficult to manage postoperatively.

Regression

Linear regression was used in order to determine to what extent anxiety, depression, and PTSD predict the outcome of ED. The overall regression model as proposed was statistically significant, $F(4,125)=8.029$, $p<.001$, $R^2=.204$. Therefore, when considering state-anxiety, trait-anxiety, depression, and PTSD as risk factors for ED, they account for 20% of the variance. Only state-anxiety was significant when entering all four of the predictor variables into the model. The regression coefficient relating state-anxiety scores and ED was B=0.112, p=.032, 95% CI=.010 to .215. When controlling for all other predictors, combat veterans with more state-anxiety had more ED symptoms.

After criterion for backward regression was met (probability of *F*-to-remove ≥0.1), the second model removed PTSD as a predictor, $F(3,126)=10.079$, $p<.001$, $R^2=.194$. Therefore, when considering state-anxiety, trait-anxiety, and depression, they account for 19% of the variance in ED. Both state-anxiety and trait-anxiety were significant when entering these three predictors into the model (respectively, B=0.114, p=.031, 95% CI=.011 to .217 and B=0.144, p=.025, 95% CI=.018 to .270).

Finally, the third model removed PTSD and depression as a predictor, $F(2,127)=14.738$, $p<.001$, $R^2=.188$. Therefore, when considering state-anxiety and trait-anxiety, they account for 19% of the variance in ED. Both predictors state-anxiety and trait-anxiety were significant in this model (respectively, B=0.107, p=.039, 95% CI=.005 to .209 and B=0.114, p=.037, 95% CI=.007 to .221).

Model		Unstandardized Coefficient (B)	β	P-value (Sig.<.05)	Confidence Interval (95%)
1	state-anxiety score	0.112	0.245	.032*	.010-.215
	trait-anxiety score	0.109	0.228	.113	-.026-.245
	PCL-M score (PTSD)	0.060	0.176	.194	-.031-.152
	PHQ score (depression)	-0.181	-0.182	.162	-.436-.074
2	state-anxiety score	0.114	0.249	.031*	.011-.217
	trait-anxiety score	0.144	0.299	.025*	.018-.270
	PHQ score (depression)	-0.102	-0.103	.371	-.328-.123
3	state-anxiety score	0.107	0.234	.039*	.005-.209
	trait-anxiety score	0.114	0.237	.037*	.007-.221

*Significant

Table 3. Regression Model Statistics

Receiver Operating Characteristic (ROC) Curve Analysis

A ROC analysis was performed to offer a recommendation to clinicians when choosing an appropriate cut-off point when using the State-Anxiety Inventory to predict ED in this population. The analysis was done with the state-anxiety test score versus a PAED ≥15. The ROC curve generated from these data accounted for 71.3% of the area under the curve. A cut-off of 39 is the recommended score, which corresponds to a sensitivity of .69 and a 1-specificity of .28. (Figure 1).

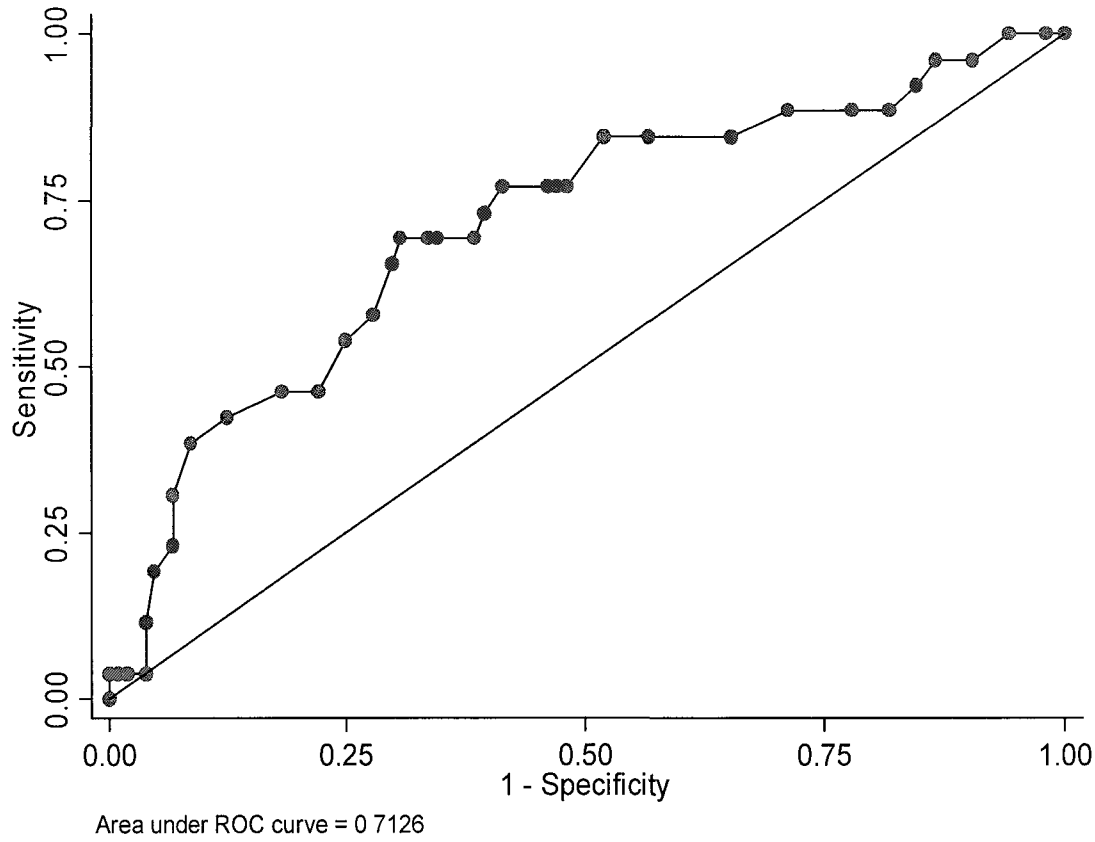

Figure 1. Receiver operating characteristic (ROC) curve for the true-positive rate (sensitivity) and false-positive rate (specificity) for the stait-anxiety score's ability to predict ED. A score of 39 on the state-anxiety score corresponds to a sensitivity of 0.69 and a 1-specificity of 0.28.

