Cognitive Disturbance among Elderly Taiwanese Patients after Elective Surgery

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Abstract

Cognitive Disturbance among Elderly Taiwanese Patients after Elective Surgery

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Acute confusion or delirium is an indicator of cognitive disturbance and is a significant health problem for the hospitalized elderly. The purposes of the study were: (1) To test a theoretical model about post-surgical cognitive disturbance; (2) To identify the most efficient items from the MMSE for assessment of cognitive function; and (3) To describe variations of cognitive/behavioral changes during the course of delirium. Data for this study came from a prospective cohort study entitled "Confusion in the hospitalized elderly patient" (Dai, Lou, & Yip, 1996). The data were collected in a medical center in Taiwan from 1995 to1997. For the first purpose, the findings showed that cognitive function ($\beta = .50$, $p < .001$), physical function ($\beta = -.34$, $p < .001$), and physiological stability ($\beta = -.21$, $p < .01$) had direct effects on post-surgical cognitive disturbance. Physical function and cognitive function also affected post-surgical cognitive disturbance indirectly through physiological stability. These variables accounted for 67% of the total variance of post-surgical cognitive disturbance.

Using item response analysis, the original 30-item MMSE was reduced to 16

items. For the 16-item MMSE, four factors were extracted. These 16 items were related to orientation to time, orientation to place, language, attention and calculation, recall and visual construction. The proposed new cutoff point for the 16-item MMSE was 11. This new cutoff point was determined for the purpose of over-identifying patients at risk in order to ensure early detection and prevention from the onset of cognitive disturbance.

The findings for the third purpose of the study showed that surgery was a stressful event to the elderly, especially for those less cognitively intact. Subjects who experienced delirium had significantly lower scores on the MMSE and all other measures than the non-delirious subjects at every stage of hospitalization. The major changes in behavior were noted in orientation, registration, and recall abilities.

The findings from this study suggest that mental status and physical functioning assessments on admission are necessary to identify patients at risk for post-surgical cognitive disturbance. These findings can be incorporated into routine nursing care that will increase the efficiency of nursing.

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COGNITIVE DISTURBANCE AMONG ELDERLY TAIWANESE PATIENTS AFTER ELECTIVE SURGERY

CHAPTER I

INTRODUCTION

Statement of the Problem

The older population is growing larger and living longer. It is estimated that 12.8% of the United States population is 65 years of age or older (Treas & Longino, 1997). In Taiwan, the older population accounted for 8.44% of total population in 1999. With the elder population increasing, a higher number of elderly patients are likely to be hospitalized. Therefore, health problems among the elderly are becoming increasingly important.

Acute confusion or delirium is an indicator of cognitive disturbance and is a significant health problem for the hospitalized elderly (Rudberg, Pompei, Foreman, Ross, & Cassel, 1997; Smita, Parika, & Chung, 1995). Delirium has been defined as "a transient organic brain syndrome characterized by the acute onset of disordered attention and cognition, accompanied by disturbance of psychomotor behavior and perception." It is the final common pathway of brain failure from many acute diseases (Lipowski, 1990, p. 41). The reported incidence of delirium in acutely ill elderly patients during hospitalization ranges from 7% to 73.5% in the United States. Differences in diagnostic criteria and study population account for the wide variation of rates in the results of these studies (Dyer, Ashton, & Teasdale, 1995; Foreman, 1989; Francis et al., 1990; Inouye & Charpentier, 1996; Francis, 1992a; Marcantonio, Flacker, Michaels, & Resnick, 2000; Mentes et al., 1999; O'Keeffe & Lavan, 1997; Smita et al., 1995). In elderly patients, delirium is often an early indicator of pathophysiological and psychological disturbances. If delirium goes undetected or untreated, the patient's cognitive function, well-being, and even chances of survival can become seriously threatened. Delirium is associated with higher mortality rates, longer hospitalization, more intensive nursing care, greater hospital costs and higher level of care after discharge (Francis et al., 1990; Smita et al., 1995).

Cognitive disturbance is complex and multidimensional. Research in the last two decades has identified several precipitating and host-related factors for cognitive disturbance (delirium) in a variety of settings and populations. Some precipitating factors identified from prior research for cognitive disturbance (delirium) are infection and psychoactive medication used. Some host-related risk factors are advanced age, pre-existing cognitive disturbance, and multiple illnesses (Foreman, 1989; Francis et al., 1990; Inouye & Charpentier, 1996). These factors are complex and inter-related. However, most of the studies focused mainly on risk factors and precipitating factors. Few studies have tested theories that integrate the potential influences of several personal and physiological factors on cognitive disturbance. Moreover, what is known about risk factors for cognitive disturbance comes predominantly from Western perspectives. Only one study has been conducted to study delirium in Taiwan (Dai, Lou, Yip, & Huang, 2000). It focuses on the incidence rate and risk factors in a population of hospitalized, post-surgical elderly patients. There is no other empirical research that has been conducted to study delirium in the context of Taiwanese patients. There is a need to test a set of predictors of cognitive disturbance as well as their relationships in elderly Taiwanese patients.

Several tools have been developed for diagnosis, screening, and rating for cognitive disturbance and behavioral symptoms (Fraser, 1988; Smith, Breitbart, & Platt, 1995; Vermeersch, 1990). Screening tools for cognitive disturbance are the most common used by nurses for early detection of delirium, but the weakness of each tool limits its unconditional use in the acute care setting. Among these tools, the Mini-Mental State Examination (MMSE) is the most frequently cited bedside cognitive screening instrument. But it was reported that every item in the MMSE is not equally efficient for identifying persons with cognitive disturbance (Braekhus, Laake, & Engedal, 1992). A tool that is valid and reliable, easy to administer, and less strenuous for respondents is needed for the actual clinical setting for cognitive assessment.

The incidence and risk factors of cognitive disturbance have been identified from literature. Previous studies have focused predominantly on changes in overall cognitive function (Milisen, Abraham, & Broos, 1998). However, little has been considered about differential changes in specific neurocognitive dimensions. Close attention to which cognitive dimension tends to vary in the post-operative period, and how the change overtime will help nurses to develop more targeted and sensitive clinical interventions for patient care.

In summary, from past studies, post-surgical cognitive disturbance is receiving more and more attention from researchers. Investigators have identified the risk and precipitating factors for cognitive disturbance. What is known about post-surgical cognitive status comes predominantly from Western perspectives. It is necessary and important to understand the factors that influenced on the cognitive status of hospitalized elderly from the Taiwanese social context as well as what specific neurocognitive dimensions change during the post-operative period. A shorter and more efficient tool for cognitive assessment is needed and will be more useful for a clinical setting.

Study Aims

The aims of this study were:

1. To test a theoretical model represented in Figure 2.1 to understand the influences of age, cognitive function, physical function, physiological stability, surgical stress and psychoactive medication use in post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery. The predicting variables are age, cognitive function, physical function, physiological stability, surgical stress and psychoactive medication use. The outcome variable is the severity of post-surgical cognitive disturbance.

2. To identify valid, reliable and efficient items from the MMSE for assessment of cognitive function in Taiwanese elders, and

3. To describe variations of cognitive/behavioral change in general and in selected cognitive dimension during the course of delirium in elderly Taiwanese patients after elective surgery.

Significance

The study has the following significant contributions to the phenomena of cognitive disturbance by increasing the understanding of the factors by which cognitive disturbance occur. This study tests a theoretical model of cognitive disturbance that specifies the effect of personal and physiological factors. Causal models of cognitive disturbance are used to test the relationship of these factors. A model to identify the relationships among predictors of post-surgical cognitive disturbance and their influence provides valuable information and enriches the knowledge base about cognitive disturbance. It also validates the model in the Taiwanese social context. Patient outcomes can then be promoted by early identification and proper monitoring of cognitive disturbance.

The item analysis from the MMSE helps to identify items that are significant in assessing the delirious patient. This tool is valid, reliable, easy to administer in the clinical setting, less strenuous for the respondent and specific to delirious patients.

In summary, the study results broaden the knowledge base of post-surgical cognitive disturbance, aid curriculum and in-service education design, and further develop the targeted nursing intervention to manage cognitive disturbance.

CHAPTER II

THEORETICAL FRAMEWORK AND LITERATURE REVIEW

There are numerous causes for cognitive disturbance in elderly patients; one of the most common is delirium. In this literature review, post-surgical delirium as a cognitive disturbance is the focus of this review. There are six parts in this chapter: (1) theory of cognitive aging, specifically reduced information processing and global cerebral insufficiency, (2) state of the research related to cognitive disturbance: delirium, (3) the theoretical framework about post-surgical cognitive disturbance, (4) literature support for the theoretical framework, (5) assessment for altered cognition and delirium, and (6) the variations of cognitive/behavioral change during the post-surgical period.

Theory of Cognitive Aging

Reduced Information Processing

Cognition refers broadly to various mental operations that acquire and use information permitting people to generate an adaptive response to environmental or internal needs (Filley, 1995). Cognitive functions can be defined as all the processes that allow a person to obtain, integrate, and retain information about themselves, other people, the environment, and enable them to share this information and act on it (Vroman, Cohen, & Volkman, 1994, p. 97).

Human information processing is a model of human thinking that applies the concept of information flow through a computer as an analogy to human thought (Jagmin, 1998; Reeves, 1996). The processing resources have three characteristics: (1)

they are limited in quantity, (2) the cognitive processing and performance are enhanced, when greater amounts of resources are available, and (3) they are relevant to a broad range of cognitive process (Salthouse, 1988; Schroots, 1996). Cognition can be conceived of as an information processing model consisting of input-processing-output, storage or memory, and operators or processors. The operators represent strategies for problem solving to generate a useful solution (Reeves, 1996; Vroman et al., 1994). The theory describes human behavior as an interaction between information processing (the problem solver) and a task environment.

The information processing theory postulates that the human mind, when engaged in a problem-solving task, can be viewed as an information processing system. In this process, the task environment is represented as a problem space (within the individual's mind) and it is organized into two main thinking processes: an understanding process, and a solving process. The understanding process is responsible for assimilating the stimulus that poses the problem and for producing mental information structures that constitute the person's understanding of the problem. The understanding process converts the problem stimuli into the initial information needed by the solving process. The solving process is derived from the understanding process and it is responsible for finding the solution to the problem and it consists of creating subgoals that generally move along the solution processes until the goal is met (Groen & Patel, 1991; Reeves, 1996).

This theory assumes that human information processing capacity is limited, and effective problem solving depends on the individual's ability to adapt his/her information processing resources to the demands of the task environment. Information for the problem-solving task is believed to be stored in several types of memory; each type of memory has different capacities and assessment characteristics. These types include a sensory storage of a very brief duration, a short-term memory of limited capacity and duration, and long term memory of large capacity and relatively permanent duration (Grobe, Drew, & Fonteyn, 1991; Groen & Patel, 1991; Taylor, 1997). The information processing theory offers a framework that has proved useful in analyzing human cognition.

There are many reasons why older people are vulnerable to cognitive problems. Aging leads to a reduction in the quantity of processing resources, such as attention, short-term memory, and the speed of at which information is processed (Schroots, 1996). Aging also involves several neurobiological mechanisms that may develop cognitive disturbance. As neurons are lost with age, neurologic disturbances that are tolerated well in younger people may no longer be tolerated as well, thus decreasing the amount of the information received from the environment by the remaining neurons. The ability to maintain orientation and interpretations of environmental stimuli is impaired (Blass, Nolan, Black, & Kurita, 1991).

Some factors causing impairment have little connection with cognitive abilities and these might be better described as conditions typical of an aging population. For example, physical or social isolation can reduce the quality and quantity of incoming information. Isolation reduces the opportunity to exercise one's cognitive abilities. Another common example is "cognitive overload" where cognitive function becomes overburdened and no longer functions well. Other conditions such as medication, dehydration, hypothermia, infection, and metabolic dysfunction, can cause cognitive function deterioration. These conditions are amenable to intervention (Vroman et al., 1994).

According to Neelon and Champagne (1992), delirium is a disturbance in information processing resulting from a reversible, diffused impairment of higher cortical function that includes the loss of attention and orientation as well. To process information successfully, people need to acknowledge significant information in the environment, encode it, and then store it in either short-term or long-term memory for later retrieval. Alteration in any phase can contribute to the occurrence of delirium (Jagmin, 1998; Neelon & Champagne, 1992).

Global Cerebral Insufficiency

Delirium is considered to be a nonspecific psychopathological manifestation of global cerebral dysfunction as a response to a variety of threats to the brain (Gray, Lai, & Larson, 1999; Mast, 1996). Delirium results from widespread but reversible interference with the function of cortical neurons, decreases in cerebral metabolic rate, impairment of neuronal metabolism, and of neurotransmission (especially cholinergic neurotransmission) (Blass et al., 1991). The clinical manifestations of delirium reflect the varying pattern of neurons involved and the extent of their impairment. With aging, both normal changes in the brain, the increasing incidence of brain disease and physiological dysfunction predispose elderly people to cognitive disturbance. Delirium results from the combined effects of a number of underlying conditions, such as medication, electrolyte imbalance, glucose metabolic rate, and cerebral blood flow (Blass et al., 1991; Francis, 1992a). So, the conditions which cause global cerebral dysfunction are associated with alterations in overall cerebral metabolism.

Researchers have tried to match the cognitive disturbances to specific brain damage, such as EEC and computer tomography (CT). These techniques are complicated and cannot be identified from bedside care. In the following review, I will focus only on the physiological and pathophysiological changes related to cognitive disturbance that nurses are able to identify by observation or routine laboratory tests.

In this section, four issues will be addressed: (1) the selected cerebral metabolic and neurochemical changes that may lead to cognitive disturbance, (2) the impact of the physiologic stressors associated with severe illness on cognitive disturbance, (3) electrolyte imbalance that leads to cognitive disturbance, and (4) age-related changes that make the elderly more vulnerable to cognitive disturbance.

Cholinergic System

Different neurotransmitter systems in the brain may be important factors in the various symptoms and clinical presentations of delirium, and more than one pathophysiologic mechanism may be involved. Adverse cognitive effects of an elevated serum anticholinergic activity have been reported in the literature (Flacker & Lipsitz, 1999; Francis, 1992a; Miller et al., 1988). The cholinergic neurotransmitter system is widely represented throughout the brain and it is thought to be related to delirium. It is the major system regulating arousal, attention, and the memory process (Francis, 1992a; Mast, 1996). The cerebral metabolism is an important factor that supports the availability of physiological functions and neurotransmission.

Cholinergic systems are very sensitive to metabolic changes. Some metabolic alterations, such as hypoglycemia, hypoxia, and ischemia, may alter cerebral metabolism. These alterations produce an imbalance between nutrient delivery and the brain's energy demand. Glucose is a major nutrient for the brain. The synthesis of acetylcholine and its precursor, acetyl coenzyme A, is derived from the oxidation of glucose and pyruvate in the citric acid cycle. Interference with glucose delivery or with its oxidation cycle (citric acid cycle) lowers the efficiency of glucose metabolism, which reduces the synthesis of acetylcholine (Blass et al., 1991; Francis, 1992a; Mast, 1998; Trzepacz, 1994).

Anticholinergic toxicity has long been known to be a cause of delirium. Several causes, such as medication, aging, and stress response, may decrease serum cholinergic levels. Medications with anticholinergic effects are associated with delirium more commonly than in any other drug class (Tune, Carr, Cooper, Klug, & Golinger, 1993; Tune, Carr, Hoagm, & Cooper, 1992; Tune & Bylsma, 1991). Anticholinergic effects of medication may be mediated by blocking postsynaptic receptors, inhibition of presynaptic release, or actions of antimuscarinic metabolites. Aging is associated with reductions in acetylcholine release and muscarinic receptor plasticity and function. These medications may increase the risk of delirium in elderly people (Trzepacz, 1994). Serum anticholinergic activity may reflect a nonspecific stress response to illness in older people. Higher levels of serum anticholinergic activity have been found to be associated with delirium in post-operative patients and elderly medical inpatients

(Flacker & Lipsitz, 1999; Golinger, Peet, & Tune, 1987; Mach et al., 1995). Flacker and Lipsitz (1999) examined 24 nursing home residents during a febrile illness. These patients displayed serial measures of serum anticholinergic activity level by radionuclied competitive-binding assay. The study reported serum anticholinergic activity levels were significantly higher during illness than at one-month follow-up (Flacker & Lipsitz, 1999). This finding was similar to a previous report by Golinger, Peet and Tune (1987) who assessed patients in the surgical intensive care unit.

In summary, decreased synthesis of acetylcholine and cholinergic neurotransmission due to metabolic insults, medications that block the acetylcholine release or postsynaptic receptors, and illness induced high anticholinergic activity levels are important pathophysiologic mechanisms contributing to delirium development.

Cytokines

Cytokines play an important role in immune activation. In a normal situation, the level of cytokines in the central nervous system (CNS) is low. Cytokines are released from activated glia cells under stressful circumstances. Both the inflammatory and infectious process and the consequence of surgery and other stressors may cause the systematic release of cytokines. Cytokines also interfere with neurotransmitter synthesis and neurotransmission. Increased cerebral secretion of Cytokines play a major role in the pathogenesis of delirium. The activation of cytokines due to diverse physiologic circumstances is one of the underlying mechanisms of delirium. The mechanisms involving increasing cytokines are: (1) Physiologic stressors, such as infection and surgery, which may be accompanied by abnormal thyroid hormone concentrations. (2) The diminished availability of thyroid may be considered as a maladaptive response-inducing hypothyroidism. Under normal circumstances, T3 is transported via the circulation to various tissues. It affects gene expression, enhances transport of amino acids and sugars, and stimulates ATP synthesis. Under stressful circumstances, thyroid metabolism changes. The transportation of amino acids and sugars into the cell are reduced. The synthesis of ATP is reduced as well. This may lead to reduction of cerebral oxidative metabolism and imbalance of neurotransmission, which induces delirium (Blass et al., 1991; Mast, 1998).

Electrolyte Imbalance

Surgical patients are at risk to certain specific disorders resulting from their underlying conditions and from the individual surgical procedures they undergo. Post-operative electrolyte imbalance is common among elderly patients. Incalzi, Gemma, Capparella, Terranova, Sanguinetti, and Carbonin (1993) followed 180 elderly orthopedic patients from admission to discharge to assess the incidence of post-operative electrolyte disorders. They reported that the incidence of post-operative electrolyte imbalance was 15%. The two most common disorders were hypokalemia and hyponatremia. These systematic disorders alter brain function by interfering with metabolism in wide areas of the brain, either directly or indirectly (Faber, Schmidt, Bear, & Narins, 1994; Gibson et al., 1991). Electrolyte imbalance has been found to be a major risk factor for development of delirium. More discussion is presented in a later section.

Age-Related Changes

Several age-related changes that may be interrelated with factors mentioned previously that cause elderly people to be prone to cognitive disturbance. The adverse effects of medication are an important cause of cognitive disorder. Several factors that may increase the risk of drug-induced cognition disorders in the elderly include: imbalanced neurotransmitters (cholinergic), age-related alterations in pharmacokinetics and pharmacodynamics, and high levels of medication (Gray et al., 1999). The major neurotransmitter change is the cholinergic function, which causes cognitive disturbance. In elderly people, the major physical changes related to the drug metabolism are reduced renal and hepatic elimination. This functional change may reduce drug clearance from the body. Also, reduced cholinergic transmission causes elderly people to be more sensitive to drugs. Elderly people tend to take multiple medications; therefore, high drug use increases the risk of adverse drug effects in the elderly.

The literature has described how either loss or excess of both salt and water may lead to acute confusional states (Cosgray, Davidhizar, Giger, & Kreisl, 1993; Guyton & Hall, 1996; Mentes, Culp, Maas, & Rantz, 1999). When the balance of water is altered, electrolyte imbalance occurs. If the fluid imbalance continues untreated, it may result in psychosis or cognitive disturbance. Multiple potential risk factors can be correlated with increased age. The two main physiological changes of aging may lead the elderly person to be more likely to have cognitive disturbance are: (1) aging reduces the adaptability of the brain to metabolic abnormalities (Mast, 1996), and (2) older people have lower body water content, a higher proportion of fatty tissue and reduced renal perfusion (Fanestil & Moore, 1994; Fretwell, 1993). The water intake worsens with insensitivity to thirst due to aging.

Besides water and electrolyte changes, many physiologic changes have been reported with normal aging, such as decreased brain volume, reduced number of neurons, and lost synapses (Mast, 1998). Aging affects the function of neurotransmitter systems. Changes in the cholinergic systems with cell loss decreases the synthesis of acetylcholine. Deterioration of the cholinergic system is related to cognitive decline, especially to arousal, attention, and memory impairment. In the elderly, low levels of thyroid hormones may be more obvious. This reduction may cause the elderly person to be less adaptive to stressful events and more prone to have delirium episodes under stressful circumstances (Blass et al., 1991; Mast, 1998).

In summary, age-related changes in metabolic and cerebral neurotransmission in the brain, increased susceptibility for stress, reduced cerebral reserve abilities, and increased use of medication make elderly people more vulnerable to cognitive disturbance.

State of the Research Related to Cognitive Disturbance: Delirium

Definition of Delirium

Delirium is a transient global disorder of cognition and consciousness. Delirium can occur at any age, but is most common in the very young and the very old. If untreated, it can cause permanent damage, turning into chronic dementia (Francis, 1992a). The main clinical features of delirium include reduced ability to focus, shift attention from one thing to another, and disorganization of thinking and speech. Less often there is an altered level of consciousness, perceptual problems such as delusion and hallucinations, disturbed sleep-wake cycles, altered psychomotor activity, disorientation, and memory impairment (APA, 1994). Some problems remain with the actual definition of delirium. These problems include time of acute onset, as it is not given a specific time frame. The definition also fails to state whether all symptoms need to coexist during a period of time or if chronic behavioral problems should be counted as symptoms. Some criteria may be difficult to assess in severely lethargic or uncooperative patients (Francis, 1992a).

Delirium has been defined as "a transient organic brain syndrome characterized by the acute onset of disordered attention and cognition, accompanied by disturbance of psychomotor behavior and perception" (Lipowski, 1990, p. 41). Delirium is the final common pathway of brain failure from many acute diseases. Delirium is a common clinical phenomenon, but research has been limited by a lack of consensus as to when to use the term. Various terms have been used synonymously with delirium including acute confusional states, acute brain syndrome, acute transient cognitive disorder, reversible dementia, cognitive failure, organic brain syndrome or organic mental disorder (Kozak-Campbell & Hughes, 1996; Smith et al., 1995). The concept of delirium is perceived in different ways by different researchers. It tends to depict varying degrees of one or several disorders of consciousness, memory, attention, inappropriate behaviors and judgement (Vermeersch, 1990). The clinical features of delirium are quite numerous and common to other psychiatric disorders such as depression, dementia and psychosis.

Incidence and Consequences of Delirium

During hospitalization, the reported incidence of delirium in acutely ill elderly patients ranges from 7% to 73.5% in the United States. Differences in diagnostic criteria and study populations account for the wide variation in rates in the results of these studies (Dyer, Ashton, & Teasdale, 1995; Foreman, 1989; Francis, 1992a; Francis et al., 1990; Inouye & Charpentier, 1996; Marcantonio, Flacker, Michaels, & Resnick, 2000; Mentes et al., 1999; O'Keeffe & Lavan, 1997; Smita et al., 1995). In elderly patients, delirium is often an early indicator of pathophysiological and psychological disturbances. If delirium goes undetected or untreated, the patient's cognitive function, well-being, and even survival can become seriously threatened. Delirium is associated with many associated results including greater functional decline, higher mortality rates, longer hospital stay, more intensive nursing care, slower rate of recovery, greater hospital costs, and higher level of care after discharge (Dolan et al., 2000; Francis et al., 1990; O'Keeffe & Lavan, 1997; Smith et al., 1995).

Etiology of Delirium

The etiology of delirium remains poorly understood. Part of the difficulty lies in its fluctuating and transient nature and in the confounding by underlying physical illness. Delirium is considered a nonspecific neuropsychiatric manifestation of a generalized disorder of cerebral metabolism and neurotransmission (Kozak-Campbell & Hughes, 1996; Rummans, Evans, Krahn, & Fleming, 1995). The lesion responsible for delirium is a functional rather than a structural change and is therefore subtler and more difficult to study. There is some evidence that delirium is mediated by a failure of cholinergic transmission. For example, the side effects of anticholinergic medications can mimic delirium (Francis, 1992a; McRae, 1999). Other causes of delirium can be grouped into four categories: physiological (such as electrolyte imbalance, acid-base imbalance, hypoxia, infections, dehydration, blood loss, medications), psychological (stress or sensory deprivation due to impaired hearing or vision), sociological (living alone) and environmental (environmental disruption as is seen in hospitals, intensive care and nursing homes, immobilization). It is generally believed that delirium has multiple causes rather than a singular one. Multiple interacting factors generally occur simultaneously in delirium; one moderates the effects of another. Factors can vary over the course of illness, with the nature of the health problem, and with the setting, each further complicating etiologic investigation (Espino, Jules-Bradley, Johnson, & Mouton, 1998; Foreman, Wakefield, Culp, & Milisen, 2001; Francis & Kapoor, 1992; McRae, 1999).

Precipitating Factors

Several major precipitating factors for delirium have been identified in recent studies, such as electrolyte imbalance, metabolic abnormality, dehydration/volume depletion. These metabolic disturbances included abnormal sodium, potassium or glucose levels, elevated BUN and blood creatinine in the studies of medical patients. Foreman (1989) identified hypernatremia, hypokalemia, hyperglycemia, hypotension, azotemia, and multiple medications as risk factors for delirium. Rockwood (1989) identified age, dementia, and unstable condition on admission as predictors of delirium.

Francis et al. (1990) found dementia, illness severity, fever/hopothermia, abnormal serum sodium, azotemia and use of psychoactive drug to be important risk factors. Schor, Levkoff and Lipstitz (1992) identified the following as associated with delirium: male gender, over 80 years of age, cognitive disturbance, fractures, infections and exposure to neuroleptic and narcotic. Inouye and Charpentier (1996) developed and validated a predictive model for delirium based on four risk factors: cognitive disturbance, severe illness, vision impairment and high BUN/creatinine ratio. In the studies of surgical patients, Williams, Campbell, Raynor, Mlynarczyk and Ward (1985a) identified age, cognitive disturbance and low pre-injury activity level as important risk factors. Gustafson, Berggren, Brannstrom, Bucht, Norbert, Hansson et al. (1988) identified age and dementia as risk factors for elderly patients with hip-fractures. Williams-Russo, Urquhart, Sharrock, and Charlson (1992) identified age, male gender and preoperative alcohol use as important risk factors for delirium among patients undergoing bilateral knee replacement surgery. Some other risk factors for the development of delirium in the elderly include hospitalization, acute illness, post-operative status, underlying psychiatric disorder, poor nutrition, acute psychosis, history of substance abuse, and impaired ambulation status (Espino et al., 1998; Lipowski, 1990). It seems that delirium is a multi-factorial disorder and multiple risk factors appear to have a multiplicative rather than simply an additive effect. Advanced age and medical frailty appear to increase risk of delirium but how much of this risk is actually due to subclinical or unrecognized dementia is not known.

Clinical Manifestations

The clinical presentation of delirium is very heterogeneous. According to DSM-IV, delirium is a disorder of consciousness, attention and cognition or perception, which develops acutely, fluctuates during the course of the day, and is attributable to a physical disorder. By definition, there is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition (APA, 1994). Delirium is an acute disorder, developing over hours to days, and fluctuates over the course of the day, often becoming worse at night. The delirious patient may have psychomotor and emotional disturbances. In most cases, delirium due to a medical disease is reversible with treatment of the underlying condition (Espino et al., 1998; Francis, 1992a; Gomez & Gomex, 1989). Several clinical subtypes of delirium have been described based on the level of psychomotor activity (Lipowski, 1990; Rummans et al., 1995). The hyperactive variant of delirium is most commonly recognized and is most apparent to the observer. It is often associated with the adverse effects of anticholinergic drugs and drug intoxication. Patients may present agitation, psychosis, and mood liability and may refuse to cooperate with medical care, may demonstrate disruptive behaviors, and may sustain injuries from falling, combativeness or pulling out intravenous (IV) lines (Rummans et al., 1995). The typical elderly patient with delirium is the hypoactive type presented as quietly confused, disoriented, and lethargic, but the hypoactive type is less frequently recognized or is dismissed as a transient, insignificant problem. The absence of disruptive behaviors contributes to the lack of recognition (Inouye, 1994; Rummans et al., 1995). Because of the multiple etiologic factors, the fluctuating course, and the individual medical comorbidities, many patients who experience delirium have a mixture of both hypoactive and hyperactive variants.

Delirium is a more transient condition than is dementia. A distinguishing feature of delirium is the fluctuation in symptoms during the course of the day. The patient is most lucid in the morning or at midday and becomes worse at night (Jacobson, 1997). Symptoms of delirium vary during the course of the event. In the early stage, patients may have confused thinking, difficulty concentrating or difficulty judging the passage of time. The patient may be irritable, lethargic or withdrawn; have a disturbance of mood; show hypersensitivity to light and noise; have perceptual distortions, insomnia, vivid dreams or hallucinations. In the stage of overt delirium, signs and symptoms such as a change in consciousness, difficulty maintaining or shifting attention, disorientation, speech abnormalities, misinterpretations, and illusions may occur (Jacobson, 1997).

Management of Delirium

Since the causes of delirium are multidimensional, so are the management strategies. Management of delirium has three components: (1) identifying and treating the underlying causes of delirium, (2) use of nonpharmacological measures to ameliorate symptoms, and (3) initiation of pharmacologic therapy for severe agitation and behavioral dyscontrol associated with delirium (Francis, 1992a; Rummans et al., 1995; Smith et al., 1995). Delirium may be prevented by eliminating or minimizing the use of medication known to affect cognitive function, ensuring adequate hydration and oxygenation and addressing the medical problem immediately. The frequently used nursing strategies for treating delirium patients include ensuring patient's physical safety, providing comfort, providing environmental support to re-orient the patient, helping the patient to use concrete reasoning skills, and supporting the patient and family members (Boss, 1991). When agitated behavior persists or other evidence of impaired judgment develops, physical restraint is often applied to patients to ensure safety and avoid harm. Yet, physical restraint will have consequences in several areas: physical (such as pressure sore develop, decline functional status), psychological (such as decline mental functioning), as well as social economic (such as increase resources utilization secondary to increase length of stay). Cognitive assessment should be incorporated into the routine care provided with clinical care. To identify the patient at risk and provide special attention can prevent the occurrence of delirium. Although many of the individual factors, such as age and chronic illness, cannot be reversed; however, other factors such as dehydration, medication, sensory impairment can be corrected by following a systematic approach (Francis, 1992a; Inouye et al., 1999; Sullivan-Marx, 1994).

Patient's Perception of Delirium

The effectiveness of management of delirium should also include the patient's perspective. It is important to understand the patient's feelings and expectations in order to provide feasible nursing care according to what the patient considers as caring. Few studies have shown how delirious patients perceived the episode of delirium. Laitinen (1996) interviewed confused patients post-cardiac surgery to understand their delirious experiences. The patients reported the importance of closeness to the professional person who provided care. The true presence of the nursing staff was significant for the patients. Through the true presence of the nurses, the patients felt safe, understood, and accepted. Schofield (1997) explored the reaction of delirious patients to an episode of delirium. They reported that the patients were able to remember short verbal commands from nurses during the episodes of altered perception. It was reported that the patients were generally willing to discuss their experiences with others. It would be helpful for nurses to provide opportunities to do so. These comments strengthen the direction that nursing care should pursue regarding delirious patients.

Knowing the patient contextually is considered central to providing effective nursing care. Whether certain actions will count as caring is dependent upon what the action is, the intent of the caregiver, and the context in which it is done (Swanson, 1999). Usually, the nurse and patient hold different values about caring such as applying restraint (from the nurse's point of view, to ensure safety) or accompanying the patient (from the patient's point of view, to have support) during a delirium episode.

Nurses' Description and Perception of Delirium

Nurses perceived delirium as a multidimensional phenomenon reflected by both cognitive and behavioral disturbances. Wu (1995) investigated perceptions of nurses about delirium through a semi-structured questionnaire. The results indicated that nurses defined delirium in several cognitive and behavioral features such as disorganized thinking, disorientation, or inappropriate behaviors.

While delirium as diagnosed by nurses is a multidimensional concept assessed through observation of the patient's behaviors, the multiple dimensions of delirium make definition and measurement difficult. Wolanin (1977) investigated the patient records of 30 confused nursing home residents in order to examine the behavioral term used to describe the patients and their progress. Forty categories of different terms were coded from the records. The results also indicated that physicians and nurses viewed delirium quite differently. Physicians tended to use terms related to cognitive inaccessibility (including changes in alertness, thought quality and memory), whereas nurses tended to describe confused patients using terms related to social inaccessibility (including changes in cooperation, response). The behaviors of the patients seemed dependent on those who worked with them. Since the perception of delirium varied considerably, it is difficult to formulate a general picture of delirium on the basis of previous study results. The inconsistent use of terms may result in confusion among practitioners about the patient's actual condition. As a result, either unnecessary diagnostic studies are performed or patient outcome is poor due to delayed evaluation and intervention. Lou (2001) interviewed four nursing students about their experiences caring for delirious patients. A model of "striving for balance" was generated from the interview result. In general, the experience of caring for delirious patients is a stressful experience. Informants reported trying to deal with unanticipated patient conditions and the unyielding workloads by balancing these two conditions. Given the condition, actions ultimately undertaken were considered the "best" one but not necessarily the "correct" one in dealing with patient problems.

Reasons for Underrecognition of Delirium

Nurses often do not recognize delirium until a patient becomes very agitated or confused. Some reasons for not recognizing delirium are failure to identify its clinical features, poor documentation of symptoms, lack of communication about the confused behavior, and acceptance of delirium as normal for older adults (Foreman, 1986; Johnson et al., 1992; Sullivan-Marx, 1994). In a study of recovery of functional capacity in elderly patients with delirium, only 2.5% of elderly medical patients over a three-month period were recognized by nurses as having delirium (Rockwood et al., 1994). This detection rate is far less than the incidence rate of delirium among elderly patients. Eden and Forman (1996) presented a case study to indicate the problems about underrecognition of delirium in critical care. They identified two major problems associated with underrecognition: (1) lack of knowledge about the criteria and methods of detecting delirium, and (2) ineffective communication between staff nurses in relaying symptoms at the onset of the disorder. Other barriers that prevent nurses from performing systematic mental status assessment of patients are fear of insulting patients and doubt about their skills as nonpsychiatric nurses to conduct a mental status exam (Eden & Foreman, 1996; Inaba-Roland & Maricle, 1992). In summary, the problems associated with underrecognition include the scope of knowledge, skill and attitude on the part of the nursing staff.

Summary

Delirium has multiple etiologies. Both chronic and acute conditions contribute to risk of delirium. A careful and systematic assessment of the patient's condition at the time of admission is important. From the literature, electrolyte imbalance and metabolic disturbance have been identified as major precipitating factors for delirium. These physiological variables were significantly associated with the onset of delirium but it is impossible to conclude whether these variables are causes, effects or just simply correlates of delirium. The physiological change of aging and research results support that these electrolyte and biochemical indicators are important variables to monitor for delirium patients. It is necessary to monitor and correct these variables at admission or before surgery to prevent or reduce the impact of post-operative delirium. It is also necessary to monitor these variables during the hospital stay to help nurses to distinguish the etiology of delirium. In each case, knowing when confusion is more likely to occur can assist in focusing more appropriate and effective efforts at detection, thereby reducing the consequences associated with confusion.

Delirium is a common clinical phenomenon, but research has been limited by a lack of consensus about when to use the term. The term is subject to various definitions and descriptions. Nurses perceive and describe delirium in different ways. Health personnel operationalize delirium quite differently. The inconsistent use of terms may result in confusion among practitioners about the patient's actual condition. Recognition of the patient's problem is the key aspect in reducing the consequences of delirious patients. Research shows a low detection rate for delirium by nurses for various reasons. The consequences of underrecognition of delirium include issues for both patient and nurse. For the patient, if delirium goes undetected or untreated, the cognitive functioning, well-being, and even survival can become seriously threatened.

For the nurse, the capacity to care for the patient will be diminished. The low detection rate of delirium indicated that nurses are missing the connection with their patients. When there is a disconnection with the patient, then effective nursing care is not possible.

Theoretical Framework

This study has developed a theoretical model for testing post-surgical cognitive disturbance. The severity of cognitive disturbance is the outcome variable in the model. Age, cognitive function at admission, physical function at admission, physiological stability, surgical stress and psychoactive medication used are independent variables. The model proposes that: (1) age, cognitive function at admission, physical function at admission, physiological stability, surgical stress and psychoactive medication used will have direct effects on the severity of post-surgical cognitive disturbance, and (2) age, cognitive function at admission, physical function at admission, will also have indirect effects through two peri-operative variables--physiological stability and surgical stress on the severity of post-surgical cognitive disturbance.