Discussion

The purpose of this research was to identify the incidence and potential risk factors for Emergence Delirium (ED) in a U. S. military combat veteran surgical population at Naval Hospital Camp Pendleton (NHCP). ED is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia and is characterized by agitation, confusion, and violent physical and/or verbal behavior.

Clinical evidence suggests that ED is increasingly seen among military personnel returning from the wars in Iraq and Afghanistan. Previous work indicates that ED is a phenomenon of concern among nurse anesthetists treating the combat veteran surgical population and supports the use of the Pediatric Anesthesia Emergence Delirium (PAED) Scale in adults (McGuire JM, unpublished data, August 2009). Research suggests that the incidence of anxiety, depression, and PTSD are higher in this population than in non-combat troops and/or non-military populations.[1]

The results of this investigation suggest that there is a relationship between anxiety, depression, PTSD, and ED in this sample of combat veterans. However, it is difficult to make direct conclusions about causality. The measure of variability between these variables and the outcome of ED ranges from 19% to 20%. This means that the remainder of the variability (80%-81%) is accounted for by other factors. These findings agree with the literature in that ED is multifactorial; there is no single cause for ED in adults.[2,3,19]

Anxiety has long been associated with the incidence of ED in the pediatric population.[21] Studies that included adults have either failed to recognized anxiety as a risk factor for ED or excluded individuals with psychiatric conditions.[2,19] The results of this study suggest that both state-anxiety and trait-anxiety are significant risk factors. In fact, state and trait-anxiety, when controlling for depression and PTSD, accounted for 19% of the variability in this population. Although PTSD and depression failed to be significant predictors for ED in this study, one cannot not ignore the biobehavioral similarities that these mental health disorders share with anxiety.[22]

Of the preoperative instruments used in this study, the authors suggest the use of the state -anxiety score serves as the best predictor for ED in this population. ROC curve analysis is a technique used for establishing a recommended cut-point when using an instrument to predict possible true cases, while minimizing the chance of a false-positive.[23] For example, if two individuals are observed postoperatively and one individual screens positive for ED (PAED ≥15) and the other does not, there is a 71.3% (area under the curve) chance that the individual without ED would score lower on the trait-anxiety inventory than the individual that screened positive for ED. A recommended cut-off score of 39 on the state-anxiety inventory would yield a sensitivity of 0.69 and a 1-specificity of 0.28, maximizing the true-positive rate while minimizing the risk for a false-positive.

Blanchard et al.[16] identified a score 50 or greater on the PCL-M as the most sensitive and specific score that leads to a later diagnosis of PTSD. Twenty-two percent of the subjects in our study scored ≥50 on the PCL-M. This rate of PTSD is slightly higher than previously described (12.2% - 19.9%).[1] However, symptoms of PTSD contributed the least variability in ED (PAED ≥15), as it was the first predictor to be eliminated in the regression model. Although there is a relationship between the PCL-M score and ED, it fails to be statistically significant when controlling for other predictors. This study suggests that PTSD is related to ED in combat veterans, but the cause is most likely due to a multitude of factors.

Five percent of the sample presented with symptoms of moderately severe to severe depression (PHQ ≥15). This rate is lower than previously described (7.1% - 14.7%).[1] There was a positive relationship between depression and ED. Although the

PHQ score was correlated with ED, it accounts for only a small percentage of the variability. Again, this suggests that ED in the combat veteran is multifactoral.

The study results suggest a relationship between post-operative pain scores, fentanyl requirement, and ED. Subjects that complained of more pain in the PACU, according to the first obtained VNRS score, presented with more symptoms of ED. This is consistent with previous research of postoperative delirium in adults, those with higher pain scores were at increased risk of delirium.[24] In addition, Radtke et al.[19] found that higher postoperative pain scores was a risk factor for ED. Not surprisingly, those combat veterans who had higher VRNS scores postoperatively also required more fentanyl in the OR and PACU. Those subjects that received minimal fentanyl had a lower incidence of ED. A limitation to these findings is that data on the use of regional anesthesia for postoperative pain control was not collected. This is important because 56% of the surgery in this study was orthopedic, often performed on the extremity where a regional anesthetic could have been used. Future research should be conducted that investigates the use of regional anesthesia and how it relates to the incidence of ED.

A further limitation to the study is the small sample size of combat veterans enrolled from one military hospital. This limits the generalizability of the findings; therefore it is difficult oversimplify these results and apply them to all combat veteran populations at other healthcare facilities. The majority of the sample included active duty members of the U. S. Marine Corps. This branch of service often carries the stigma of anxiety, PTSD, and depression that may potentially affect the way in which one completes self-report measures aimed at identifying these psychological disorders. Although great care was taken during the consent process to ensure that the veteran

understood how these measures would be used, Marines are often concerned with how these conditions might negatively effect how they are perceived as a "warrior." This may have resulted in an inaccurate assessment of anxiety, PTSD, and depression. This could explain the stronger relationship between those previously diagnosed with a psychological disorder and the higher incidence of ED. A previous diagnosis may bring about a certain amount of acceptance in the veteran concerning their condition, therefore, removing this as a barrier to accurate assessment. If this study was somehow carried out in a non-military environment with non-military investigators as members of the research team, this could limit potential error in psychological measurement.

Furthermore, future research warrants a calculation of power in order to determine the sample size necessary to detect smaller differences among study variables. To our knowledge, this was the first time ED was studied in the combat veteran population, making it difficult to predict adequate sample size. Based on the results of this study and the future researcher's plans for statistical analysis, an effect size can be calculated in order to more accurately detect differences and generalize findings to the larger combat veteran population.