Hypotheses

The theoretical model of post-surgical cognitive disturbance is presented in Figure 2.1. Inferred by each path in the model is a specific hypothesis to be tested. From right to left and top to bottom, the hypothesized paths are:

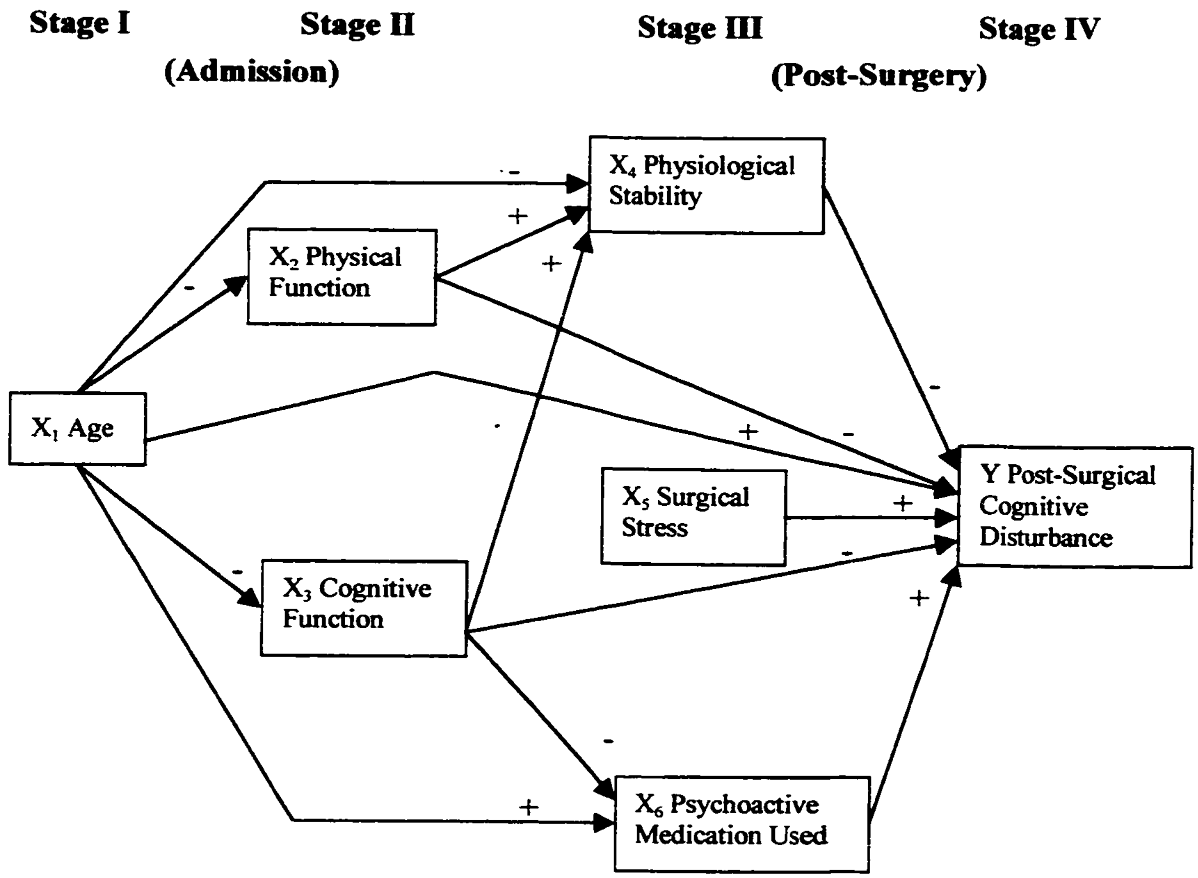


Figure 2.1 Theoretical Model of Predictors of Post-Surgical Cognitive Disturbance in Older Patients after Elective Surgery

Hypothesized Direct Paths

H1 Age will have a direct positive effect on the severity of post-surgical cognitive disturbance.

H2 Physical function at admission will have a direct negative effect on the severity of post-surgical cognitive disturbance.

H3 Cognitive function at admission will have a direct negative effect on the severity of post-surgical cognitive disturbance.

H4 Physiological stability will have a direct negative effect on the severity of post-surgical cognitive disturbance.

H5 Surgical stress will have a direct positive effect on the severity of post-surgical cognitive disturbance.

H6 Psychoactive medication use will have a direct positive effect on the severity of post-surgical cognitive disturbance.

H7 Physical function at admission will have a direct positive effect on physiological stability.

H8 Cognitive function at admission will have a direct positive effect on physiological stability.

H9 Age will have a direct negative effect on physiological stability.

H10 Cognitive function at admission will have a direct negative effect on psychoactive medication used.

H11 Age will have a direct positive effect on psychoactive medication used.

H12 Age will have a direct negative effect on physical function at admission.

H13 Age will have a direct negative effect on cognitive function at admission.

Hypothesized Indirect Paths

H14 The effect of age on post-surgical cognitive disturbance will be indirect through (a) physical function at admission, (b) cognitive function at admission, (c) physiological stability and (d) psychoactive medication used.

H15 The effect of physical function at admission on post-surgical cognitive disturbance will be indirect through (a) physiological stability.

H16 The effect of cognitive function at admission will be indirect through (a) physiological stability, and (b) psychoactive medication used.

Structure Equations Tested in this Study

E1 $X_2 = B_{21}X_1 + e1$

E2 $X_3 = B_{31}X1 + e2$

E3 $X_4 = B_{41}X_1 + B_{42}X_2 + B_{43}X_3 + e3$

E4 $X_6 = B_{61}X_1 + B_{63}X_3 + e5$

E5 $Y = B_{y1}X_1 + B_{y2}X_2 + B_{y3}X_3 + B_{y4}X_4 + B_{y5}X_5 + B_{y6}X_6 + e6$

Defining Variables in the Model

Six independent variables and one dependent variable are proposed in the theoretical model. The operational definitions of these variables are presented in the following table:

Variable Name	Definition
Age	Age is defined as the chronological age of the patient.
Cognitive Function	Cognitive function, which represents an individual's cognitive ability, is defined as a set of abilities that include orientation, registration, attention, calculation, recall, language, and visual construction. In this study, the assessment score from the MMSE is used to represent the individual's cognitive function.
Physical Function	Physical function is defined as the individual's capability to perform a series of daily activities such as dressing, grooming, and eating. In this study the assessment score from the Barthel Index is used to represent the individual's physical function.
Physiological Stability	Physiological stability is defined as the equilibrium level of the individual's biochemistry and metabolic condition. Six indicators are selected to represent the individual's physiological stability. These are serum sodium level (Na), serum potassium level (K), blood urea nitrogen (BUN), blood fasting sugar (BSAc), body temperature (BT), and dehydration indicator by the ratio of blood urea nitrogen to creatinine level (BUN/Cr.).
Surgical Stress	Surgical stress is defined as the types of the peri-operative treatment that cause the individual to be more prone to having cognitive disturbance post-surgery. Three indicators are selected to represent the individual's surgical risk. These are types of anesthesia, types of surgery and blood transfusion.
Psychoactive Medication Used	Psychoactive medication used is defined as the use of any of the five types of medications, which tend to induce cognitive disturbance. These are narcotic analgesics, sedative hypnotics, histamine 2-receptor blockers, anti-Parkinsonism agents, and anti-cholinergic drugs.
Severity of Cognitive Disturbance	Severity of cognitive disturbance is defined as the degree of cognitive disturbance by the assessment score of the MMSE. A score of less than 24 indicates cognitive disturbance. A score of 18-23 indicates mild cognitive disturbance and, 0-17 indicates severe cognitive disturbance.

Literature Support for the Theoretical Framework

The following section introduces the literature that supports each path of the theoretical model. Acute confusion or delirium is an indicator of cognitive disturbance. In this literature review, delirium as cognitive disturbance in post-surgery is the focus of this review.

Stage I Variable: Age

Aging involves an increasing vulnerability to physiologic, psychological and sociocultural insult. From the theoretical model, age affects the individual's physical function, cognitive function, physiological stability, kinds of psychoactive medication used and the severity of post-surgical cognitive disturbance.

Age and Cognitive Function

Age is always a strong predictor of cognitive performance. Cognitive disturbance is the one condition that increases consistently with advancing age. Cognitive disturbance increases with age and occurs most frequently in individuals 85 years of age and older (Kramer, German, Anthony, VonKorff, & Skinner, 1985; McDougall, 1995; Zelinski, Crimmins, Reynolds, & Seeman, 1998). Age has been identified as the major risk factor for cognitive disturbance in many reports (Dai et al., 2000; Gustafson et al., 1988; Marcantonio et al., 1994a; Martin, Stones, Young, & Bedard, 2000; Rockwood, 1989; Schor et al., 1992; Williams et al., 1985a; Williams-Russo et al., 1992) (Table 2.1). None of these studies has identified a specific age when post-surgical delirium becomes more prevalent.

Research has been shown that an individual's short-term memory declines with age. The individual's ability to learn material presented verbally declines after age 70. People over the age 60 make more errors in verbal learning tests than do younger adults (Carmen, 1997). Kramer, German, Anthony, VonKorff and Skinner (1985) reported the result of a survey among elderly residents in eastern Baltimore for mental disorders. They reported that the prevalence rates of mental disorders contrasted by age across the 18-and-over population for cognitive disturbance. The cognitive disturbance rates were based on responses of the MMSE. The cutoff point of 17 was used for severe cognitive disturbance. Among the 3,400 interviews, the rate of severe cognitive disturbance increased markedly with advanced age, from 0.5% in the age group of 18-64, 3.0% in the age group 65-74, to 9.3% in the age group 75 or higher ($p < .0001$) (Kramer et al., 1985). Milisen, Abraham and Broos (1998) reported a significant difference ($p < .0005$) of cognitive function between different age groups from admission assessment of cognitive status for 26 elderly hip fracture patients. Severe cognitively impaired patients were significantly older than patients with no cognitive disturbance. Stromberg, Lindgren, Nordin, Ohle, and Svensson (1997) investigated 256 hip fracture patients on their cognitive state at admission. They reported that cognitive decline was associated with age. From the 65-69 age group, 3 out 18 patients were cognitively impaired. But, in the group aged 90 or older, 13 out 24 patients were cognitively impaired at admission.

Age and Physiological Stability

Multiple potential risk factors correlate with increasing age. The two main physiological effects of aging that increase elderly people's chances to become cognitively impaired are (1) Reduction of the brain's ability to adapt to metabolic abnormalities. Delirium develops when the cerebral oxidative metabolism (such as oxygen, glucose or amino acid) is reduced and when the neurotransmitters in the brain are imbalanced (Mast, 1996), (2) Lowered body water content and a higher proportion of fatty tissue that reduces renal perfusion (Fretwell, 1993). Water intake worsens with insensitivity to thirst due to aging. During surgery, the loss of blood or body fluid will exacerbate this condition. It is common to use IV fluid therapy after surgery, which may cause overhydration and dilutional hyponatremia, which further develops confusion in the elderly patients. All of the above mentioned could lead elderly people to be more prone to having unstable physiological conditions that lead to a change in mental status.

Age and Physical Function

As age increases, physical function decreases. Resnick and Daly (1998) investigated the predictors of functional ability among 200 geriatric rehabilitation patients and reported that age correlated negatively with an individual's functional ability at admission. It was also reported that age directly predicted function at discharge. Older people have more difficulty with at least one ADL and/or IADL (Patrick, 1993).

Age and Medication Used

Since elders have a greater incidence of chronic disease, they are more likely to use multiple drugs that contribute to cognitive disturbance. It is estimated that elderly patients consume 25% to 40% of all prescription drugs and average 4.5 prescriptions daily, primarily because of multiple chronic diseases (DeMaagd, 1995). Alterations in pharmacokinetic action with aging and multiple drug use or misuse increase the possibility of drug reactions and drug interactions associated with cognitive disturbances or other serious consequences (DeMaagd, 1995; Robert & Lincoln, 1988). Change in cognitive performance may further contribute to poor medication compliance due to memory loss, confusion, and disorientation.

Stage II Variables: Physical Function and Cognitive Function

The individual with poor physical function may lead to poor cognitive performance and vice versa. Marcantonio, Flacker, Michaels, and Resnick (2000) examined the role of delirium in the natural history of functional recovery after hip fracture surgery in 126 elderly people participated in this study. The authors reported pre-fracture cognitive disturbance, ADL functional impairment and high medical comorbidity were risk factors to developing delirium. The person who developed delirium post-surgery was associated with poor functional recovery one month after fracture. Dolan, Hawkes, Zimmerman, Morrison, Gurber-Baldini, and Hebel, et al (2000) reported similar findings up to 24 months postsurgery. Royall, Chiodo, and Polk (2000) assessed 561 elderly in a continuing care retirement community using the Executive Interview, the MMSE and an executive clock-drawing task. They reported the individual's cognitive function had significantly affected the level of IADL function. Knight (2000) reported that cognition is one key dimension of functional status. One must "know what to do" to perform to be successful in an activity which required choosing, attending, and problem solving. The author concluded that cognitive function is a separate construct from functional status. However, several researchers reported that physical function was a precipitating factor for cognitive disturbance.

Physical Function and Physiological Stability

Physical function affects cognitive disturbance directly as well as indirectly affects cognitive disturbance through biochemical stability. Goldberg and Hagberg (1990) reported the most common and significant cause for decline in function with aging is the development of disease that resulted in biochemical instability.

Physical Function and Cognitive Disturbance

Physical function is a precipitating factor for cognitive disturbance among elderly patients. Williams, Campbell, Raynor, Musholt, Mlynarczyk, and Crane (1985b) reported that low pre-injury activity level was a risk factor for delirium development among hip fracture patients. Similar results were reported in the literature (Dai et al., 2000; Schor et al., 1992). Marcantonio, Goldman, Mangione, Ludwig, Muraca, and Haslauer. (1994a) also reported that poor functional status was a precipitating factor for delirium among 1341 surgical patients. Milisen, Abraham and Broos (1998) investigated the relationship between functional status (ADL) and the cognitive abilities among 26 hip fracture patients from admission through the fifth post-operative day. The patient's physical function was measured by the Katz ADL Scale and the cognitive function was assessed by the MMSE. They reported a relationship between functional status and cognitive function. There was a strong association between memory and psychomotor skills relative to ADL and a moderate association between linguistic ability and concentration relative to ADL. Patients with decreased cognitive status post-operatively had reduced physical performance compared to non-impaired patients (Milisen et al., 1998). Zelinski, Crimmins, Reynolds, and Seeman (1998) examined the relationship between cognitive performance, self-reported medical conditions, general health rating, and age, using a large survey data set. The sample included 6,646 elderly people aged 70 to 103. They reported that the presence of stroke, diabetes and poorer health ratings predicted poorer performance on recall and mental status tasks. Age interacted with medical conditions including high blood pressure, and diabetes in predicting mental status. They concluded that chronic physical conditions were associated with cognitive deficits.

Cognitive Function and Physiological Stability

Individuals who are cognitively impaired suffer major adverse consequences from illness. For example, they are particularly susceptible to respiratory complications and subsequent mortality due to unstable physiological functions (McDougall, 1995). Robert and Lincoln (1988) examined the predictors of cognitive disturbance among 94 hospitalized and 78 institutionalized elders. They reported neural function was the only variable that significantly associated with greater cognitive disturbance in both groups.

Cognitive Function and Psychoactive Medication Used

From the literature, psychoactive medication use is a precipitating factor for delirium development. However, it was often difficult to establish whether psychoactive drugs were causing the delirium or whether the drugs were prescribed after the symptoms of delirium appeared (Tune, 1991). The hypothesis for this study is that the less cognitive function pre-surgical patients have the greater the amount of post-surgical psychoactive medication use, further worsening the individual's cognitive function.

Cognitive Function and Post-surgical Cognitive Disturbance

Pre-operative cognitive function is an important predicting factor for treating cognitive disturbed elderly patients post-surgery. Pre-operative poor performance on cognitive testing was one of the predictors for delirium development post-surgery (Williams et al., 1985b). Similar results were reported from Gustafson et al. (1988), Francis et al. (1990), Schor et al. (1992), Pompei et al. (1994), Marcantonio et al. (1994a), and Dai et al. (2000).

Stage III Variables: Physiological Stability, Surgical Stress and Psychoactive Medication Used

Physiological Stability and Cognitive Disturbance

Delirium usually has multiple causes. Medication, metabolic disturbance, and dehydration are all possible causes. Delirium has been identified with many physiological indicators. Fluid and electrolyte imbalance, especially hypo-, or hypernatremia and hypo- or hyperkalemia, is the third most common cause of acute confusion; metabolic disturbance is the fourth most common cause (Bruera, Franco, Maltoni, Watanabe, & Suarez-Almazor, 1995; Foreman & Zane, 1996). Some reports have suggested that fever, infection and dehydration can induce delirium also (Inouye & Charpentier, 1996). From the literature, most of the studies recorded these physiological indicators as background information and used them as risk factors for delirium. Table 2.1 lists the selected studies of delirium in older patients. Metabolic risk factors have been identified in some of the research (Elmstahl, Wahlfrid, & Jerntrop, 1995; Foreman, 1989; Francis et al., 1990; Marcantonio et al., 1994a). These metabolic disturbances included abnormal sodium, potassium or glucose level, elevated BUN and blood creatinine.

The following research results demonstrate that electrolyte imbalance is a cause for delirium. In Koizumi, Shiraishi, Ofuku, and Susuki's study, they reported 72.7% of the cases of delirium had electrolyte imbalance. Among the delirious patients with electrolyte imbalance, they classified four types of electrolyte imbalance: hypokalemic type (40.6%), hyponatremic-hypochloremic type (25.0%), hypokalemic-hyponatremic-hypochloremic type (18.8%), and irregularly fluctuating electrolyte type (15.6%). By correcting electrolyte imbalance to treat the delirium, the mean duration of delirium was 9.4 days, whereas the mean duration of delirium without the electrolyte correction was 25.7 days. The mean duration of delirium in cases without the electrolyte imbalance was 25.0 days. From these results, the duration of delirium with electrolyte imbalance has been significantly shortened by the correction of electrolyte imbalance. They concluded that electrolyte correction should be done systematically for the delirious patients as a treatment for the disorder (Koizumi, Shiraishi, Ofuku, & Susuki, 1988).

Seymour, Henschke, Cape, and Campbell (1980) investigated the etiology of delirium in physically ill old people and reported that the presence of dehydration/volume depletion at the time of admission was a significant indicator for poor mental function. They checked the mental status and the blood biochemical profile, which included blood urea nitrogen, serum sodium, potassium, osmolality and creatinine. The person's age and the initial blood tests were not significantly correlated. The BUN/creatinine ratio, sodium, and osmolality showed a significant negative correlation with the initial mental score. They concluded the BUN/creatinine ratio was an indicator for plasma dehydration/volume depletion, which was correlated with low mental performance. Inouye, Viscoli, Horwitz, Hurst, and Tinetti (1993) and other researchers used BUN/creatinine ratio higher than 18 as an index of dehydration and concluded that this is a major predicting factor for delirium. Adequate hydration of patients might prevent the development of delirium. Bruera, Franco, Maltoni, Watanabe, and Suarez-Almazor (1995) conducted a study to understand the relationship between hydration and the incidence of agitation and impaired mental status in oncology patients. Patients who presented with early characteristics of cognitive disturbance received immediate subcutaneous hydration. The hydration status was assessed by daily physical examination, presence of sweating and dryness of the mucosa as well as by urine output and electrolyte, creatinine and blood urea nitrogen determinations. They reported patients who received hydration (n=162) had significant lower incidence (26% vs 10%) of agitated impaired mental status from those who did not (n=117). This was also reflected by a lower mean dose of haloperidol, and less frequent use of other psychoactive drugs such as neuroleptics and benzodiazepines. They suggested that hydration is one of the strategies that may reduce the incidence of agitated impaired mental status in terminal cancer patients (Bruera et al., 1995).

Foreman (1989) investigated 71 medical patients to examine the psychophysiologic variables associated with the onset of confusion. For assessment of the physiological variables related to delirium, electrolyte, BUN, and creatinine levels were obtained daily and serum glucose was obtained every four hours because of increased variability. It was reported that the confused patients who were hypernatremic, hypokalemic, hyperglycemic, hypotensic and had elevated blood levels of creatinine and urea nitrogen, received more medications, were more frequently perceived by nurses as confused, had more orienting objects in their immediate environment and fewer interactions with significant others.