The results of this study suggest that the incidence of ED among the combat veteran population is higher (20%) when compared to the general adult population (5%).[2,19,25] The military population is exposed to unique stressors when they perform their required duties, combatants arguably being the most vulnerable to mental health problems. The percentage of study subjects whose responses met screening criteria for anxiety, PTSD, and depression was higher than found in the general adult population. As mental health problems increased in this sample population, so did the incidence of ED.

These results could be beneficial to military perianesthesia practitioners and to those professionals that care for combat veterans. A review of the documented history of these psychological disorders may alert anesthesia providers to a possible delirious episode following surgery. This information may aid the provider as they tailor their anesthetic in order to curb the incidence of ED. As suggested, clinicians could administer the State-Anxiety Inventory (or any simple self-report measure) preoperatively in order to obtain a more accurate description of their current health status.

Future research is required before the PAED Scale can be used with adults in the clinical setting. However, this study suggests that the PAED Scale is a valid and reliable instrument for use in clinical research. A study of ED among combat veterans should be conducted with a larger sample, across multiple centers in order the increase the generalizability of the findings. A broader representation of military service branches should be included as there are inherent differences in mission requirements and exposure to deployment stressors.

Dexmedetomidine has been recently studied as a new and novel preventive therapy for ED in the pediatric population.[26] A randomized-controlled trial should be conducted that focuses on this as a possible preventive treatment. Conducting a study among combat veterans using dexmedetomidine when compared to a control group, would identify whether or not this would be an effective preventive treatment in this high risk population.

In conclusion, this study describes the incidence of ED in a sample population of combat veterans and identifies anxiety, PTSD, and depression as risk factors. As the

number of U. S. combat veterans continues to rise with the on-going conflict in the Middle East, it is imperative that we research the problems that are inherent to their service. Continued research in this area may someday provide the tools necessary to identify the individuals that are at high-risk for emergence delirium and prevent its occurrence.

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Appendix A

Research Participant Consent Form

Title of Research Study: *A Survey of Certified Registered Nurse Anesthetists regarding the Concept of Emergence Delirium.*

Introduction

Jason McGuire, MS, CRNA is a doctoral student in nursing at the Hahn School of Nursing and Health Science at the University of San Diego. You are invited to participate in a study he is conducting for the purpose of exploring emergence delirium (ED) in adult patients.

Procedures . The research project will involve filling out a survey that will take about 10 minutes. Jason will ask you to fill out a questionnaire that will ask you information about yourself and how you view emergence delirium in patients. A typical item on this questionnaire is, "How descriptive are the following symptoms for patients with ED: Moaning; restlessness; involuntary physical activity. " You will be asked to rate these symptoms for their relevance. You will also be asked general questions about yourself such as your age, gender, if you've been in the military, and how long you've practiced as a CRNA. Finally, you'll be asked for any ideas or comments you might have about ED.

Risks. There may be a risk that you may feel tired or fatigued while filling out the questionnaires. You can stop at any time to rest, decide not to fill out all the forms, or withdraw from the study anytime.

Sometimes when clinicians are asked to think about difficult patient situations, they feel anxious or sad. If you would like to talk to someone about your feelings at any time, you can call**: the San Diego Mental Health Hotline *on a 24 hour a day basis, 7 days a week* at 1-800-479-3339**. If you would like to talk to someone in your local area after you return home, you can still dial this number, and ask to be referred to a number in your area. You can also dial 411 and ask for "mental health services" in your area.

Benefits: The benefit to participating will be in knowing that you helped CRNAs and other clinicians know more about what emergence delirium is like in their patient populations.

Participant Costs: The only cost to you is 10 minutes of your time.

Confidentiality: Any information provided and/or identifying records will remain confidential and safeguarded in a locked file in the researcher's office for a minimum of five years. All data collected from you will be coded with a number and not your name.

The results of the research project may be made public and information quoted in professional journals or meetings, but information from this study will only be reported as a group, and not individually.

Voluntary Participation and Withdrawal

Participation in the research project is entirely voluntary and you can refuse to answer any question and/or quit at any time. Should you choose to quit, no one will be upset with you. Deciding not to participate or answer some of the questions will have no effect on your membership in AANA, your status as a CRNA, your job status, or any other services/benefits to which you are entitled.

More Information

If you have any additional questions about this research project, please contact Jason McGuire, MS, CRNA, at [redacted] or by email at [redacted]. You may also contact Dr. Joseph Burkard, the professor who is supervising this research, at the University of San Diego School of Nursing [redacted] or by email at [redacted] for additional information.

I have read and understand this form, and consent to the research it describes to me. I have received a copy of this consent form for my records.

Signature of Participant Date

Name of Participant (Printed)

Signature of Investigator Date

Appendix B

Survey of Certified Registered Nurse Anesthetists regarding the Concept of Emergence Delirium

Purpose: To gain the perspective of practicing CRNAs clinical experiences with emergence delirium as it occurs in the young adult population, specifically the combat and/or psychological trauma victim.

Directions: Please read each question carefully and answer it to the best of your ability from your recollection. Complete the entire survey as to ensure good data collection. Please sign and date the release consent on the previous page so that your answers can be used for analysis and reporting.

Demographic Information:

Please mark ☒one of the following-

1.	☐Military CRNA	☐Non-military CRNA
	☐Former-military CRNA	
2.	☐Male	☐Female

Please write in-

3.	Age in Years:_____
4.	Number of years in anesthesia practice:_____

5. Considering the population you serve, please represent the percentage of the following age groups in regards to frequency of anesthetics provided: (total must equal 100%)

_____ infants (birth to 2 years)

_____ children (ages 3-12 years)

_____ adolescents (ages 13-17 years)

_____ young adults (ages 18-29 years)

_____ adults (ages 30-65 years)

_____ elderly (>65 years-old)

_____ TOTAL % (must equal 100%)

6. To the best of your knowledge, what percentage of your total caseload involves caring for patients with known psychological disorders? e.g. anxiety, depression, cognitive dysfunction (write in percent)

_____%

7. What percent of your total caseload involves the care of combat veterans?

_____%

8. If you care for combat veterans, to the best of your recollection, what percentage of those have documented post-traumatic stress disorder (PTSD), depression, or other related anxiety disorder? (write in percent)

_____%

When reading and interpreting the concept of "Emergence Delirium" in the following questions, please utilize the following definition:

> Emergence delirium (ED) is a post-anesthetic phenomenon that occurs immediately following emergence from general anesthesia in adults and children. It is characterized by agitation, confusion, and violent physical and verbal behavior in the operating room or the post-anesthesia care unit.

Model Case (Example):

> A 24 y/o male presents to the operating room requiring general anesthesia for an ORIF revision (extraction/placement) of a right tibial nailing following a blast injury. Past medical history reveals sleep disturbances related to his general anxiety disorder. He emerges one hour later in the operating room following extubation, confused, agitated, and attempting to roll off the operating room table. He is yelling incoherently and is unresponsive to verbal commands to remain still while physically restraining him in order to provide a safe environment.

9. Considering the definition of Emergence Delirium (ED) offered, please read the list of descriptive words and phrases below. Please grade each item on a scale from 1 to 7, 1 if you consider the item not descriptive at all, 7 if you consider the item very descriptive of this post-anesthetic event.

not at all descriptive very descriptive

1 2 3 4 5 6 7

(#)		(#)	
	Moaning		Lack of cooperation
	Restlessness		Angry
	Involuntary physical activity		Frightened
	Thrashing about		Yelling
	Crying		Violent
	Confusion		Verbally abusive
	Hallucinations		Combative
	Delusions		Incoherent speech
	Agitation		Weeping

10. At this time, please feel free to write down any and all descriptive words or phrases (not listed previously) that you believe would help describe the situations of ED that have occurred in your practice.

11. Previous research has identified six categories of ED behaviors:

(1) Cognitive (arising from purposeful thought) behavior

(2) Behavioral response to environmental stimuli

(3) Behavior threatening patient safety

(4) Motor behavior

(5) Affective (arising from emotions) behavior

(6) Vocal behavior

Please place a number of one (1) of the six categories above next to each scale item below that you believe best corresponds to it's description.

(#)

	A. patient can focus attention on caregiver
	B. patient pulls at the monitoring equipment or IV that is connected
	C. patient behavior threatens his/her safety
	D. patient movements are disruptive
	E. patient mood is irritable
	F. patient makes eye contact with caregiver
	G. patient has hyperactive motor behavior
	H. patient actions are purposeful
	I. patient is agitated when touched by caregiver
	J. patient has behavior that requires supervision
	K. patient is restless
	L. patient is combative toward the caregiver who tries to comfort them
	M. patient behavior makes postoperative care difficult
	N. patient is aware of his/her surroundings
	O. patient is distressed by the monitoring equipment connected to him /her
	P. patient is inconsolable
	Q. patient's behavior is uncontrollable
	R. patient seems panic stricken
	S. patient interacts purposefully with caregiver
	T. patient is hypersensitive to tactile stimuli
	U. patient is attentive to his/her surroundings

12. Please read the following scale items again. Place the number of one of the six categories above in front of the scale items that you believe best describes that behavior. Then rate (circle) the relevance of each scale item to the definition of ED provided. 1 = Not at all relevant, 7 = Extremely relevant.

A. **patient can focus attention on caregiver**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

B. **patient pulls at the monitoring equipment or IV that is connected**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

C. **patient behavior threatens his/her safety**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

D. **patient movements are disruptive**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

E. **patient mood is irritable**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

F. **patient makes eye contact with caregiver**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

G. **patient has hyperactive motor behavior**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

H. **patient actions are purposeful**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

I. **patient is agitated when touched by caregiver**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

J. **patient has behavior that requires supervision**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

K. **patient is restless**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

L. **patient is combative toward the caregiver who tries to comfort them**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

M. **patient behavior makes postoperative care difficult**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

N. **patient is aware of his/her surroundings**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

O. **patient is distressed by the monitoring equipment connected to him /her**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

P. **patient is inconsolable**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

Q. **patient's behavior is uncontrollable**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

R. **patient seems panic stricken**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

S. **patient interacts purposefully with caregiver**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

T. **patient is hypersensitive to tactile stimuli**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

U. **patient is attentive to his/her surroundings**

not at all relevant						extremely relevant
1	2	3	4	5	6	7

13. If you care for victims of psychological disorders and/or combat veterans, what percentage of those patients emerge from general anesthesia with symptoms of ED? (write in percent)

_____%

14. If ED occurs in your practice, do you pharmacologically treat the symptoms?

(mark ☒ one)

☐Yes	☐No

15. If yes, what method do you most frequently employ? (mark ☒ one)

☐ Opioid	☐ Benzodiazepine
☐ Physostigmine	☐ Other_____

Consider the statements below and mark ☒ agree or disagree:

16. I consider ED, as it occurs in the adult, a phenomena of interest.

☐ Agree	☐ Disagree

17. I would find it helpful if an instrument were available to aid in the recognition of ED in this population.

☐ Agree	☐ Disagree

18. Please use the space below to contribute any comments or ideas you have in regards to the phenomena of emergence delirium (ED) as it occurs in the combat and/or psychologically traumatized victim.

Thank you!

Appendix C

NAVAL MEDICAL CENTER

SAN DIEGO, CALIFORNIA 92134-5000

CONSENT BY A *SUBJECT* FOR VOLUNTARY PARTICIPATION IN A CLINICAL INVESTIGATION (RESEARCH) STUDY

1. You, _____, have been asked to voluntarily participate in a research project entitled, **"Emergence Delirium in the U. S. Military"** being conducted at the Naval Hospital Camp Pendleton by medical researchers from the Department of Anesthesiology.

2. WHY IS THE STUDY BEING DONE?

The purpose of this research project is to: Discover the connection, if any, between your experiences as a veteran of combat or combat related deployment to the possible occurrence of waking from surgery confused and restless.