Based on these initial works mentioned above on electrolyte and metabolic indicators for delirium, researchers investigated the relationship of metabolic disturbance with delirium. Francis, Martin and Kapoor (1990) reported abnormal sodium level and azotemia were associated with high risk of delirium. The reported odds ratio was 6.2 for abnormal sodium and 2.9 for azotemia. They also compared delirious patients according to the time their delirium manifested. The only significant difference was in the frequency of fluid or electrolyte disorders. These contributed to the etiology of delirium in 40% of patients with delirium on initial evaluation but in no cases of delirium developing after admission. It seems the initial assessment for electrolyte imbalance was a predictor of future delirium. Elmstahl, Wahlfrid, and Jerntrop (1995) examined medical records of 221 confused elderly patients retrospectively and reported that the metabolic disturbance was the second leading

(30%) precipitating factors for acute confusion. The metabolic disturbance included hyponatremia, hyperkalemia, hypercalcemia, uremia, hyperglycemia, hypoglycemia and acidosis. Marcantonio et al. (1994a) used admission information to predict further delirium for surgical patients. They concluded abnormal (either hypo or hyper) pre-operative serum sodium, potassium or glucose levels were the major risk factors.

It has been described in the literature how loss or excess of both salt and water may lead to an acute confusional state (Cosgray et al., 1993; Guyton & Hall, 1996; Mentes et al., 1999). Inouye (1994) suggested that detailed history and physical examination, review of medication, and targeted laboratory testing should be adequate to identify most potential underlying causes of delirium. The targeted laboratory evaluation includes complete blood count, electrolytes, blood urea nitrogen, creatinine, glucose, calcium, phosphate, and liver enzyme. This suggestion supports that metabolic disturbance was a common predisposing factor for delirium. Monitor of these variables could help us to distinguish the various clinical presentations of delirium.

In conclusion, delirium has multiple etiologies. Both chronic and acute conditions contribute to the risk of delirium. The added model of risk factors has been reported in the literature (Inouye et al., 1993). A careful and systematic assessment of the patient's condition at the time of admission is important. From the literature, electrolyte imbalance and metabolic disturbance have been identified as major precipitating factors for delirium. These physiological variables were significantly associated with the onset of delirium, but it is impossible to conclude whether these variables are causes, effects or just simply correlates of delirium. The physiological changes of aging and the research results support that these electrolyte and biochemical indicators are important variables to monitor for delirium patients. It is necessary to monitor and correct these variables in admission or before surgery to prevent or reduce the impact of post-surgical delirium. It is also necessary to monitor these variables during the hospital stay to help health personnel to distinguish the etiology of delirium. In each case, knowing when confusion is more likely to occur can assist in focusing on more appropriate and effective efforts at detection, thereby reducing the consequences associated with confusion.

Surgical Stress and Cognitive Disturbance

Surgery and anesthesia make elderly people more prone to cognitive disturbance. Surgery and anesthesia also have the potential for neurological insults to elderly patients (Jagmin, 1998). Martin, Stones, Young, and Bedard (2000) reported surgery was one of the risk factors for delirium development during hospitalization. For surgical treatment, literature revealed that the type of surgery, blood transfusion, and anesthesia affect the cognitive functioning of the elderly postoperatively. Marcantonio et al. (1994) reported that patients who received non-cardiac thoracic surgery or had aortic aneurysm surgery were at risk for delirium. Dai, Lou, Yip, and Huang (2000) reported that patients who had orthopedic surgery or received blood transfusion peri-operatively and after surgery were at higher risk for delirium development post-surgery. Berggren, Gustavsson, Eriksson, Bucht, Hansson, and Reiz et al. (1987) reported that patients who had femoral neck fractures experienced delirium three times more than patients having non-orthopaedic surgery. From the review of Ritchie, Polge, Roquefeuil, Djakovic, and Ledesert (1997), cognitive disorder varies according to the type of surgery, with rates of 0% to 44% being reported for ophthalmic surgery, 25% to 48% for orthopedic surgery, and more than 80% for cardiac surgery.

Anesthesia has been identified as one of the precipitating factors in postoperative delirium (Berggren et al., 1987; Lipowski, 1990). Medications used to produce and maintain anesthesia are known to act both directly on the central nervous system and indirectly by causing anoxia through depression of the respiratory system. Even small doses of anesthesia have been shown to influence mental functioning. Significant cognitive dysfunction was found to be common in elderly patients one to three days after surgery. Confusion and cognitive disturbance are relatively common in the days following surgery (30% to 80%), with a much smaller percentage (16% to 57%) of cases persisting over six months (Ritchie et al., 1997). Smith, Carter, Sevel, and Yate (1991) assess the influence of age and preoperative mental status score on post-operative mental function using the Clifton Assessment Procedure for the Elderly and the reaction time on 112 elderly patients. All the patients received general anesthesia. They reported the variability in reaction time performance was increased 24 hours after anesthesia in transurethral patients. Factors contributing to increased variability of reaction time after operation were reduced mental status score before operation, extent of surgery, postoperative pain and postoperative sedative drugs.

However, several authors report that general anesthesia is not the cause of a cognitive disturbance that remains after the awakening period (Berggren et al., 1987;

Stromberg et al., 1997). Berggren et al. used randomized control trial on 57 elderly patients with femoral neck fracture to understand if the anesthetic technique influenced the incidence of postoperative confusion. They reported no difference in the incidence of confusion between the group that received epidural anesthesia and the group that received general anesthesia (Berggren et al., 1987). Williams-Russo et al. (1992) compared the effect of analgesia using epidural versus intravenous infusion on the incidence of post-surgical delirium after bilateral knee replacement surgery in elderly patients. Fifty-one patients were randomly assigned to two groups. Patients who were randomly chosen to receive epidural analgesics in order to reduce the risk of narcotic-induced delirium showed no reduction in risk of delirium. The overall incidence of delirium was high (41%), with no difference between these two groups. Other factors such as the stress of the surgical procedure, and the prolonged recovery period were stronger contributors to delirium than the type of anesthesia (Williams-Russo et al., 1992). Williams-Russo, Sharrock, Mattis, Szatrowski and Charlson (1995) continued their previous work and reported the similar results on 262 older patients with total knee replacement surgery who had been randomized into two groups. One group received general anesthesia and the other group received epidural anesthesia. These two groups were similar at baseline in age, sex, comorbidity, and cognitive function. They reported no significant differences between the epidural and general anesthesia groups on the cognitive tests at either one week or six months after surgery. They concluded the type of anesthesia does not affect the magnitude or pattern of postoperative cognitive disturbance in older adults undergoing elective total knee replacement. Dyer, Ashton, and Teasdale (1995) reviewed 80 studies from 1966 through 1992 related to postoperative delirium. They concluded that the insufficient sample size and inconsistent application of various diagnostic tools were the major factors for the inconsistent findings from the research. They indicated age, pre-operative cognitive disturbance, and the use of anticholinergic drugs were significantly associated with post-operative delirium, but gender, type and route of anesthesia were not.

Whether or not type of anesthesia may be an important factor for post-surgical cognitive disturbance is still uncertain. Some possible explanations were raised, such as: the post-operative cognitive decline was the existence of an undiagnosed neuropsychiatric disorder that continue to follow its course postsurgery, a preoperative physical condition, an alteration in cerebral blood flow and metabolism due to factors other than anesthesia, and the medication given in conjunction with anesthesia (Ritchie et al., 1997). In this theoretical model, I assume that general anesthesia will induce cognitive disturbance.

Psychoactive Medication Used and Cognitive Disturbance

Any medication that lowers the patient's attentive power will reduce how much he or she registers and remembers. If a patient takes any medication or multiple medications, it is often worthwhile to investigate the cognitive impact of those medications. Many drugs and drug combinations have been associated with acute onset of delirium. Literature has suggested that an etiologic relationship exists between decreased levels of neurotransmitters in the brain, such as acetylcholine, and delirium

(Jacobson, 1997; Parente & Herrmann, 1996; Smita et al., 1995). Impairment of the cholinergic-activating pathways results in disorder of the arousal, alertness, and sleep states. Thus, treatment with drugs that affect cholinergic pathways and interfere with arousal or alertness and sleep cycles, or that alter the concentrations of neurotransmitters in the central nervous system increase the risk of delirium (Berggren et al., 1987; Levkoff, Cleary, Liptzin, & Evans, 1991; Smita et al., 1995). Tune, Carr, Cooper, Klug, and Golinger (1993) examined 25 patients in the surgical intensive care unit over a three-week period. They studied the cumulative anticholinergic effects of these patients' medications. They reported that the risk of delirium could be estimated by an anticholinergicity drug score generated according to exposure to drugs with measured anticholinergic effects. The delirious patients had significantly higher cumulative anticholinergic effects than those of non-delirious patients.

Gustafson et al. (1988) reported that anticholinergic drugs was one of the precipitating factors for delirium in femoral neck fracture patients. Rudberg, Pompei, Foreman, Ross, and Cassel (1997) reported that medication was the leading cause for delirium for medical-surgical elderly patients. Other researchers reported that use of multiple medications (Foreman, 1989; Inouye & Charpentier, 1996; Martin et al., 2000), narcotics or sedatives (Francis et al., 1990), neuroleptic or narcotics (Schor et al., 1992), alcohol (Marcantonio et al., 1994b; Pompei et al., 1994; Williams-Russo et al., 1992), and psychoactive drugs (Dai et al., 2000) precipitated delirium development.

Berggren et al. (1987) used randomized control trial on 57 elderly patients with femoral neck fractures to understand the influential factors of postoperative confusion.

They reported that the patients who developed confusion were correlated closely to the use of drugs with anticholinergic effects ($p < .005$).

Summary

From the literature review, a theoretical model has been developed that includes six predictors affecting cognitive disturbance and their interrelationships. Age, physical function at admission, cognitive function at admission, physiological stability, surgical stress, and psychoactive medication used post surgery all impact the severity of post-surgical cognitive disturbance. The literature supports all the directions of the relationships. These variables are significantly associated with cognitive disturbance but it is inconclusive whether these variables are causes, effects or just simply correlate to cognitive disturbance. However, these variables can be placed in sequential order during the hospital stay.

Table 2.1 Selected Studies of Delirium in Older Patients

Reference	Population	Frequency and Method of Assessment	Rate of Delirium/ Cognitive Disturbance	Risk/Precipitating Factors
Williams et al., 1985	Hip fracture patients (N= 170)	Daily assessment by nurses from admission to post-surgical day 5 on presence of any of 4 behaviors	51.5% incidence	Age Preoperative poor performance on cognitive testing Low pre-injury activity level
Gustafson et al. 1988	Femoral neck fracture patients (N=111)	Daily assessment for two weeks post surgery using DSM-III	33% prevalence before surgery, 28% incidence after surgery	Age Dementia Anticholinergic drugs Depression Operative hypotension
Rockwood. 1989	Medical patients (N=80)	Daily assessment using DSM-III	16% prevalence, 13% incidence	Age Unstable illness Dementia
Forman, 1989	Medical patients (N=71)	Daily assessment from admission to post-surgical day 6 by MMSE, CAC[1] and VAS-D[2]	38% incidence	Hypernatremic Hypokalemic Hyperglycemic Hypotensive Elevated blood creatinine Elevated BUN Multiple medication
Francis et al., 1990	Medical patients, 70 years of age or more(N=229)	Assessment every 48 hours until discharge using DSM-III-R	22%, did not separate prevalent and incident cases	Abnormal sodium Illness severity Dementia Fever Use of narcotics or sedative Azotemia

Table 2.1 Selected Studies of Delirium in Older Patients (continue)

Reference	Population	Frequency and Method of Assessment	Rate of Delirium/ Cognitive Disturbance	Risk/Precipitating Factors
Schor et al., 1992	Medical and surgical patients (N=325)	Daily assessment for 14 days using DSM-III	31% incidence	80 years of age or more Chronic cognitive impairment Fracture on admission Neuroleptic or narcotic use Infection Male
Williams-Russo et al., 1992	Bilateral knee replacement patients (N= 51)	Daily assessment from recovery room to post-surgical day 7 by DSM-III	41% incidence	Age Male gender Pre-operative alcohol use
Inouye et al. (1993)	General medical patients (N=107)	Daily assessment by CAM[3]	25% incidence	Vision impairment Severe illness Cognitive disturbance High blood urea nitrogen/creatinines ratio
Pompei et al., 1994	Medical and surgical patients (N=323)	Daily assessment by DSM-IIIR	15%, did not separate prevalent and incident cases	Cognitive disturbance Comorbidity Depression Alcoholism
Marcantonio et al., 1994	Surgical patients (N=1341)	Prediction rule by using admission assessment. Delirium was determined by CAM[3].	9% incidence	Age Alcohol abuse Poor cognitive status Poor functional status Abnormal preoperatvie serum sodium, potassium or glucose level Noncardiac thoracic surgery Aortic aneurysm surgery

Table 2.1 Selected Studies of Delirium in Older Patients (continue)

Reference	Population	Frequency and Method of Assessment	Rate of Delirium/ Cognitive Disturbance	Risk/Precipitating Factors
Elmstahl et al., 1995	Acute medical unit (N=221)	Retrospectively assessment from medical records by DSM-III-R	--	Dementia Metabolic disturbance Cardiovascular diseases
Williams-Russo et al. 1995	Total knee replacement older patients (N= 262)	Assessed preoperatively and repeated 1 week and 6 months postopeartively by neuropsychological assessment	5% showed a long-term clinically significant deterioration in cognitive function	--
Inouye et al., 1996	Medical patients (N= 196)	Assessed every other day by clinical researcher and nurse from admission to hospital day 9 by CAM[3]	18% incidence	Use of physical restraint Malnutrition More than 3 medications added Use of bladder catheter Iatrogenic event
O'Keeffe,& Lavan, 1997	Acute geriatric unit (N=225)	Assessed every 48 hours by DSM-III-R	42% prevalence 24% incidence	Chronic cognitive disturbance Severe acute illness Multiple comorbid condition Functional disability
Stromberg et al., 1997	Hip fracture patients (N= 256)	Assessment on day of admission, postoperatively, after one week and on discharge by SPMSQ[4]	37% prevalence and 13 % incidence	not mentioned
Milisen et al., 1998	Hip fracture patients (N=26)	Assessed at admission and on the first, third and fifth postoperative days by the MMSE	73%, did not separate prevalent and incident cases	not mentioned

Table 2.1 Selected Studies of Delirium in Older Patients (continue)

Reference	Population	Frequency and Method of Assessment	Rate of Delirium/ Cognitive Disturbance	Risk/Precipitating Factors
Jagmin, 1998	Hip surgery patients (N= 70)	Assessment in admission and assessed twice in post-surgical day one1 to day five5 by MMSE and NEECHAM	not mentioned	not mentioned
Mentes et al. 1999	Long term care Minimum Data Set (N=2318)	--	14.0% incidence	Inadequate fluid intake Dementia Fall in the last 30 days
Marcantonio et al. 2000	Hip fracture patients (N=126)	Assessment in admission and daily interviews with MMSE and Delirium Symptom Interview	41% prevalence, persisted in 39% at discharge	Age over 80 ADL impairment Medical comorbidity
Martin et al. (2000)	Medical and surgical patients (N= 156)	Assessed daily by CAM[3]	17.9% incidence	Age Cognitive dysfunction Surgery Intensive care requirement High number of medication High number of procedures
Dai et al. 2000	Surgical patients (N=701)	Assessed by nurse and RA from admission and every 48 hours until post surgical day 5 by DSM-IV	5.1% incidence	Age Abnormal BUN Lower ADL function Lower MMSE score Blood transfusion Psychoactive drug used Type of surgery

[1]CAC: Clinical assessment of confusion

[2]VAS-D: Visual analogue scale for confusion

[3]CAM: Confusion assessment method

[4]SPMSQ: The short portable mental status questionnaire

Assessment of Cognitive Disturbance

There are many screening tools developed to provide brief, objective measures of cognitive functions. Examples include the clinical assessment of confusion (CAC), the mental status examination (MSE), the Mini-Mental State Examination (MMSE), the cognitive capacity screening examination (CCSE), mental status questionnaire (MSQ), and the short portable mental status questionnaire (SPMSQ) (Fraser, 1988; Vermeersch, 1990). These instruments have been developed for or used in the measurement of cognitive functioning of the elderly in a variety of settings and for a variety of subject conditions. Although all of the instruments are adequate for the purpose of identifying cognitive disturbance and to some extent, quantifying the level of impairment, few have been generally accepted (Stromberg et al., 1997). For clinical assessment, the MMSE is the most widely used tool for assessing cognitive disturbance. It is the most frequently cited bedside cognitive screening instrument. In this session, I will review literature about the MMSE and take into consideration the psychometric characteristics and factor structures of each test.

Items and Scores of the MMSE

The MMSE was developed by Folstein, Folstein and McHugh (1975, Table 2.2). It consists of 30 items of dichotomous questions that combine for a total score of 30. There are seven dimensions in this scale, which include orientation to time (five points), orientation to place (5 points), registration of three words (3 points), attention and calculation (5 points), recall of three words (3 points), language (8 points), and visual construction (1 point). It takes about 5-10 minutes to complete. The assessment

Table 2.2 The Mini-Mental State Examination

Maximum Score	Score	Questions
		ORIENTATION TO TIME
5	( )	What is the (year) (month) (date) (day) (season)?
		ORIENTATION TO PLACE
5	( )	Where are we: (town) (hospital) (floor) (room) (bed)?
		REGISTRATION
3	( )	Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until the patient learns all 3. Count trials and record.
		LANGUAGE
8	( )	Name a pencil, and watch (2 points) Repeat the following "No ifs, ands, or buts.: (1 point) Read and obey the following: "Close your eyes.: (1 point) Write a sentence (1 point) Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor." (3 points)
		RECALL
3	( )	Ask for 3 objects repeated above. Give 1 point for each correct.
		ATTENTION AND CALCULATION
5	( )	Serial 7s. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.
		VISUAL CONSTRUCTION
1	( )	Copy design (overlapping pentagons, 1 point)
TOTAL SCORE	( )	

Mini-Mental State Examination form. (From Folstein, Folstein & McHugh, 1975) provides a standard set of questions for health care providers to evaluate a patient's cognitive function. A score of less than 24 indicates cognitive disturbance (Folstein, Folstein, & McHugh, 1975; Tombaugh & McIntyre, 1992).

Psychometric Characteristics of the MMSE

The psychometric properties of the MMSE have been tested in different situations with different subjects. The test-retest reliability was .56-.98. Inter-rater reliability was .82. Internal consistency was .96. Criterion-related validity was .78. The sensitivity was .87 and the specificity was .82 (Folstein et al., 1975; Foreman, 1987; Tombaugh & McIntyre, 1992). The instrument demonstrates satisfactory reliability, construct validity, and criterion validity (Smith et al., 1995; Tombaugh & McIntyre, 1992). The MMSE has been translated into Chinese with a little modification based on sociocultural differences of the Chinese population. The cut off point for the MMSE is 24. A score of 23 or less indicated the presence of cognitive disturbance. A score of 18-23 indicated mild cognitive disturbance, and 0-17 indicated severe cognitive disturbance.