3. HOW LONG WILL YOU BE PARTICIPATING IN THE STUDY?

If you agree to participate in this study you will be involved from now until being discharged from the hospital after surgery.

4. WHAT IS INVOLVED IN THE STUDY?

Your involvement in this study includes completing a series of paper-and-pencil tests and a questionnaire the day you perform your pre-operative anesthesia interview, which usually occurs the day before or days before your scheduled surgery. The questionnaire and tests take approximately 30 minutes of your time to complete. The questionnaires involve asking you about your past and present experiences and emotions, some of them ask about your deployment or combat experiences. Questions also concern your physical and mental health, as you perceive them. As part of this project, these tests and the questionnaire will be analyzed and interpreted by medical and psychology professionals and used to determine relationships between medical conditions and how they might be related. Your involvement in this study continues on the day your surgery is scheduled. A member of the

project team will ask you some simple questions. For example, you will be asked about what medications you are taking. You will also be asked as part of this study to rate the intensity of your pain, if any, using a 0-10 scale. A "0" on this scale will indicate "No Pain," and a "10" will indicate "The Worst Pain Imaginable".

Your surgical procedure and anesthetic will go as planned according to the agreement you have reached with your surgeon and your anesthesia provider. A member of the project team will be present at certain times to observe and collect information. Specifically, a member of the project team will be present during the period of time in which you wake up from your anesthesia, both in the operating room and the post-anesthesia care unit. Observations will be made in regard to the manner in which you wake up from anesthesia. For example, the purposefulness of your actions, your level of awareness at certain times and the degree of restlessness, if any. These behaviors will be graded and recorded for the purposes of the study. These observations and their recordings are not part of your medical record. Additional information will be obtained from your anesthesia record, recovery room record and/or your anesthesia provider and post-anesthesia care nurse. This information will be your level of pain, details on the type of anesthetic your received and any additional medications you may have received as part of your care.

5. WHAT IS THE EXPERIMENTAL PART OF THE STUDY?

Specifically, you should be aware that there is no "experimental" part of this research study. It is a "correlational" study or an "observational" study. Information collected from your participation will be used to make a statistical "connection", if any, to the results of the tests/questionnaire given before surgery, to any behavioral signs observed, if any, in the time immediately following surgery. The research team will at no time be a part of deciding on the care you receive or provide any of that care. We are simply there to observe and record.

6. HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

A total of 133 active duty, reserve, or separated service members with combat and/or deployment experience are expected to participate in this study. Your participation in this study is just one day and the total duration of the project is approximately 6 months.

7A. WHAT ARE THE RISKS OF THE STUDY?

The risks or discomforts, which are possibly related to your participation in this study, are minimal. In other words, no greater risk than those experienced in everyday life. Included in that risk is the experience of unpleasant emotions such as fear, anxiety and sadness. This would more than likely occur during or after your completion of the surveys and questionnaire, a day or days prior to your surgery. The nature of some of the questions can lead a person to experience these unpleasant emotions because it can remind you of unpleasant memories of your past. An additional minimal risk is fatigue. The surveys and questionnaire portion of your participation involves sitting and requires your attention to the paper-and-pencil tasks for approximately 30 minutes. This can bring about both physical and mental fatigue.

8. ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You should understand that your participation in this research study may or may not be of direct benefit to you personally. However, the results of this study may help the investigator gain important knowledge about certain potential risk factors associated with the occurrence of emergence delirium or aid in future medical evaluation and treatment of other patients.

9. WHAT OTHER OPTIONS ARE THERE?

If you decide not to participate in this research study, you may decline now or at any time. This study is not an "experiment" and does not change or modify the care surrounding your surgical experience in any way. Your surgery and anesthetic is not modified in any way, regardless if you participate or decide not to participate, without retribution, expressed or implied. This research study is not designed to treat any medical condition that you may have. Therefore, there are no alternative procedure(s) or course of treatment that would be advantageous to you.

10. WILL I BE PAID TO PARTICIPATE?

You will not be financially compensated for your participation in this study.

11. WHAT IF I AM INJURED AS A RESULT OF PARTICIPATION IN THIS STUDY?

If you should suffer any injury directly related to your participation in this research study, immediate medical attention is available at the Naval Hospital Camp Pendleton or at another closer military medical treatment facility, if applicable. You should understand that although no financial compensation is available, any injury resulting from your participation in this study will be evaluated and treated in keeping with the benefits or care to which you are entitled under applicable Navy, Department of Defense, and other state or Federal regulations.

12. WHAT ABOUT CONFIDENTIALITY?

In all publications and presentations resulting from this research study, information about you or your participation in this project will be kept in the strictest confidence and will not be released in any form identifiable to you personally. However, authorized personnel from the Navy Medical Department may have access to your research file in order to verify that your rights have been adequately protected.

PATIENT AUTHORIZATION TO USE AND/OR DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH (HIPAA)

(In Keeping with the Health Insurance Portability and Accountability Protection Act)

What is Confidentiality of records all about?

The Naval Hospital Camp Pendleton makes every effort to maintain the confidentiality of protected health information we obtain about you. However, we cannot absolutely guarantee confidentiality because other people may need to see your information in the course of this research study. Most people and organizations will protect the privacy of your information, but may not be required to do so by the law. Also, if the results of this research study are presented at meetings or are published, your name will not be used.

What is HIPAA all about?

The Health Insurance Portability and Accountability Act (HIPAA) requires that we get your permission to use protected health information about you that is either created by or used in connection with this research study. This permission is called an Authorization. The information we use includes your entire research record and supporting information from your medical records,

results of laboratory test, X-rays, MRIs, CT scans and observations made by a physician or nurse which are both clinical and research in nature.

What will we do with this information?

Your protected health information will be collected and used during the course of the research study, to monitor your health status, to measure the effects of drugs or devices or procedures, to determine research results, and to possibly develop new tests, procedures, and commercial products.

Your research investigator will use this information to report the results of research to sponsors and federal agencies. The information may also be reviewed when the research study is audited for compliance. When the study is over, you have the right to see the information and copy it for your records.