Critiques of the MMSE

The MMSE was not designed to assess delirium. It is not able to distinguish between delirium and dementia and does not assess features of delirium, such as acute onset, fluctuating course or disturbance in psychomotor behavior. Content analyses revealed the MMSE was highly verbal and not all items were equally sensitive to cognitive disturbances. The MMSE has been criticized for insensitivity to mild cognitive dysfunction, limited memory assessment, and lack of standardized administration procedures (Broshek & Marcopulos, 1999). Items measuring language were judged to be relatively easy and lacked utility for identifying mild language deficits. The assessment also included a drawing activity, which is impractical for bedridden patients. The MMSE can be used only for screening an individual's mental status but it is recommended that the MMSE be used with age- and education-corrected norms and supplemented with other cognitive measures. People with low scores may indicate mental retardation or may suffer from dementia, depression, or a neurologic disorder or a low educational level. Accurate diagnosis depends on careful clinical evaluation, such as psychiatric history, full mental status examination, the physical status and laboratory data. Study results shown the overall MMSE scores are affected by age and education (Broshek & Marcopulos, 1999; Kramer et al., 1985; Stromberg et al., 1997; Tombaugh & McIntyre, 1992).

Factor Structures of the MMSE

The items of the MMSE were not equally efficient for identifying cognitive disturbance. Item analyses have shown that certain items are more sensitive to detect the changes than others (Smith et al., 1995). Shortening the test and making it less strenuous for the respondent but still maintaining good psychometric properties would make it a better test and easier to administer. Several authors (Table 2.3) explored the possible empirical structures of the MMSE, attempting to find a more differentiated factor structure representing common neurocognitive dimensions (Abraham et al., 1994; Braekhus et al., 1992; De-Leon, Baca-Garcia, & Simpson, 1998; Fillenbaum, Heyman, Wilkinson, & Haynes, 1987; Hill & Backman, 1995; Tinklenberg et al., 1990). This factor structure represents commonly recognized dimensions of neurocognitive ability and assesses functioning across several neurocognitive areas.

Magaziner et al. (1987) successfully reduced the MMSE items into a shorter form consisting of seven items. These seven items could be used to reliably predict the total MMSE scores. These items were Date, Month, Backward, Recall, Phrase repetition, Three-stage command and Pentagons. These items accounted for 94% to 96% of the variance. When compared with the full MMSE score, which used 23/24 as a cut-off point, the shorter form had a sensitivity of 100% and specificity ranged from 93% to 100%. The authors reported four age-by-education specific scoring equations to calculate for specific age and education ranges (Magaziner, Basset, & Hebel, 1987).

Fillenbaum, Heyman, Wilkinson, and Haynes (1987) assessed 36 elderly patients with probable Alzheimer's disease using the MMSE and reported a two-factor structure, which accounted for 66% of the variance from the MMSE. The first factor consisted of items regarding concentration, language and praxis; the second factor consisted of items regarding orientation to time, orientation to place and recall.

Tinkleberg, Brooks, Tanke, Khalid, Poulsen, and Kraemer et al. (1990) assessed 63 elder persons with probable Alzheimer's disease using the MMSE and reported a two-factor structure accounted for 62% of variance. These two factors were general functioning and concentration ability. To measure the patient's status and rate of change, they repeated testing every six months up to one and a half years. Repeated assessments for this group reported a five-factor structure accounting for 75% of variance. These five factors were orientation and concentration, obeying commands, learning and repetition, language and recall.

Braekhus, Laake, and Engedale (1992) used the 14 subitems of the MMSE for both exploratory and confirmatory factor analysis from 850 elderly people. They reported that both analyses yielded a two-factor solution that included recent memory and praxis, and orientation to place. Four items (country, town, hospital, floor) were loaded on both factors. The authors did not report the percentage of variance explained in this study. Using factor analysis, they reduced the MMSE items to 12 items with only 3% misclassifications when compared with the original cut-off point of 23/24.

Abraham, Manning, Snustad, Brasbear, Newman, and Wofford (1994) identified a four-factor structure explaining 56.1% of the variance of the MMSE from 892 nursing home residents. These four factors were executing psychomotor commands, memory, concentration, and language.

Hill and Backman (1995) examined the relationship between the MMSE items and selected cognitive performance in a sample of 251 non-demented adults over 75 years of age. They reported a three-factor solution, which accounted for 49.6% of the total variance from this analysis. These three factors were memory, spatial skill and the ability to follow commands. De-Leon, Baca-Garcia, and Simpson (1998) reported a three-factor structure (frontal, memory and spatial) of the MMSE, which accounted for 61% of the variance in 80 schizophrenic patients.

The individual items of the MMSE varied in level of difficulty. From these studies, few authors reported the difficulty levels of each MMSE item. Fillenbaum et al. reported 96% of their participants answered the registration questions correctly. In items that measured orientation to time, patients had the most difficulty answering the date. Only 22% of the participants answered this question correctly, but 47% of the participants identified the season and the month correctly. Of the items that measured orientation to place, 14% of the participants named the county, 75% named the state. It was reported that 86% of the participants immediately repeated the three objects, but only 6% could recall all three objects. When asked language questions, 50-75% of the participants answered correctly and 33% copied the design correctly (Fillenbaum et al., 1987). In Abraham et al.'s (1994) study, they reported that the questions on registration were the easiest for participants (99.6% correct) and copying the design was the most difficult (32.6% correct). For the remaining items, correct response rates ranged between both with a mean of 74.2% and a standard deviation of 19.6%. This indicated the variability of difficulty level in the MMSE items (Abraham et al., 1994).

In Hill and Backman's (1995) study, the authors dichotomized the performance of each MMSE item to 11 binomial scores. A score of one was assigned when subjects correctly answered the specific category, which had only one item. A score of zero was given to a partial or complete failure of the item. For some categories that have several items in the category, a score of one was assigned when subjects correctly answered all the items in the category and score of zero was assigned to those who answered these items at least one item incorrectly. From these 11 binomial content domains, only seven had sufficient variability to predict cognitive disturbance. Participants correctly answered more than 97% on the following items, verbal registration, confrontation naming, repeat a sentence and written command. All participants had 100% correct responses on items of verbal registration and confrontation naming. Episodic recall was the most frequently missed item, with 77% of the participants making one or more errors. The correct response rates ranged from 71% to 95% for the rest of the items (Hill & Backman, 1995).

Dai et al. (1999) used the MMSE to investigate the cognitive function of 801 elderly Taiwanese patients on admission. They reported a mean correct response rate of 88.3% of all the participants. Among the MMSE items, items on attention received the highest correct response rate (99.7%). Ability to copy the design received the lowest correct response rate (66%). The other items had a range of 77-94% correct response rate (Dai, Yip, Huang, & Lou, 1999).

Although the MMSE is a widely used instrument, few studies examine the pattern of relations among items. For the performance across the specific MMSE items, the results indicated that participants seldom erred on items low in cognitive demand, such as verbal and registration and language ability. Participants frequently missed more cognitively demanding items, such as memory. The MMSE measured broad cognitive capacity rather than specific neurocognitive domains. In Folstein et al.'s (1975) original paper, the MMSE covers a variety of cognitive dimensions. However, from the above research summaries, these MMSE factor analytical studies suggested that only a few factors were needed to describe the full MMSE items and the results have shown inconclusive factor structures between studies. These efforts did not derive consistent dimensions from the MMSE. For instance, items factored differently, items loaded on a factor differently, and simple descriptors for the factors were not derived across these studies. This may be due to the different samples. Most of the studies were based on a single assessment of the MMSE and most of the sample sizes were small. These reasons may contribute to the unstable conceptual structures across these studies.

Cognitive/ Behavioral Changes Related to Post-surgical Cognitive Disturbance (Delirium)

The clinical features of delirium include reduced ability to focus, shift attention, and thinking and speech disorganization. Less often, delirious patients experienced altered levels of consciousness, delusions and hallucinations, disturbed sleep-wake cycles, altered psychomotor activity, disorientation, and memory impairment (APA, 1994). The term "delirium" is subject to various definitions and descriptions. It tends to depict varying degrees of one or several disorders of consciousness, memory, attention, inappropriate behaviors and judgment (Vermeersch, 1990). The evaluation of specific neurocognitive functions such as memory, language ability, attention and psychomotor executive skills can help to plan and organize the post-operative nursing care to identify and manage delirium.

Variation in Neurocognitive Function

Research in delirium is confusing because of the inconsistent diagnostic classification system. Multiple terms are used to refer to similar cognitive disorders such as acute confusional states and cognitive failure. DSM-IV classification system is the gold standard for cognitive disturbance. However, the essential features of delirium have been changed from DSM-III-R to DSM-IV. In DSM-IV criteria for delirium, the acute onset of disordered attention and cognition are retained while continuing to recognize the importance of acute onset and organic etiology. Associated phenomena such as psychomotor behavioral changes, perceptual disturbances, hallucinations or delusions are no longer viewed as essential features of delirium (Breitbart, Bruera, Chochinov, & Lynch, 1995; Smith et al., 1995). Researchers need to address neurocognitive symptoms and related issues because these are important features of cognitive disturbance.

Acute confusion among the elderly differs from the young in many aspects. The elderly are likely to have longer episodes of confusion with less dramatic presentation, and carry an adverse prognostic outcome (Choo, Lee, Owen, & Jayaratnam, 1991). More differentiated assessment of neurocognitive functioning over time is needed for guiding a more targeted selection of nursing activities for the elderly. This may reduce the length of the cognitive impaired episode. However, little is known about the attributes of cognitive disturbance and how these attributes change during the course of delirium among post-surgical elderly patients.

Stromberg et al. (1997) explored the cognitive change in 256 hip fracture patients. These researchers used SPSMQ to screen patient's cognitive function on admission, discharge, post-surgical day three, and post-surgical one week. They reported 37% were cognitively impaired on admission, of those, 51% reached normal test scores while in the hospital.

Foreman (1990) investigated the cognitive and behavioral change of 238 acutely confused elderly hospitalized patients. The patients were interviewed daily from admission for a maximum of eight days or until discharged. Among these patients, 113

(47.5%) developed acute confusion within six days of hospital admission. In order to understand the representative pattern of cognitive deficits and psychomotor behavior for acute confusion, this study examined the items of the MMSE and the CAC-B (clinical assessment of confusion) using exploratory factor analysis. It was reported that a five-factor solution, including both cognitive and behavioral dimensions, represented 29.8% of the variance from these items. These five factors included cognition, orientation, perception, motor behavior and higher integrative functions. To determine the essential features of acute confusion, the researcher used stepwise discrimination function analysis using the items of the MMSE and the CAC-B. Nine of these cognitive and behavioral features were diagnostic of acute confusion with 90.3% of correctly classified rates when compared with the original items. The nine items included: spell WORLD backward, observe if the patient has slurred or garbled speech, calculate serial 7's, draw a pentagon, observe if the patient was generally cooperative and pleasant, able to perform some ADLs, observe if the patient had minor forgetfulness, and ask the patient to recall people form the past and recall three objects. The sensitivity was 80% and the specificity was 99% for the diagnosis of acute confusion by using these nine items (Foreman, 1990). From the results, both the cognitive and behavioral aspects of confusion are represented by these nine items; but these nine items represent only three of the five factors derived from the factor analysis. In assessment of acute confusion in the hospital, nurses tended to target their effort toward collecting evidence of disorientation and agitated motor behaviors. However, the findings of the nine items indicated orientation and motor behavior were not very useful in detecting acute confusion. On the other hand, focusing on a patient's ability to concentrate and attend to stimuli was found to be useful in differentiating an acutely confused patient from one who was not confused.

Delirium in hospitalized elderly patients varies over time. Rudberg et al. (1997) assessed 432 elderly patients on a daily basis to understand the presentation, course, and duration of delirium. Among these patients, 15% (N=64) had delirium and 69% had delirium on a single day. Among those with delirium on multiple days (N=20), there were no changes over time (Rudberg et al., 1997). This may be due to some important characteristics of delirium such as attention level or level of consciousness, which are not measured in the delirium rating scale (DRS). They also concluded that there is no single pattern of delirium. Patients with multiple days of delirium did not display decreasing DRS total scores between the first and the last day of delirium and there were no differences in the average item scores from those with delirium on a single day. In fact, the DRS scores among the patients with multiple day delirium presented much more variety and heterogeneity (Rudberg et al., 1997).

Milisen, Abraham and Broos (1998) described the neurocognitive variations among 26 elderly hip fracture patients postsurgery. They used the MMSE to assess the patient's cognitive function from admission through the fifth postoperative day. They reported cognitive status, especially recall ability and psychomotor executive skills and found that these two skills were the most vulnerable to becoming impaired after hip surgery. For patients without cognitive disturbance, significant changes were found on overall cognitive function ($p < .0001$) and on the memory subscale ($p < .0005$). For the overall MMSE score, there was a small decrease from baseline to the first post-operative day but this score increased again through the third and fifth postoperative day. The same pattern was noted on the memory ability subscale. Patients with moderate cognitive disturbance had moderately impaired psychomotor executive skills and memory abilities but their attention and language abilities remained intact. Patients with severe cognitive disturbance had significant changes in the total MMSE scores over time ($p < .05$) and on the neurocognitive dimension of attention ($p < .05$). Total scores decreased from baseline to the first post-operative day, but gradually improved through the third and fifth post-operative day. Psychomotor executive skills and memory function remained impaired during the entire period with a very large decrease in memory function (Milisen et al., 1998).

Elmstahl, Wahlfrid and Jerntorp (1995) investigated the common clinical features of acute confusional state (ACS) among 221 patients by medical record review. Among the 221 patients, 65 fulfilled the DSM-III-R criteria for acute confusional state. The most common clinical features of ACS were reduced attention (100%), memory impairment (100%), disorientation (75%), changes in psychomotor activity (30%), and perception disturbance (25%). Patients who did not fulfill the criteria for acute confusional state, 14 were disoriented and another 9 patients had reduced psychomotor activity or perceptual disturbances (Elmstahl et al., 1995). A potential problem of this study includes incomplete and inconsistent documentation of changes in cognition and ability to concentrate and attend to stimuli. These symptoms are more difficult to detect than changes in psychomotor functions.

From the research results, heterogeneity in neurocognitive manifestations reflects biological variability in the disease process. Delirium may occur any time during a hospital stay. Understanding the relationships of specific patterns of cognitive disturbance may shed light on this complex and varied syndrome. Nurses should remain alert for delirium throughout the course of the patient's hospital stay.

Summary of Literature Review

The literature presented in this section supports the variables related to post-surgical cognitive disturbance and the complexity of the inter-relationship of these variables. The proposed variables include age in Stage I, physical function and cognitive function in Stage II, physiological stability, surgical stress, and psychoactive medication used in Stage III to predict the outcome in Stage IV, that is the severity of post-surgical cognitive disturbance. The literature reviewed relates to all the directions of the relationships in the theoretical model. Besides this, a review of the assessment tool, the MMSE, and the neurocognitive variations after surgery are also presented. Based on the knowledge from the literature review, the methodology of the study is developed. In chapter III, the methodology used to reach the research aims are described.

Table 2.3 Selected Studies of Factor Structure of the MMSE

Reference	Population	No. of Factor Retained	Name of the Factor	Variance Explained
Filenbaum et al. (1987)	* N = 36 (12M, 24F) * Patients with probable Alzheimer's disease * 54-75 yesrs * Test-retest for reliability test	2	1. Concentration-language-praxis 2. Orientation for time-place-recall	66%
Tinklenberg et al. (1990)	* N =63 (44M, 19W) * Patients with probable Alzheimer's disease * 56-90 years * Repeated assessment for 1.5 years	2 (static) 5 (dynamic)	1. General functioning 2. Concentration 1. Orientation and concentration 2. Obeying commands 3. Learning and repetition 4. Language 5. Recall	62% 75%
Braekhus et al. (1992)	* N= 850 (74% F) * Elderly persons (Norweigian) * 54-99 years * Retrospective survey data	2	1. Recent memory 2. Praxis and orientation to place	--
Abraham et al. (1994)	* N= 892 (77.6% M) * Nursing home residents * 71-97 years * One time assessment	4	1. Executing psychomotor commands 2. Memory 3. Concentration 4. Language	56.1%

Table 2.3 Selected Studies of Factor Structure of the MMSE (continue)

Reference	Population	No. of Factor Retained	Name of the Factor	Variance Explained
Hill & Backman (1995)	* N=251 (51M, 200F) * Non-demented adults (Sweden) * 75-96yrs * One time assessment	3	1. Memory 2. Spatial skill 3. Follow command	49.6%
De-Leon et al. (1998)	* N= 80 (56M, 24F) * Schizophrenic patients * Mean age = 38 * One time assessment	3	1. Frontal 2. Memory 3. Spatial	61%

CHAPTER III

METHODOLOGY

The purposes of this study were (1) to test a theoretical model about post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery; (2) to identify the valid, reliable and efficient items from an existing mental status screening tool (the MMSE) for assessment of mental status in elderly Taiwanese patients; and (3) to describe variations of cognitive/behavioral changes in general and in selected cognitive dimensions such as orientation, attention, memory, calculation, during the course of delirium. This chapter describes the research method and procedures used to achieve these purposes. These include: (1) study design, (2) sample selection and data collection procedures, (3) data source for the proposed study, (4) measures used in this study, and (5) protection of human subjects.

Study Design

Secondary data analysis with subgroup analysis was used to achieve the study purposes. Data for this study comes from a prospective cohort study entitled "Confusion in the hospitalized elderly patient." The data were collected in a medical center in Taiwan from 1995 to1997. The specific grant for the data collected were funded by the National Science Council (NSC 85-2331-B002-088 and NSC 86-2314-B002-279) of the Republic of China of which Dr. Yu-Tzu Dai was the Principal Investigator and Meei-Fang Lou was the Co-Investigator (Dai, Lou, & Yip, 1996).

Sample Selection and Data Collection Procedures

The inclusion criteria for this study were (1) 65 years of age or older; (2) ability to communicate orally in Chinese; (3) not unconsciousness, delirious, deaf, or aphasic on admission. This study consisted of 801 elderly patients undergoing selected orthopedic or urological surgery. At admission, patients' demographic data, functional level and cognitive function were assessed. The patient's functional level was assessed by the Barthel Index. The patient's cognitive function was assessed by the Mini Mental State Examination (MMSE). Among the 801 patients, 106 patients were closely observed during their post-operative period. During the first to fifth postoperative day, nurses assessed patients using a confusion-screening tool. To further validate organic etiology of delirium, 41 patients with signs of delirium were closely examined for change of behavioral and cognitive status, vital signs, and laboratory data.. Another 65 patients who had no signs of delirium by nurses' assessment were also closely assessed from post-surgical day one to day five for comparison.

Data Source for this Study

Different data were used to achieve the research purpose. To achieve purpose (1) to test a theoretical model about post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery, the data for the 106 patients which included admission functional status, admission and post-surgical mental assessment data, selected laboratory data and medication administered, were used to test a theoretical model of post-surgical cognitive disturbance.

To achieve purpose (2) to identify the valid, reliable and efficient items from an existing mental status screening tool (the MMSE) for assessment of mental status in elderly Taiwanese patients, the admission assessment of mental status for the 801 patients were used to identify the most efficient items for mental status assessment.