Who will we share your information with?

Your information may be shared with any of the following:

- The sponsor of the study, or its agents, such as data repositories
- Other medical centers, institutions, or research investigators outside of the Naval Hospital Camp Pendleton, participating in this research study
- State and Federal agencies which have authority over the research, the Naval Hospital Camp Pendleton or patients. Good examples are: the Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), the National Institute of Health (NIH), the Office of Human Research Protections (OHRP), and the Department of Social Services (DSS) or other.
- This hospital or clinic.
- Accrediting agencies, such as JCAHO.
- A data safety monitoring board, if applicable
- Clinical staff who may not be involved directly in the research study, but who may become involved in your care, if it is possibly related to treatment

For this research study, the study investigator may share this authorization form and records which identify you to comply with regulatory requirements or for purposes related to this research to:

All documented Principal, Associate, and Sub-investigators, and the Medical Monitor (if one is assigned).

What if you want to revoke or cancel away your Authorization?

If you decide to participate in this research study, your Authorization for this study will not expire unless you revoke or cancel it in writing to the research investigator. If you revoke your Authorization, you will also be removed from the study, but standard medical care and any other benefit to which you are entitled will not be affected in any way.

Revoking your Authorization only affects the use and disclosure (sharing) of information after your written request has been received. Federal law requires sending study information to the FDA for studies it regulates, like studies of drugs and devices. In a case like this, your information may need to be reported to them and cannot be removed from the research records once it is collected.

Do you have to sign this form?

You have the right to refuse to sign this Authorization form and not be a part of this study. You can also tell your study investigator you want to withdraw from the study at any time without revoking the Authorization to use your health information. By signing this research Authorization form, you authorize the use and/or disclosure of your protected health information described above.

This authorization expires 25 years from the date of signature.

13. WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions regarding this research study, you may contact **LCDR Jason McGuire at [redacted].**

If you have any questions about your rights as an individual while participating in a research study at the Naval Hospital Camp Pendleton, you may contact **CAPT David Tanen, MC, USN, Chairman, Institutional Review Board at [redacted], or CAPT Peter Linz, MC, USN, Head, Clinical Investigation Department at [redacted].**

If you believe that you have been injured as a result of your participation in this research study, you may contact **CDR Mary Ellen Moss, JAGC, USN, Naval Medical Center, San Diego, Legal Department, at [redacted]**

14. WHAT ARE MY RIGHTS AS A PARTICIPANT?

Your participation in this project is entirely voluntary and your decision not to participate will involve no penalty or loss of benefits to which you are entitled under applicable regulations. If you choose to participate, you are free to ask questions or to withdraw from the study at any time. If you should decide to withdraw from the research project, you will notify **LCDR Jason McGuire** at [redacted] to ensure your timely removal from the study. Your withdrawal will involve no prejudice to your future health care or any loss of rights or benefits to which you are otherwise entitled. Any new significant finding developed during the course of this study, which might affect your willingness to continue participation will be communicated to you.

California Experimental Subject's Bill of Rights

(a) Be informed of the nature and purpose of the experiment.

(b) Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

(c) Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

(d) Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

(e) Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

(f) Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

(g) Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

(h) Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

(i) Be given a copy of the signed and dated written consent form as provided for by Section 24173 or 24178.

(j) Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

15. CAN I BE TERMINATED FROM THE STUDY?

The investigator may terminate your participation in this study for the following reasons: Your failure to comply with the study procedures or the investigator determines that the procedures are unsafe.

16. SIGNATURE

You are making a decision whether or not to participate in the research project above. Your signature indicates that you have had this information presented to you, have had the opportunity to ask questions about the research and your participation, and agree to participate in the study. Further, your signature indicates that you have been provided with a copy of this consent document, a Health Information Portability and Accountability Act (HIPAA) Patient Authorization form and a document entitled, "California Experimental Subject's Bill of Rights."

SIGNATURES AND **DATE** SIGNED: **PRINTED** OR **TYPED IDENTIFICATION**:

Patient / Subject (Date) Name

Investigator/Researcher (Date)Name / Grade or Rank

Appendix D

ED Study Data Collection Sheet

Subject #_____ *Complete the following prior to surgery:*

Age (years)_____	Gender (mark one ☒) ☐ Male ☐ Female
Ethnicity or Race: (mark one ☒) ☐ American Indian or Alaskan Native ☐ Asian ☐ Black or African American ☐ Native Hawaiian or other Pacific Islander ☐ Hispanic or Latino ☐ White	Years of formal education: (mark one ☒) *High school education or GED = 12 years* ☐ 12 ☐ 13-16 ☐ 17-18 ☐ 19 or greater
Relationship status: (mark one ☒) ☐ Married ☐ Divorced ☐ Widowed ☐ In relationship ☐ Single	Branch of service: (mark one ☒) ☐ Marine Corps ☐ Navy ☐ Army ☐ Air Force ☐ National Guard ☐ Coast Guard
Current military service: (mark one ☒) ☐ Active ☐ Reserve ☐ Separated	Current rank/last rank obtained: (mark one ☒) ☐ E1-E3 ☐ E4-E5 ☐ E6 ☐ E7 or greater ☐ O1-O3 ☐ O-4 ☐ O-5 ☐ WO1 ☐ WO2 ☐ WO3 ☐ WO4
Number of service deployments since 2001: (mark one ☒) ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ other_____	
Deployment **1**: Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant	Deployment **2**: (if applicable) Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant
Deployment **3**: (if applicable) Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant	Deployment **4**: (if applicable) Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant
Deployment **5**: (if applicable) Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant	Deployment **6**: (if applicable) Year_____ AOO_____ (mark one ☒) ☐ Combat zone ☐ Combatant

Do you have a known history of any psychiatric condition? ☐ Yes ☐No If yes, please identify_____	Please list any medications you are currently taking: _____
Number of surgeries since 2001: (including current surgery)_____	

Complete the following on the day of surgery:

Type of surgery: (mark all that apply ☒) ☐ Ortho ☐ ENT ☐ General ☐ Oral ☐ Gyn ☐ Neuro ☐Vascular ☐ Other _____	Anatomical location of surgery: ☐ Arm ☐ Leg ☐ Hand ☐ Foot ☐ Chest ☐ Abdomen ☐ Head ☐ Pelvic ☐ Other _____	Medications used during surgery:(mark all that apply☒) ☐ Benzo, Amount (eg-Versed 2mg)_____ ☐ Opioid, Amount (eg-Fentanyl 100mcg_____ ☐N_2O ☐ Sevo ☐ Forane ☐ Des ☐ Propofol ☐ Ketamine ☐ Reglan ☐ Droperidol
Length of surgery: (round to nearest half-hour) Hours_____	Number of surgeries since 2001: (including current surg.) _____	First obtained VAS score upon emergence: (0-10) _____

Appendix E

Adult Emergence Delirium Scale (AEDS)

Directions for clinician rater: Please circle (rate) what you believe to be the most appropriate description of each of the ten (10) behavioral responses below while caring for your patient upon emergence from general anesthesia.

Subject # _____Location: (circle one) OR PACU

	not at all	just a little	quite a bit	very much	extremely
1. The patient makes eye contact with caregiver.	4	3	2	1	0
2. The patient's actions are purposeful.	4	3	2	1	0
3. The patient is aware of his/her surroundings.	4	3	2	1	0
4. The patient is restless.	0	1	2	3	4
5. The patient is inconsolable.	0	1	2	3	4
6. The patient behavior threatens his/her safety.	0	1	2	3	4
7. The patient has behavior that requires supervision.	0	1	2	3	4
8. The patient's behavior is uncontrollable.	0	1	2	3	4
9. The patient seems panic stricken.	0	1	2	3	4
10. The patient is hypersensitive to tactile stimulation.	0	1	2	3	4

Appendix F

Posttraumatic Stress Disorder Check List – Military

Instructions: Below is a list of problems and complaints that veterans sometimes have in response to stressful military experiences. Please read each one carefully, then circle one of the numbers to the right to indicate how much you have been bothered by that problem in the past month.

	Not at all	*A little bit*	*Moderately*	*Quite a bit*	*Extremely*
1. Repeated, disturbing *memories, thoughts, or images* of a stressful military experience?	1	2	3	4	5
2. Repeated, disturbing *dreams* of a stressful military experience?	1	2	3	4	5
3. Suddenly *acting or feeling* as if a stressful military experience *were happening again* (as if you were reliving it)?	1	2	3	4	5
4. Feeling *very upset* when *something reminded you* of a stressful military experience?	1	2	3	4	5
5. Having *physical reactions* (e.g., heart pounding, trouble breathing, sweating) when *something reminded you* of a stressful military experience?	1	2	3	4	5
6. Avoiding *thinking about or talking about* a stressful military experience or avoiding *having feelings* related to it?	1	2	3	4	5
7. Avoiding *activities or situations* because *they reminded you* of a stressful military experience?	1	2	3	4	5
8. Trouble *remembering important parts* of a stressful military experience?	1	2	3	4	5
9. *Loss of interest* in activities that you used to enjoy?	1	2	3	4	5
10. Feeling *distant or cut off* from other people?	1	2	3	4	5
11. Feeling *emotionally numb* or being unable to have loving feelings for those close to you?	1	2	3	4	5
12. Feeling as if your *future* somehow will be *cut short*?	1	2	3	4	5
13. Trouble *falling or staying asleep*?	1	2	3	4	5
14. Feeling *irritable* or having *angry outbursts*?	1	2	3	4	5
15. Having *difficulty concentrating*?	1	2	3	4	5
16. Being "*superalert*" or watchful or on guard?	1	2	3	4	5
17. Feeling *jumpy* or easily startled?	1	2	3	4	5

Appendix G

Patient Health Questionnaire (PHQ-9)

Over the *last 2 weeks*, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
	0	1	2	3

1. Little interest or pleasure in doing things

2. Feeling down, depressed, or hopeless.

3. Trouble falling/staying asleep, sleeping too much.

4. Feeling tired or having little energy.

5. Poor appetite or overeating.

6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down.

7. Trouble concentrating on things, such as reading the newspaper or watching television.

8. Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual.

9.Thoughts that you would be better off dead or of hurting yourself in some way.

Appendix H

State-Trait Anxiety Inventory (STAI)

University of San Diego

06/15/09

Institutional Review Board
Project Action Summary

Action Date: June 15, 2009 *Note: Approval expires one year after this date.*

Type: __New Full Review _X__New Expedited Review ___Continuation Review ___Exempt Review
____Modification

Action: _X__Approved ___Approved Pending Modification ___Not Approved

Project Number: 2009-06-126
Researcher(s): Jason McGuire Doc SON
Dr. Joseph Burkard Fac SON
Project Title: A survey of Certified Registered Nurse Anesthetists regarding the Concept of Emergence Delirium

Note: We send IRB correspondence regarding student research to the faculty advisor, who bears the ultimate responsibility for the conduct of the research. We request that the faculty advisor share this correspondence with the student researcher.

Modifications Required or Reasons for Non-Approval

None

The next deadline for submitting project proposals to the Provost's Office for full review is N/A. You may submit a project proposal for expedited review at any time.

[redacted]
Dr. Thomas R. Herrinton
Administrator, Institutional Review Board
University of San Diego
[redacted]

Office of the Vice President and Provost
Hughes Administration Center, Room 328
5998 Alcalá Park, San Diego, CA 92110-2492
Phone (619) 260-4553 • Fax (619) 260-2210 • www.sandiego.edu

University of San Diego

Institutional Review Board
Project Action Summary

Action Date: September 3, 2010 *Note: Approval expires one year after this date.*

Type: __New Full Review __X_New Expedited Review ___Continuation Review ___Exempt Review
____Modification

Action: _X__Approved ___Approved Pending Modification ___Not Approved

Project Number: 2010-09-001
Researcher(s): Jason McGuire Doc SON
Dr. Joseph Burkard Fac SON
Project Title: Emergence Delirium in the US Military

Note: We send IRB correspondence regarding student research to the faculty advisor, who bears the ultimate responsibility for the conduct of the research. We request that the faculty advisor share this correspondence with the student researcher.