To achieve purpose (3) to describe variations of cognitive/behavioral changes in general and in selected cognitive dimensions during the course of delirium, the four assessments of mental status by the MMSE were used to understand the cognitive/behavioral changes among the post-surgical patients. The four assessments included admission assessment, onset of delirium, the second day post delirium, and the fourth day post delirium for delirious patients. The assessment also included admission, post-surgical day one, day three and day five for non-delirious patients. This data were also used to compare the cognitive/behavioral differences among patients who developed post-surgical delirium and those who did not.

Measures Used in This Study

Measures reflecting the variables of interest in Figure 2.1 were selected from the data set. These include: (1) measures used for the theoretical model testing, (2) the measure used for cognitive assessment, and (3) the measure used for the cognitive/behavioral characteristics for patients. The reliability and validity of the measures were summarized in Table 3.1.

Measures Used for the Theoretical Model Testing

Age

The patients' chronological age was used in the model testing.

Cognitive Function

The MMSE was used to assess the cognitive function of the patients. The MMSE was developed by Folstein, Folstein and McHugh (Folstein et al., 1975) from clinical

Table 3.1 Reliability and Validity of Measurements

Concept	Measures	Reliability	Validity
Physical Function	Barthel Index (0-100)	*Inter-rater reliability Kappa: .70- .88 $\alpha = .91$ (this study)	*Face validity: measure ADL *Construct validity: single domain *Concurrent validity *Predictive validity
Cognitive Function	MMSE (0-30)	*Test-retest reliability: .56-. 98 *Inter-rater reliability: .82 *Internal consistency: .96. KR-20: .86 (this study)	Criterion-related validity: .78.
Surgical Stress	Three Items[1]		Face validity
Physiological Stability	Six Items[2]		Face validity
Psychoactive Medication Used	Five Items[3]		Face validity
Severity of Post-Surgical Cognitive Impairment	MMSE 3 levels[4]		

[1]Type of surgical, Anesthesia, Blood transfusion

[2]Na, K, BSAC, BT, BUN, BUN/Cr

[3]Narcotic analgesics, Sedative hypnotics, Histamine 2-receptor blockers, anti-Parkinsonism agents, and anti-cholinergic drugs

[4]MMSE 24-30 as 1, 18-23 as 2, 0-17 as 3

observations of patients. The MMSE is the most widely used tool for assessing cognitive impairment. It is found to be the most frequently cited bedside cognitive screening instrument. The MMSE has been translated into Chinese with a small amount of modification based on sociocultural differences of the Chinese population. This exam consists of 30 dichotomous items with a total score of 30. It takes about 5-10 minutes to complete. It provides a standard set of questions for health care providers to evaluate a patient's cognitive functions. A score of less than 24 indicates cognitive impairment. A score of 18-23 indicated mild cognitive impairment and, 0-17 indicates severe cognitive impairment (Dolan et al., 2000; Tombaugh & McIntyre, 1992).

The psychometric properties of the MMSE have been tested in different situations with different subjects. The reported test-retest reliability was .56-. 98. Inter-rater reliability was .82. Internal consistency was .96. Criterion-related validity was .78. The sensitivity was .87 and the specificity was .82 (Folstein et al., 1975; Foreman, 1987; Tombaugh & McIntyre, 1992). The internal consistency (KR-20) of the MMSE in the original study was .86. The inter-rater assessment agreement obtained in the original study was higher than 90%. The instrument demonstrates satisfactory reliability, construct validity, and criterion validity.

Physical Function

The Barthel Index was used to measure an individual's function in performing activities of daily living (ADL) at admission. It is one of the most popular assessment scales in measuring the individual's functional ability. The Barthel Index is used to assess an individual's ability to manage his or her own care. This Index contains ten items with a maximum score of 100, which indicates total independence in ADL (Mahoney & Barthel, 1965; Resnick & Daly, 1998). These ten items include bowel control, bladder control, grooming, toilet use, feeding, transferring, mobility, dressing, stair climbing, and bathing (Mahoney & Barthel, 1965; Wade & Collin, 1988).

The reported inter-rater reliability (Kappa coefficient) ranged from .70- .88 (Loewen & Anderson, 1988). Richards et al. (2000) used the Barthel Index to compare a nurse's assessment and a non-clinical research assistant's assessment to the same patient. The percentage of agreement ranged from 64% to 99% for each of the ten items. The Barthel Index certainly has "face validity" because it covers items usually included in ADL indices. Factor analysis, which represents construct validity, has confirmed that it is measuring a single domain (Wade & Collin, 1988). These reports support the reliability and validity of the index. The inter-rater assessment agreement obtained in the original study was higher than 90%. The internal consistency (Chronbach's α) obtained in the original study was .91.

Surgical Stress

Three indicators regarding surgical treatments were selected in this study as a risk index to test the theoretical model. These included types of surgery, types of anesthesia and blood transfusion. These items were coded as "yes" or "no." The total score ranges from 0 to 3. The higher the score, the more risk for cognitive impairment the individual would have after surgery.

Physiological Stability

Six indicators regarding physiological stability were used in this study to test the theoretical model. These include blood sodium (Na), potassium (K), blood urea nitrogen (BUN), fasting blood glucose (BSAC), body temperature (BT) as fever and infection indicator, and the ratio of BUN to creatinine as a dehydration indicator (BUN/Cr.). The subject's most recent test values obtained during his/her hospital stay were used in the analysis. From the suggestion of literature (Davis, 1993), the following cutoff point was used: Na, 135-146mmol/L, K, 3.0-5.9mmol/L, BUN, 9-33mg/dL, BSAC, 70-110mg/dL, BT, ≦37.7℃ (99.8℉), BUN/Cr., ≦18. The data were coded as normal vs. abnormal based on the cutoff point. The total score ranges from 0 to 6. The higher the score, the more stable the physiological condition of the individual.

Psychoactive Medication Used

A checklist of twenty-six medications with psychoactive action was used to record whether these medications were used during post-surgical period. The list included those medications indicated in the literature to be significantly related to delirium such as morphine, meperidine, atropine, etc. (Marcantonio et al., 1994a; Smita et al., 1995). In data analysis, the medications were categorized into five types: narcotic analgesics, sedative hypnotics, histamine 2-receptor blockers, anti-Parkinsonism agents, and anti-cholinergic drugs. The total score ranges from 0 to 5. The higher the score, the more psychoactive medication was used.

The Outcome Variable: Severity of Cognitive Disturbance

The mental status, which was assessed by the MMSE, will be used as the outcome variable. For delirious patients, the assessment at onset of delirium will be used; for non-delirious patients, the assessment on post-surgical day one will be used in the analysis. Patients will be categorized on the basis of cognitive status into three levels as follows: no cognitive impairment (MMSE $\geqq$ 24), moderate (MMSE $\leqq$ 23 but $\geqq$ 18) and severe impairment (MMSE $\leqq$ 17). The higher the level, the more severe the cognitive impairment (Dolan et al., 2000; Milisen et al., 1998; Tombaugh & McIntyre, 1992).

Measure Used for Cognitive Assessment at Admission

The MMSE was used to assess the cognitive function. The psychometric of MMSE has been presented in the above section.

Measure Used for Cognitive/Behavioral Characteristic

The MMSE was used to assess the cognitive function from admission through the post-surgical period. The psychometric of the MMSE has been presented in the above section.

Data Analytic Procedure

The following presents the analysis plan to achieve each research purpose. To achieve purpose (1) to test a theoretical model about post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery, the analysis include (1) case-related issues such as the accuracy of data input, missing data, and outliers, (2) distributional relational issues such as normality, linearity, and homoscedasticity, and (3) regression analysis to test for each path in the model.

Linearity and homescedasticity are two aspects of multivariate normality that will be evaluated through the inspection of bivariate scatterplots. The skewness index was measured by the skewness divided by its standard error. Data sets with absolute values of univariate skew indexes greater than 1.96 were extremely skewed (Duffy & Jacobsen, 2001). These data were transformed.

The Correlation matrix was used to present the correlation of the variables. Multicollinearity occurs when intercorrelations among some variables are so high that certain mathematical operations are either impossible or the results are unstable because some denominators are very close to zero. The variance inflation factor (VIF) was used as the index of multicolleineartiy among predicting variables. The VIF is the ratio of a variable's total variance in standardized terms to its unique variance. If the ratio is greater than 10, then, the variable may be redundant with others (Kline, 1998).

Standardized regression coefficients (β) were used to present the final result. Path coefficients were considered meaningful if they are statistically significant ($p < .05$). Adjusted R^2 (Adj. R^2) was used to present the total variance explained by the independent variables to the outcome variable. Both direct and indirect effects to the outcome variable were calculated.

To achieve purpose (2) to identify the valid, reliable and efficient items from an existing mental status screening tool (the MMSE) for assessment of mental status in elderly Taiwanese patients, the one-parameter (Rasch model) and two-parameter (Birnbaum model) Item Response Theory (IRT) models were used. The RASCAL program will be used to test the one-parameter model. The XCALIBRE program was used to test the two-parameter model. Testing the fit of the data to the IRT model is equivalent to a test of the theoretical construct validity and adequacy of the scale. The data derived from the MMSE will be fitted to the IRT one-parameter and two-parameter models, operationalized by the unconditional maximum likelihood approach (Assessment Systems Corporation, 1995; Baker, 1985; Wright & Stone, 1979). The problematic items were defined as if the difficulty level were less than -2.95 or higher than 2.95, or if the discrimination level were less than .3, or if the standardized residual were higher than 1.96. The cutoff point for the reduced MMSE will be determined by the item information curve (Assessment Systems Corporation, 1995; Baker, 1985).

After the items have been selected from the analysis, the following procedures were used to further understand the factor structure and correct classification rate of the reduced MMSE:

(1) Principal component analysis with Varimax rotation to determine the factor structure of the final reduced MMSE. A communality cutoff point of .3 was used for inclusion of a variable in interpretation of a factor.

(2) Compare the correct classification rate of the reduced MMSE with the new cutoff point with the original MMSE and its cutoff point.

To achieve purpose (3) to describe variations of cognitive/behavioral changes in general and in selected cognitive dimension during the course of delirium, the following procedures will be used:

(1) After checking data for normality, descriptive statistics were used to determine the mean, standard deviation, frequencies of the total score of the MMSE and in each

cognitive dimension between the delirious and non-delirious groups.

(2) Inferential statistical procedures, which include Student t test, chi-square and repeated measures of analysis of variance will be used. Statistical significance is established as $p < .05$ with all tests being two-tailed.

(3) Graphs were used to plot the trends of total score of the MMSE and in each cognitive dimension between the delirious and non-delirious groups.

Protection for Human Subjects

To use of the data for secondary analysis, permission was obtained from the principal investigator of the original research (Appendix A). The research proposal was submitted for evaluation and has approved by the Human Subjects Review Committee of the University of Washington (Appendix A). All the data have been entered into the SPSS statistical package with no identifiers on the notes. A code number was assigned to each patient. There were no patients' names on the data file. Only the investigator and her advisory committee had access to the data set. Thus, the confidentiality was maintained.

Summary

This chapter presented the methodology to achieve the study purposes. Secondary data analysis was used in this study. The measures for the major variables and their validity and reliability were presented. Besides these, the sample selection, data analysis and protection of human subjects were also presented in this chapter.

CHAPTER IV

RESULTS

The purpose of this study were (1) to test a theoretical model about post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery; (2) to identify the valid, reliable and efficient items from an existing mental status screening tool (the MMSE) for assessment of mental status in elderly Taiwanese patients; and (3) to describe variations of cognitive/behavioral change in general and in selected cognitive dimensions such as orientation, attention, memory, calculation, during the course of delirium. Secondary data analysis was used to achieve each study aim. This chapter presents the results of the data analysis in three parts; each part presenting the results for each study purpose, is included in this section.

Testing a Model of Post-Surgical Cognitive Disturbance

To achieve purpose (1) to test a theoretical model about post-surgical cognitive disturbance among elderly Taiwanese patients after elective surgery, the path analysis was used. Four parts are included in this section. The first part presents the description of the sample and univariate analysis of the major variables. The second part presents the bivariate correlations among major variables of this model. The third part is related to testing of the theoretical model by path analysis. The forth part presents the revised empirical model.

Description of the Subjects and Univariate Analysis of the Major Variables

One hundred and six subjects were in the data set. The data were entered into an SPSS data file. Upon inspection of the data matrix, it was noted that four subjects did not complete the MMSE and another nine did not have the complete biochemistry data for analysis. Therefore, a total of 93 subjects with complete data were used to test the model. Univariate analysis on demographic variables (Table 4.1) showed the ages of the study sample ranged from 65-93 years of age with a mean of 74.3 and standard deviation (SD) of 6.5. The number of male and female subjects were almost equal. The majority of the subjects (76.3%) were literate. The average year of education was 6.9 years (SD = 5.3). More than 80% of the subjects had family members or hired attendants accompanying them 24 hours during the hospital stay. Most of the subjects (80.6%) received orthopaedic surgery.

Table 4.2 presents the frequency for items in the variables of physiological stability, surgical stress and psychoactive medication used. Six items combined to represent the subject's physiological stability. Of these subjects, 98% had normal blood potassium level, but only 54% had normal blood glucose. Three items combined to represent the subject's level of surgical stress. Most of the subjects received spinal anesthesia (72%), had blood transfusion (90%) and orthopaedic surgery (81%). Five items combined to represent the amount of psychoactive medication used by the subject. Of these subjects, 73% of subjects had narcotics and 31% had sedative hypnotic post-surgery. Table 4.3 presents the descriptive analysis of the major variables. The mean age of these subjects was 74.3 years (SD = 6.5). The mean of the Barthel ADL total score, indicating the subject's physical function, was 89.46 (SD = 23.06). The mean of the MMSE total score, indicating the subject's cognitive function, was 25.41 (SD = 5.28). The mean scores of physiological stability and surgical stress were 4.7 (SD = 1.06), 2.0 (SD = .79), respectively. On average, the subjects used 1.33

Table 4.1 Demographic Data of the Study Subjects (N=93)

Variable	Number	%	Mean ± SD	Range
Age			74.3 ± 6.5	65-93
Gender				
Male	46	49.5		
Female	47	50.5		
Literacy (ability to read)				
Yes	71	76.3		
No	22	23.7		
Years of Education			6.9 ± 5.3	0-18
Accompanied by a Person in the Hospital				
24 hrs Family Member	65	69.9		
24 hrs Family Member or Hired Attendant	12	12.9		
24 hrs Hired Attendant	2	2.2		
Partial Hours by Family Member	10	10.8		
Other	4	4.4		
Unit				
Orthopaedic	75	80.6		
Urological	18	19.4		

SD: Standard Deviation

Table 4.2 Univariate Analysis of Items in Major Variables of the Model (N=93)

Variable	N	%	Variable	N	%
Physiological Stability			**Psychoactive Medication Used**		
K			Narcotics		
Normal	91	97.8	Yes	68	73.1
Abnormal	2	2.2	No	25	26.9
Na			Sedative-Hypnotic		
Normal	78	83.9	Yes	29	31.2
Abnormal	15	16.1	No	64	68.8
BUN			Histamine Blocker		
Normal	81	87.1	Yes	13	14.0
Abnormal	12	12.9	No	80	86.0
Glucose			Anti-Parkinsonism		
Normal	50	53.8	Yes	1	1.1
Abnormal	43	46.2	No	92	99.9
Dehydration			Anticholinergics		
Normal	54	58.1	Yes	13	14.0
Abnormal	39	41.9	No	80	86.0
Body Temperature					
Normal	81	87.1			
Abnormal	12	12.9			
Surgical Stress					
Anesthesia					
General	26	28.0			
Spinal	67	72.0			
Blood Transfusion					
Yes	84	90.3			
No	9	9.7			
Type of Surgery					
Orthopaedic	75	80.6			
Urological	18	19.4			

Table 4.3 Univariate Analysis of Major Variables in the Model (N=93)

Variable Name	Number of Items	Possible Range	Actual Range	Mean	Standard Deviation	Skewness Index
X_1 Age	1	65 and above	65-93	74.33	6.54	3.11
X_2 Physical function at admission	10	0-100	0-100	89.46	23.06	-11.08
X_3 Cognitive Function at admission	30	0-30	6-30	25.41	5.28	-5.36
X_4 Physiological stability	6	0-6	2-6	4.68	1.06	-2.13
X_5 Surgical Stress	3	0-3	0-3	1.99	.79	-2.66
X_6 Psychoactive Medication used	5	0-5	0-4	1.33	.93	1.17
$X_{2.1}$ Transformed of physical function at admission		.01-1	.01-1	.66	.45	-2.36
$X_{3.1}$ Transformed of cognitive function at admission		0-1.49	0-1.40	.55	.43	.51
Y Severity of post-surgical cognitive disturbance		1-3	1-3	1.70	.89	2.55

Skewness Index = Skewness/Standard Error of Skewness

(SD = .93) types of psychoactive medication post-surgery.

To test the assumption of normal distribution, the distribution of the major variables was examined by histograms (Figure B.1 to B.6 in Appendix B). While examining the distribution of the major variables and their skewness indexes (Table 4.3), the scores of physiological stability, and psychoactive medication used were shown to have normal distribution. The distribution of age was slightly positively skewed, indicating a higher number of younger subjects in this sample. The score of surgical stress was slightly negatively skewed, indicating that more subjects had high scores on surgical stress. The total Barthel ADL score and the total MMSE score were negatively skewed. The skewness indexes were -11.08 and -5.36, respectively. This skewness indicates that more subjects had high scores in these two variables. These two variables were transformed by the suggestions of Tabachnick and Fidell (Tabachnick & Fidell, 1996). From Tabachnick and Fidell (1996), when the distribution of the variable is substantially negatively skewed, the reflect and the logarithm transformation can be used to produce normality. When the distribution of the variable is severely negatively skewed, the reflect and the inverse can be used to produce normality. The logarithm transformation was applied to transform the total MMSE score (New score = LG_{10} (31-Old score). After logarithm transformation, the original higher scores of the MMSE converted to lower new scores. The inverse transformation was applied to transform the total Barthel score (New score = 1/ (101-Old score)). After transformation, the original higher scores of the Barthel score converted to higher new scores. After transformation, the skewness indexes for these two variables were .51 and -2.36, respectively (Table 4.3). The transformed data were used for further analysis.

Bivariate Correlation among Variables of the Model

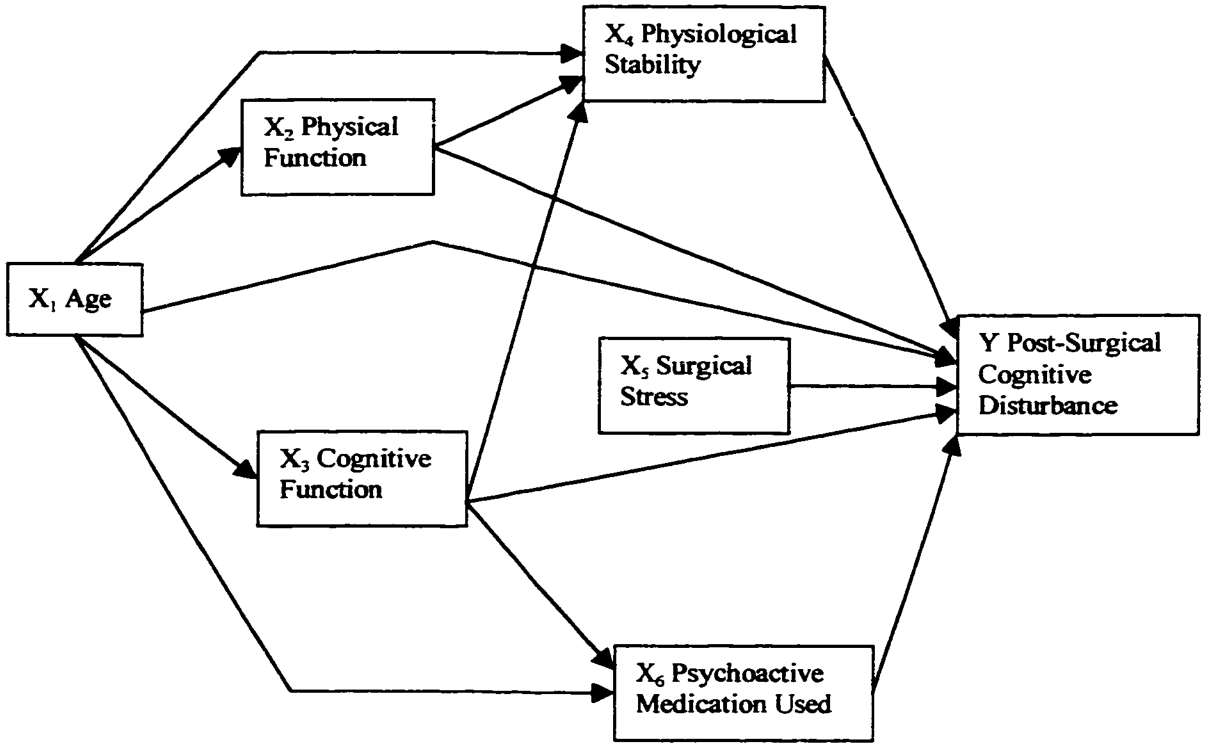
Zero order correlations among these seven variables in the theoretical model were presented in Table 4.4. All the dependent variables, except the score of psychoactive medications used, were significantly correlated with the outcome variable. The correlation coefficients ranged from .06 (age and total psychoactive medication used) to .72 (cognitive function at admission and severity of post-surgical cognitive disturbance) among these variables. This was the one strong correlation (correlation coefficient higher than .65) found from the major variables. The score of cognitive function was highly correlated with the outcome variable, the severity of post-surgical cognitive disturbance. It indicates subjects who had higher scores of cognitive functioning had lower levels of cognitive disturbance. Five moderate correlations (correlation coefficients between .40 to .65) were found. They were age and physical function, age and cognitive function, physical function and cognitive function, physical function and post-surgical cognitive disturbance, and physiological stability and post-surgical cognitive disturbance. These indicate that subjects who were more stable on physiological indicators, more independent in activities of daily living, had lower level of cognitive disturbance. The subjects who were more stable on physiological indicators had higher score of physical function. Subjects who had higher scores on physical function also had higher scores on cognitive function.

Table 4.4 Bivariate Correlation of the Major Variables (N=93)

Var.	X_1	X_2	X_3	X_4	X_5	X_6	Y
X_1	1.00						
X_2	-0.45**	1.00					
X_3	-0.42**	-0.44**	1.00				
X_4	-0.07	0.34**	-0.30**	1.00			
X_5	-0.09	-0.27	0.10	-0.39**	1.00		
X_6	0.06	0.25*	0.07	0.18	0.29**	1.00	
Y	0.39**	-0.64**	0.72**	-0.48**	0.23*	0.15	1.00

X_1: age, X_2: Transformed total Barthel ADL score at admission, X_3: Transformed total MMSE score at admission, X_4: Physiological stability, X_5: Surgical stress, X_6: Total psychoactive medication used, , Y: Severity of post-surgical cognitive disturbance

*$p < .05$, **$p < .01$



Structure Equation

$X_2 = B_{21}X_1 + e1$

$X_3 = B_{31}X1 + e2$

$X_4 = B_{41}X_1 + B_{42}X_2 + B_{43}X_3 + e3$

$X_6 = B_{61}X_1 + B_{63}X_3 + e5$

$Y = B_{y1}X_1 + B_{y2}X_2 + B_{y3}X_3 + B_{y4}X_4 + B_{y5}X_5 + B_{y6}X_6 + e6$

Figure 4.1 Theoretical Model

When independent variables were highly correlated to each other, researchers should be cautious to use them in the same analysis. The problem of multicollinearity could occur (Tabachnick & Fidell, 1996), which would make multivariate regression analysis inappropriate. The squared multiple correlation (Ri^2) or tolerance ($1-Ri^2$) among independent variables showed that multicollinearity is not a problem. A very low value of tolerance indicates multicollinearity among variables. The tolerance of these independent variables ranged from .61- .88. This tolerance means only .12- .39 of variance is shared by other independent variables.

Testing of the Theoretical Model by Path Analysis

A theoretical model predicting post-surgical cognitive disturbance was tested in this section (Figure 4.1). The following hypotheses were tested:

H1 Age has a direct positive effect on the severity of post-surgical cognitive disturbance.

H2 Physical function at admission has a direct negative effect on the severity of post-surgical cognitive disturbance.

H3 Cognitive function at admission has a direct negative effect on the severity of post-surgical cognitive disturbance.

H4 Physiological stability had a direct negative effect on the severity of post-surgical cognitive disturbance.

H5 Surgical stress has a direct positive effect on the severity of post-surgical cognitive disturbance.

H6 Psychoactive medication used has a direct positive effect on the severity of post-surgical cognitive disturbance.

H7 Physical function at admission has a direct positive effect on physiological stability.

H8 Cognitive function at admission has a direct positive effect on physiological stability.

H9 Age has a direct negative effect on physiological stability.

H10 Cognitive function at admission has a direct negative effect on psychoactive medication used.

H11 Age has a direct positive effect on psychoactive medication used.

H12 Age has a direct negative effect on physical function at admission.

H13 Age has a direct negative effect on cognitive function at admission.

H14 The effect of age on post-surgical cognitive disturbance is indirect through (a) physical function at admission, (b) cognitive function at admission, (c) physiological stability and (d) psychoactive medication used.

H15 The effect of physical function at admission on post-surgical cognitive disturbance is indirect through (a) physiological stability.

H16 The effect of cognitive function at admission is indirect through (a) physiological stability, and (b) psychoactive medication used.

Path analysis was used to examine the theoretical model (Figure 4.1). Multiple regression equations were used to compute regression coefficients in the theoretical model. The standardized regression coefficient (beta) was used to present the direction and magnitude of the path, and also for comparison the magnitude of the path from each other. The adjusted R^2 (R^2 adj.) was used to present the variance accounted for by the independent variables in the equation. To test the theoretical model, five standardized multiple regression equations were constructed from the theoretical model. They were:

$X_2 = B_{21}X_1 + e$

$X_3 = B_{31}X1 + e$

$X_4 = B_{41}X_1 + B_{42}X_2 + B_{43}X_3 + e$

$X_6 = B_{61}X_1 + B_{63}X_3 + e$

$Y = B_{y1}X_1 + B_{y2}X_2 + B_{y3}X_3 + B_{y4}X_4 + B_{y5}X_5 + B_{y6}X_6 + e$

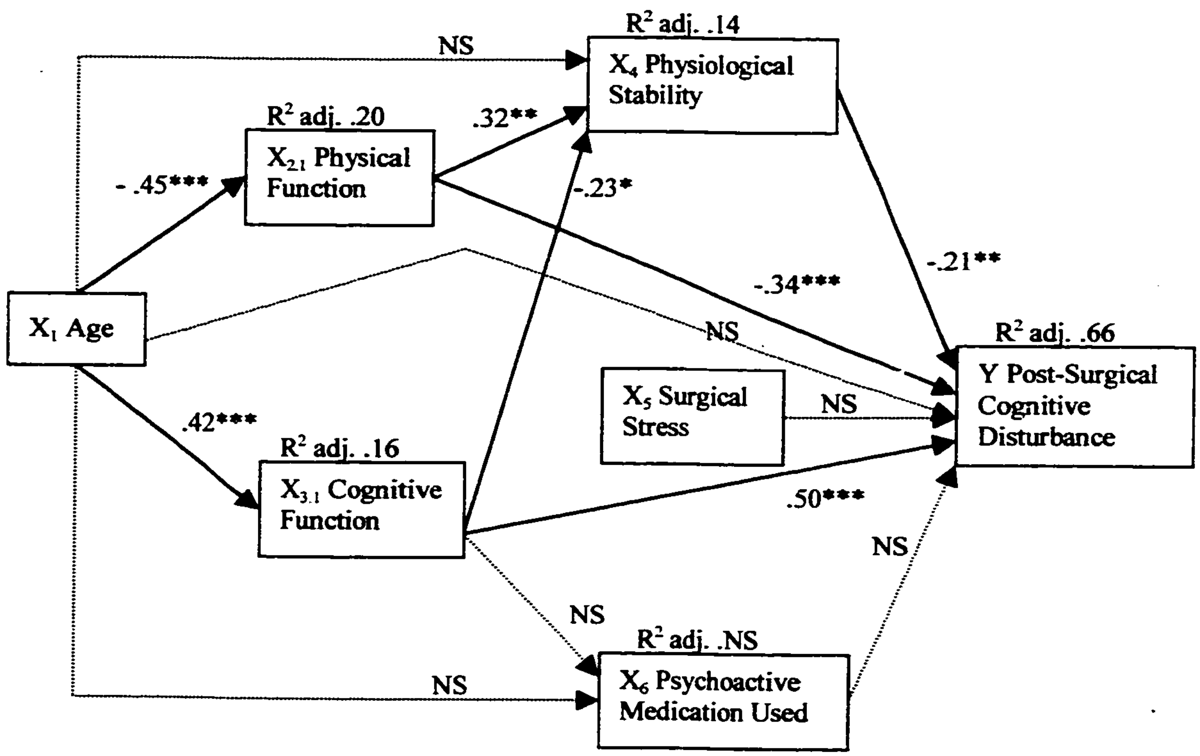
Where

X_1 = age, X_2 = physical function, X_3 = cognitive function, X_4 = physiological stability, X_5 = surgical stress, X_6 = psychoactive medication used, Y = severity of post-surgical cognitive disturbance, Bij = the regression coefficient for the jth predictor variable in the model for the ith dependent variable, e = error term.

Before analysis, the assumptions of multiple regression analysis were tested. Scatterplots of residuals of dependent variables of selected equation were presented in Figure B.7 and Figure B.8 in Appendix B. The scatterplots were used to examine the assumptions of normality, linearity, and homoscedasticity of residuals. Scatterplots of all variables showed a spread out distribution of the residuals against the expected values. Thus, the assumption was met on all major variables.

Figure 4.2 showed the path coefficients for the theoretical model. Seven out of the 13 paths were significant at $p < .05$ or $p < .001$ level. These six predictors explained 66% of the total variance in subjects' post-surgical cognitive disturbance. Age strongly predicted physical function ($\beta = -.45$, $p < .001$) and cognitive function at admission ($\beta = .42$, $p < .001$) for the Stage II variables. The more advanced in age that subjects were, the less physical function and cognitive function was preserved. Physical function and cognitive function at admission, but not the age, significantly predicted the severity of post-surgical cognitive disturbance directly ($\beta = -.34, .50$, respectively, $p < .001$). Subjects more cognitively intact and physically functional at admission were less cognitively impaired after surgery. For the stage III variables, physical function and cognitive function had direct effects on physiological stability ($\beta = .32, -.23$, $p < .01, .05$, respectively). These two variables explained 14% of variance in physiological stability. Cognitive function and age had no significant impact on psychoactive medication used. Physiological stability directly predicted the severity of post-surgical cognitive disturbance ($\beta = -.21$, $p < .01$). Individuals more physiologically stable were less affected by post-surgical cognitive disturbance. However, the surgical stress and psychoactive medication used had no significant impact on post-surgical cognitive disturbance.

In summary, the path analysis supports the empirical model partially. These six predictors explained 66% of the total variance in subjects' post-surgical cognitive disturbance. The results support Hypotheses 2, 3, 4, 7, 8, 12, 13,15,16, but not the rest of the seven hypotheses.



Mathematical Equations:

Physical function = (-.45)Age + e

Cognitive function = (.42)Age + e

Physiological stability = (NS)Age + (.32)Physical function + (-.23)Cognitive function + e

Psychoactive medication used = (NS)Age + (NS)Cognitive function + e

Severity of post-surgical cognitive disturbance = (NS)Age + (-.34)Physical function + (.50)Cognitive function + (-.21)Physiological stability + (NS)Surgical stress + (NS)Psychoactive medication used +e

$^*p < .05$. $^{**}p < .01$. $^{***}p < .001$.

----: Non significant path

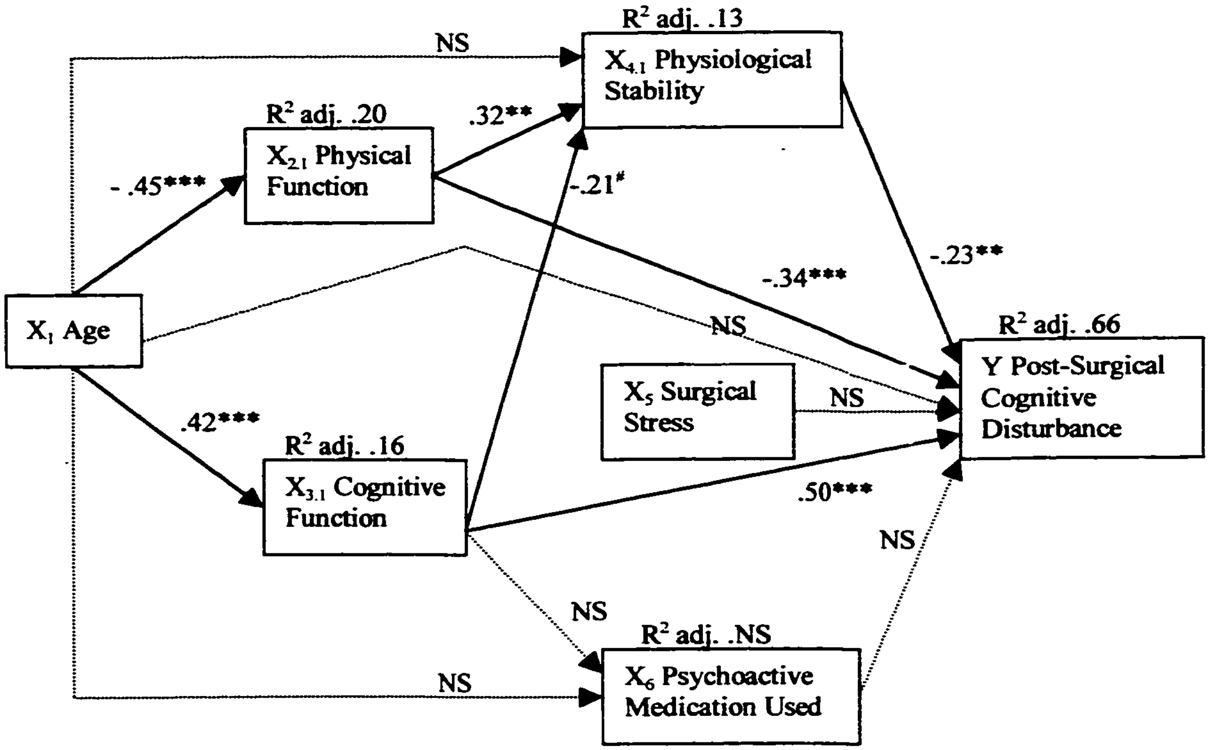
NS: non-significant

Figure 4.2 Standardized Regression (Path) Coefficients for the Original Empirical Model (N=93)

Revised Empirical Model

Two empirical models were tested after the results of the path analysis for the original model. The only change of the revised empirical model was in the items for the variable of physiological stability. In the original empirical model, six items including blood sodium, blood potassium, blood urea nitrogen, blood glucose, body temperature and dehydration index were combined for the variable of physiological stability. For the first revised model, five indicators for physiological stability were used for model testing. Because only two subjects had abnormal blood potassium (Table 4.2), this item was removed from the analysis. The rest of five items combined into a new score for the subject's physiological stability. Figure 4.3 presents the results of the path analysis by using five indicators as physiological stability. These six predictors explained 66% of the total variance in subjects' post-surgical cognitive disturbance. The results were similar to the original empirical model except the path from the cognitive function to physiological stability. The significant level of this path decreases to the .1 level. In this first revised model, the path from the cognitive function to physiological stability was not statistically significant based on the pre-determined .05 level but had a trend level ($\beta = -.21$, $p < .1$) effect on the dependent variable.

The second revised model used the subjects' pre-surgical biochemistry data instead of the most recent available data as indicators for physiological stability. Four indicators for physiological stability were used for model testing. Most of the subjects had normal blood sodium and potassium; these two items were removed from the



Mathematical Equations:
Physical function = (-.45)Age + e
Cognitive function = (.42)Age + e
Physiological stability = (NS)Age + (.32)Physical function + (-.21)Cognitive function + e
Psychoactive medication used = (NS)Age + (NS)Cognitive function + e
Severity of post-surgical cognitive disturbance = (NS)Age + (-.34)Physical function + (.50)Cognitive function + (-.23)Physiological stability + (NS)Surgical stress + (NS)Psychoactive medication used +e
#$p < .1$. **$p < .01$. ***$p < .001$.
----: Non significant path
NS: non-significant

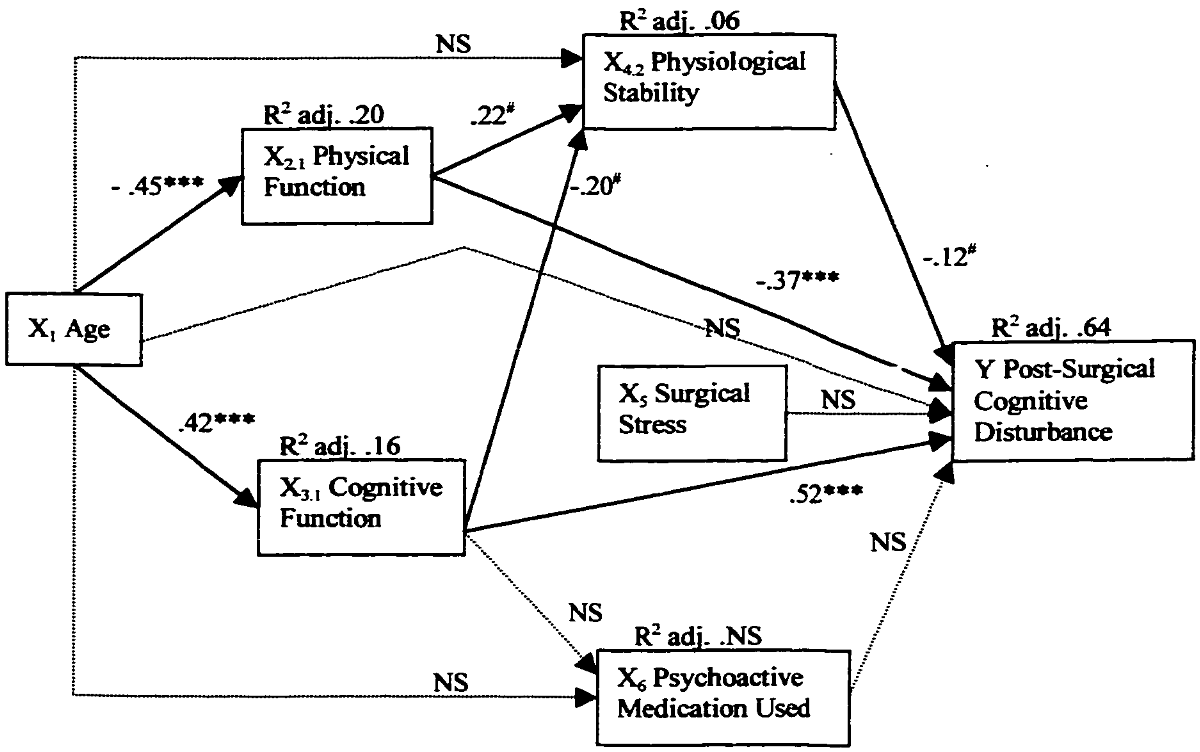
Figure 4.3 Standardized Regression (Path) Coefficients for the Original Empirical Model by Use 5 Indicators for Physiological Stability in the Analysis (N=93)

The rest of four items combined into a new score for the subject's physiological stability. Figure 4.4 presents the results of the path analysis by using four indicators as physiological stability. These six predictors explained 64% of the total variance in subjects' post-surgical cognitive disturbance. The results were similar to the previous two empirical models except the paths from the physical and cognitive function to physiological stability. The significant level decreases to .1 level. Although they were not statistically significant in terms of the pre-determined .05 level, but they have trend levels that affect the dependent variable.