Modifications Required or Reasons for Non-Approval

None

The next deadline for submitting project proposals to the Provost's Office for full review is N/A. You may submit a project proposal for expedited review at any time.

[redacted]
Dr. Thomas R. Herrinton
Administrator, Institutional Review Board
University of San Diego
[redacted]

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CLINICAL INVESTIGATION DEPARTMENT
Naval Medical Center San Diego
34800 Bob Wilson Drive, Suite 5
San Diego, CA 92134-1005
Tel: [redacted]
E-mail: [redacted]

20 August 2010

From: Head, Clinical Investigation Department (CID)
To: LCDR Jason McGuire, NC, USN

Subj: **FINAL APPROVAL OF CLINICAL INVESTIGATION PROGRAM (CIP) STUDY CIP #NHCP.2010.0125, "Emergence Delirium in the U.S. Military"**

Ref: (a) NAVMEDCEN SDIEGOINST 6500.9A

1. The Institutional Review Board (IRB) has reviewed and approved this application to involve humans as research subjects, as reported in the **14th July 2010** IRB meeting minutes. This included a review of all documents attached to the original submission. Naval Medical Center San Diego holds Office of Human Research Protections Federal Wide Assurance number **FWA00002342** and **DOD Navy Assurance number 40005.**

2. **COMMENT**: the **expiration date** of this protocol is **13 July 2011**; ***an application for renewal will be sent to you approximately 60 days in advance.*** The IRB wants to remind you according to the Department of Health and Human Services (DHHS) and NMCSD the renewal of research projects is the Investigator's responsibility and it is required ***at least*** annually for all projects involving humans as subjects.

3. **PROTOCOL NUMBER**: **CIP # NMCSD.2010.0125**
This number is the clinical investigation program number and should be used on all correspondence, consent forms, and research data files.

4. **IRB APPROVAL DATE**: **14 July 2010**
Type of Review: __X__ Full Committee

5. **EXPIRATION DATE**: **13 July 2011**. If the project is to continue, it must be renewed ***by the expiration date.*** See the Research Administration Division (RAD) for assistance with the Continuing Review requirements.

6. **ADVERSE EVENT REPORTING**: All problems having to do with subject safety must be reported to the IRB within five days; serious AEs must be reported within 24 hours. All deaths, whether or not they are directly related to study procedures, must be reported. Please review the Research Investigator Handbook for additional examples of adverse events, unexpected problems or protocol deviations which must be reported.

7. **MODIFICATIONS**: Prior IRB approval is required before implementing any changes to the consent documents or any changes in the protocol including investigator additions or deletions.

8. **QUESTIONS**: Please contact the IRB Research Administration Division (RAD) if you have any questions:

Mary Massello at [redacted] or
Kelsey Preston at [redacted] or
Jeanna Basnett at [redacted]

9. Articles/abstracts for publication must be submitted to the CID Medical Editing staff. The Lead Editor, Ms. Waine Macallister can be reached at ([redacted] or the Editorial Assistant, Ms. Susana Hazelden at [redacted]. They will assist in their preparation, will ensure proper acknowledgment of BUMED as sponsor, will obtain command approval and submit them to journals and publications.

[redacted]
P. E. LINZ
[redacted]

Template Updated last 05/27/09

HUMAN RESEARCH PROTOCOL PROPOSAL

Cover Sheet

Title: Emergence Delirium in the U. S. Military

CIP #: NHCP.2010.0125

[Use accompanying instructions.]

Principal Investigator (PI or PI(A))	Last Name: McGuire	First Name: Jason	MI: M	Rank & Degree: LCDR/CRNA/PhDc
	Department/Division: Anesthesiology	Department Code:		
Institution: Naval Hospital Camp Pendleton				
DOD Assurance Number: # 40008	E-Mail Address: m[redacted]			
[redacted]	DSN:	Fax:	Fax DSN:	
NUMBER OF HUMAN SUBJECTS TOTAL: 133	Control: 0	Experimental: 0	Minors: 0	
Retrovirology Research: N/A				
Investigational Drugs, Devices, or Biologics: No	IND/IDE #			
Personnel/Environmental Hazards: No				
Proposed Start Date/Duration: August 2010, 5 months				
Budget/Payment Schedule				
FY: $	FY: $	FY: $	Total: $	
CRADA/MOU (Yes or No): No	If Yes, Name:			

Signatures: We accept responsibility for the conduct of the project, as specified in the attached assurance statement, and agree to provide any required progress reports.

Print: Jason M. McGuire			Print: Amy Mortensen	
Sign: [redacted]	Date 14 July 2010		Sign: [redacted]	Date 8 June 2010
Principal Investigator		Department	Department Chair Anesthesiology	
Approv[redacted] for IRB Review				
Sign: [redacted]	Jun 2010	[redacted]		[redacted] Date

Reviewed and approved by the IRB in accordance with the common rule and other governing regulations.

Date of IRB Review: July 14th, 2010 Risk Category: next CR 12 Months Minimal Risk

Chairman, IRB Approval: ( )

D. A. Tanen, CAPT, MC, USN (Date)

The official signing below certifies that the information provided within this document is correct, all supporting agreements are in place, future reviews will be performed as required, and certification will be provided.

Print or Type:

Sign: Date

Commanding Officer, Naval Hospital Camp Pendleton

NHCP.2010.0125-IRB-CONV-A

Reviewer Com

Joseph Carney Comments - [357722-1] Emergence Delirium in the U. S. Military

Reviewer Comments:

As the 1st Vice Chair I have reviewed the changes/modifications for the study and approve

Recommendation: Approve

Last Updated: 08/21/2010 02 24 PM

☑ Mark my personal review as complete

Completed Date: 08/21/2010 02 24 PM