When the insignificant paths were deleted and the regression analysis was run again from the original empirical model, 67.0% of total variance in subjects' post-surgical cognitive disturbance was accounted for in the reduced model (Figure 4.5). Age, physical and cognitive functions at admission, and physiological stability were the four significant predictors for the severity of post-surgical cognitive disturbance. Age had direct effect to physical function and cognitive function. Physical function and cognitive function affected post-surgical cognitive disturbance directly, also indirectly through physiological stability.

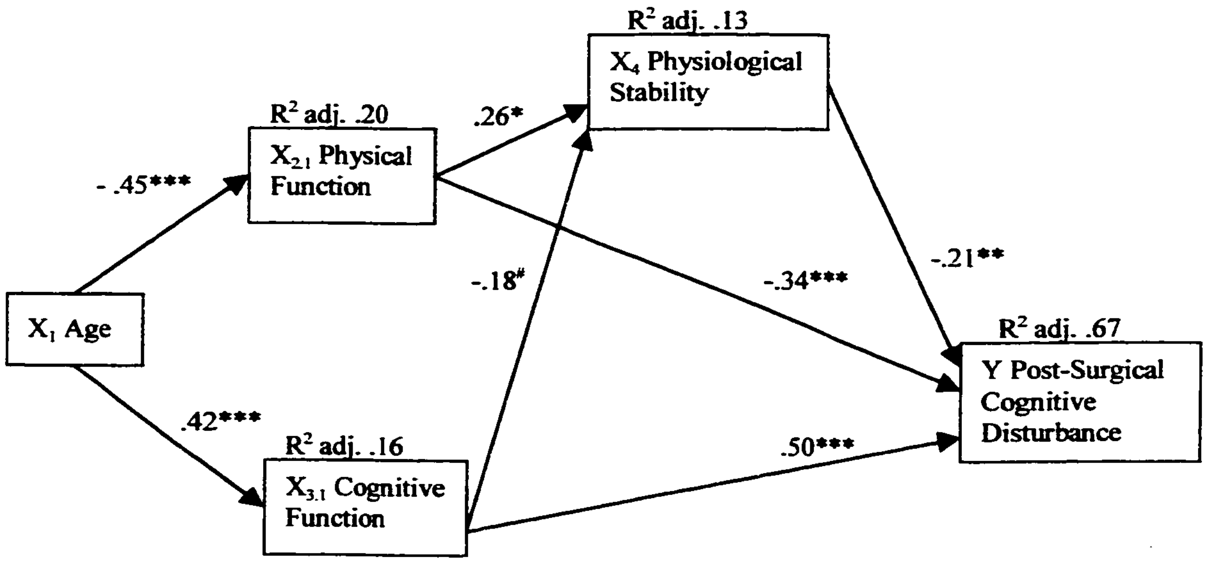
Summary

The empirical model was partially supported by the path analysis and seven out of the 13 paths were supported. Age affects the physical function and cognitive function directly and negatively. Physical function and cognitive function affects the physiological stability directly and positively. They also affect post-surgical cognitive



Mathematical Equations:
Physical function = (-.45)Age + e
Cognitive function = (.42)Age + e
Physiological stability = (NS)Age + (.22)Physical function + (-.20)Cognitive function + e
Psychoactive medication used = (NS)Age + (NS)Cognitive function + e
Severity of post-surgical cognitive disturbance = (NS)Age + (-.37)Physical function + (.52)Cognitive function + (-.12)Physiological stability + (NS)Surgical stress + (NS)Psychoactive medication used +e
#$p < .1$. ***$p < .001$.
----: Non significant path
NS: non-significant

Figure 4.4 Standardized Regression (Path) Coefficients for the Empirical Model by Use Pre-Surgery Biochemistry Data as Indicators for Physiological Stability in the Analysis (N=93)



Mathematical Equations:

Physical function = (-.45)Age + e

Cognitive function = (.42)Age + e

Physiological stability = (.26)Physical function + (-.18)Cognitive function + e

Severity of post-surgical cognitive disturbance = (-.34)Physical function + (.50)Cognitive function + (-.21)Physiological stability +e

#$p < .1$. *$p < .05$. **$p < .01$. ***$p < .001$.

Figure 4.5 Reduced Empirical Model for Predicting Severity of Post-surgical Cognitive Disturbance (N=93) disturbance directly and negatively. These two variables also affect post-surgical cognitive disturbance indirectly and negatively through physiological stability. Physiological stability affects post-surgical cognitive disturbance directly and negatively. A total of 66% of total variance in subjects' post-surgical cognitive disturbance is accounted for in the original empirical model. When testing the model with different numbers of indicators in physiological stability, the total variance explained decreased slightly (66% to 64%) but the patterns of significant paths are similar. When the insignificant paths are removed from the original empirical model, 67% of total variance in subjects' post-surgical cognitive disturbance is accounted for in the reduced model. Age, physical function, cognitive function and physiological stability are the four predictors for predicting the severity of post-surgical cognitive disturbance.

Identifying the Most Efficient Items from the MMSE

To achieve purpose (2) to identify the valid, reliable and efficient items from an existing mental status screening tool (the MMSE) for assessment of mental status in elderly Taiwanese patients, the one-parameter (Rasch model) and two-parameter (Birnbaum model) Item Response Theory (IRT) models were used. The RASCAL program was used to test the one-parameter model. The XCALIBRE program was used to test the two-parameter model. Testing the fit of the data to the IRT model is equivalent to a test of the theoretical construct validity and adequacy of the scale. The data derived from the MMSE was fitted to the IRT one-parameter and two-parameter models, operationalized by the unconditional maximum likelihood approach

(Assessment Systems Corporation, 1995; Baker, 1985; Wright & Stone, 1979). The problematic items were defined if the difficulty level is less than -2.95 or higher than 2.95, or if the discrimination level is less than .three, or if the standardized residual is higher than 1.96. The cutoff point for the reduced MMSE was determined by the item information curve (Assessment Systems Corporation, 1995; Baker, 1985). Three parts are included in this section. The first part presents the result of the preliminary analysis. The second part presents the item response analysis of the MMSE, which includes one parameter (1PL) and two parameter (2PL) model testing. The last part presents the factor analysis for the reduced MMSE items.

Preliminary Analysis

The admission assessment of mental status for the 801 patients was used to identify the most efficient items for cognitive function assessment. There were 801 complete MMSE assessments and the subjects' demographic data in the data file. Among these subjects, 42.6% (341) were male and 57.4% (460) were female. The subjects ranged in age from 65 to 98 with a mean of 72.72 years and standard deviation of 6.29. Twenty-nine percent (232) received urological surgeries and 71% (569) received orthopaedic surgery. The total score of the MMSE ranged from 7 to 30 with a mean of 26.5 and standard deviation of 4.0. Twenty-three percent of subjects (n=181) answered all the questions correctly and had total score of 30. Twenty percent of subjects scored 23 or lower. The internal consistency (KR-20) of the MMSE was .86. Four items (items 14, 19, 20, and 21) had negative inter-item correlation. The correct response rate for each item ranged from 1.00 (items 11-16, items related to registration and language) to .66 (item 30, visual construction). For a correct response of 1.0, this meant that items 11 to 16 were easy items. All of the subjects answered these items correctly. Another six items (items 5, 6, 7, 19, 20, and 21, were items related to orientation to place, and language) had a 98%-99% correct response rate. These were easy items, too. From principal components analysis with Varimax rotation for the 30-item MMSE, nine components were extracted (eigenvalue higher than 1) which explained 72% of the variance (Table C.1 in Appendix C). A scree plot revealed four major components that accounted for 41.4% of total variance. The communalities ranged from .487- .978. Seven items load more than one component. Table 4.5 listed these nine components and their corresponding items and loadings. For the first four major components, Component 1 consisted of four items explaining 13.5% of variance; Component 2 consisted of five items explaining 12.3% of variance; Component 3 consisted of four items explaining 7.9% of variance; Component 4 consisted of three items explaining 7.7% of variance.

Item Response Analysis

The item response analysis was operationalized by the unconditional maximum likelihood approach (Assessment Systems Corporation, 1995; Baker, 1985; Wright & Stone, 1979). There are two conditions, which the maximum likelihood estimation procedures failed to yield an ability estimation. The first one of these conditions is that the subject answers none of the items correctly, the corresponding ability estimate is negative infinity. The second one of these conditions is that the subject answers all the items correctly in the test, the corresponding ability estimate is positive infinity. In the

Table 4.5 Component Matrix of the 30-Item MMSE

Item/ loading	Comp. 1	Comp. 2	Comp. 3	Comp. 4	Comp. 5	Comp. 6	Comp. 7	Comp. 8	Comp. 9
1		0.307			0.442	**0.507**			
2						**0.741**			
3						**0.756**			
4						**0.554**	0.334		
5							**0.826**		
6	0.435						**0.716**		
7			**0.513**				0.384		
8			**0.627**				0.457		
9			**0.817**						
10			**0.782**						
11	**0.979**								
12	**0.979**								
13	**0.979**								
14								**0.931**	
15	0.348							**0.786**	
16	**0.879**								
17					**0.732**				
18					**0.813**				
19				**0.907**					
20				**0.901**					
21				**0.795**					
22									**0.641**
23									**0.745**
24									**0.630**
25		**0.600**							
26		**0.772**							
27		**0.825**							
28		**0.861**							
29		**0.847**							
30		0.319			**0.723**				

Comp.: Component

analysis, subjects who had a zero score or a perfect score were eliminated for further analysis (Baker, 1985).

During item analysis, only one- and two-parameter models were tested because the MMSE asks questions that have exact answers. They were assessed in face to face interviews. The chances for guessing were minimal, so the three-parameter model, which models the items by item difficulty, item discrimination and the level of guessing, was not tested in this analysis. While using ITEMAN to analyze the data, the point biserial correlation ranged from .02-. 73. Four items (items 14, 19, 20, and 21) had point biserials lower than .2 in item-total correlation. The discrimination index ranged from .00- .78. Twelve items (items 5, 6, 7, 11, 12, 13, 14, 15, 16, 19, 20, and 21) had a discrimination index less than .1. When the item-total correlation is near zero, it does not produce a satisfactory statistical criterion for validating an item. When the discrimination function is low, it does not differentiate between the subjects who have intact cognitive function or not. These items were deleted in later analysis. However, since the MMSE is a well-developed and widely used tool, the whole 30 items were used to do further analysis before any deletion of items.

One-Parameter Model

The RASCAL program that centered on difficulty level was used to analyze the one-parameter model. The RASCAL converged after seven loops indicating the average difficulty parameter changed at .0003. Table 4.6 presented the final parameter estimates from these 30 items. For nine degrees of freedom, a chi-square value in excess of approximately 16.92 may indicate a poor fit to the model at the .05 level.

Table 4.6 Final Parameter Estimates of the Initial 1PL Model from the 30-Item MMSE

Item	Difficulty	Std. Error	Chi Sq.	df	Scaled Diff
1	1.849	0.114	18.955	9	2
2	1.062	0.135	22.243	9	1
3	2.362	0.104	25.673	9	2
4	1.062	0.135	20.615	9	1
5	-1.226	0.277	9.002	9	-1
6	-2.045	0.374	4.857	9	-2
7	-1.910	0.356	7.824	9	-2
8	-0.525	0.217	14.794	9	-1
9	0.803	0.144	21.458	9	1
10	0.742	0.147	20.847	9	1
11	-3.545	0.692	0.887	9	-4
12	-3.545	0.692	0.887	9	-4
13	-3.545	0.692	0.887	9	-4
14	-4.249	0.951	0.416	9	-4
15	-3.122	0.577	1.414	9	-3
16	-3.122	0.577	2.786	9	-3
17	2.929	0.098	17.284	9	3
18	1.212	0.130	43.821	9	1
19	-2.572	0.460	93.714	9	-3
20	-2.045	0.374	57.619	9	-2
21	-1.304	0.285	47.862	9	-1
22	2.060	0.109	95.677	9	2
23	2.246	0.106	122.487	9	2
24	2.473	0.103	138.626	9	2
25	0.570	0.154	18.141	9	1
26	2.668	0.100	16.857	9	3
27	2.351	0.105	40.929	9	2
28	2.403	0.104	69.323	9	2
29	2.828	0.099	53.420	9	3
30	3.134	0.096	20.300	9	3

So, from Table 4.6, 19 items had fit problems in this model (items 1-4, 9-10, 17-25, and 27-30) with chi-square values higher than 16.92. Item 14 had a difficulty level of -4.249. It was the easiest item. Although from the previous section, item 14 had a low item-total correlation (.11), it fit the model very well (chi-square value .416). Items 11-13 were the next easiest items but they fit the model well also. These four items (items 11-14) were retained in the next analysis. Ten items showed that they had severe fit problems (items 18, 19, 20, 21, 22, 23, 24, 27, 28, and 29, chi-square values higher than 40) were deleted from the second analysis. The analysis converged after 12 loops. For seven degrees of freedom, a chi-square value in excess of approximately 14.07 indicated a lack of fit to the model at .05 level. Still, six items had chi-square values higher than 14.07. Since too many variables had fit problems in the one-parameter model, it represented that the one-parameter model did not fit the data well.

__Two-Parameter Model__

The XCALIBRE program, which calibrates difficulty level and discrimination function, was used to analyze the two-parameter model (2PL). The starting prior distribution values were set to (a) mean equals 1 and standard deviation equals .12 for discrimination function, and (b) mean equals 0 and standard deviation equals 1 for difficulty level. The analysis converged on loop four when the parameter change was less than .05. The final parameter for discrimination value (a) was 1.34. This means moderate discrimination. The final parameter for difficulty level (b) was -2.05, suggesting the items were easy. From the pre-determined criteria for deleting an item, two items (items 4 and 18) had fit problems for this model because their standardized residuals were higher than 1.96. Eleven items (items 6, 7, 11, 12, 13, 14, 15, 16, 19, 20, and 21) were potential problematic items (indicated "P" in Table C.2 in Appendix C). They had high discrimination functions but were very easy items. Their difficulty levels were less than -2.95 (b< -2.95). This suggests that most of the subjects scored these items correctly. They provided little variation in the analysis.

All the problematic items (11 items), the two revised items and item 5 (PC= .98, b= -2.9) were deleted from the second analysis. Sixteen items remained in the second analysis. The analysis converged on loop three when the parameter change was less than .05. The final parameter values for discrimination value (a) was 1.37. This suggests high discrimination. The final parameter for difficulty level (b) was -1.33, suggesting the items were moderately easy (Baker, 1985). Table 4.7 presented the final parameter estimates for the final 2PL model. All the standardized residuals for these 16 items were less than 1.96. This indicates that the model fits the data very well. The correct response rates ranged from 66% to 97%. The item-total correlation ranged from .28 (item 23) to .77 (item 29).

The test characteristic curve and the test information curve of the 16-item MMSE for the two-parameter model were presented in Figures 4.6 and 4.7. The test characteristic curve is a graphic depiction of the estimated proportion of correct scores for subjects of varying levels of the latent trait. This curve can be used to evaluate the probability of correct response at each ability level. From Figure 4.6, the final test characteristic curve was a smooth curve. The final test characteristic curve suggests

Table 4.7 Final Parameter Estimates of the Final 2PL Model from the 16-Item MMSE

Item Lnk Flg	a	b	c	Resid	PC	PBs	PBt
1	1.54	-1.21	0.00	1.25	0.82	0.66	0.61
2	1.53	-1.65	0.00	1.51	0.89	0.63	0.54
3	1.02	-1.11	0.00	1.84	0.76	0.54	0.52
4-7 -- Deleted --							
8	1.59	-2.45	0.00	0.36	0.97	0.50	0.42
9	1.47	-1.80	0.00	1.74	0.91	0.59	0.51
10	1.62	-1.80	0.00	1.27	0.91	0.61	0.53
11-16 -- Deleted --							
17	1.03	-0.74	0.00	0.92	0.69	0.56	0.58
18-21 -- Deleted --							
22	0.61	-1.79	0.00	1.69	0.80	0.35	0.29
23	0.56	-1.69	0.00	1.67	0.78	0.33	0.28
24	0.55	-1.51	0.00	1.53	0.75	0.33	0.29
25	1.56	-1.90	0.00	1.01	0.92	0.58	0.51
26	1.79	-0.74	0.00	0.80	0.73	0.69	0.71
27	1.88	-0.90	0.00	0.71	0.77	0.74	0.73
28	2.01	-0.86	0.00	1.55	0.76	0.79	0.76
29	1.93	-0.64	0.00	1.26	0.70	0.76	0.77
30	1.20	-0.56	0.00	0.94	0.66	0.61	0.63

a: discrimination parameter

b: difficulty parameter

c: guessing parameter

Resid: standardized residual

PC: probability of correct

PBs: point biserial correlation

```
   1.00 I                                         ****************
        I                                ********* 
        I                             ***
        I                           **
        I                         **
E       I                          *
s       I                         *
t       I                        *
i       I                       *
m       I
a 0.75  I                         *
t       I                     *
e       I
d       I                     *
        I                   *
P       I
r       I                   *
o       I                  *
p       I
o       I                 *
r 0.50  I                   *
t       I
i       I               *
o       I               *
n       I
        I             *
C       I              *
o       I
r       I            *
r       I           *
e 0.25  I              *
c       I          *
t       I        *
        I       *
        I      *
        I    **
        I  **
        I**
        I------------------------------------------------------------------------------------
       -3.0     -2.0     -1.0      0.0      1.0      2.0      3.0
                                        ability
```

Figure 4.6 Test Characteristic Curve of the 2PL Model from the 16-Item MMSE

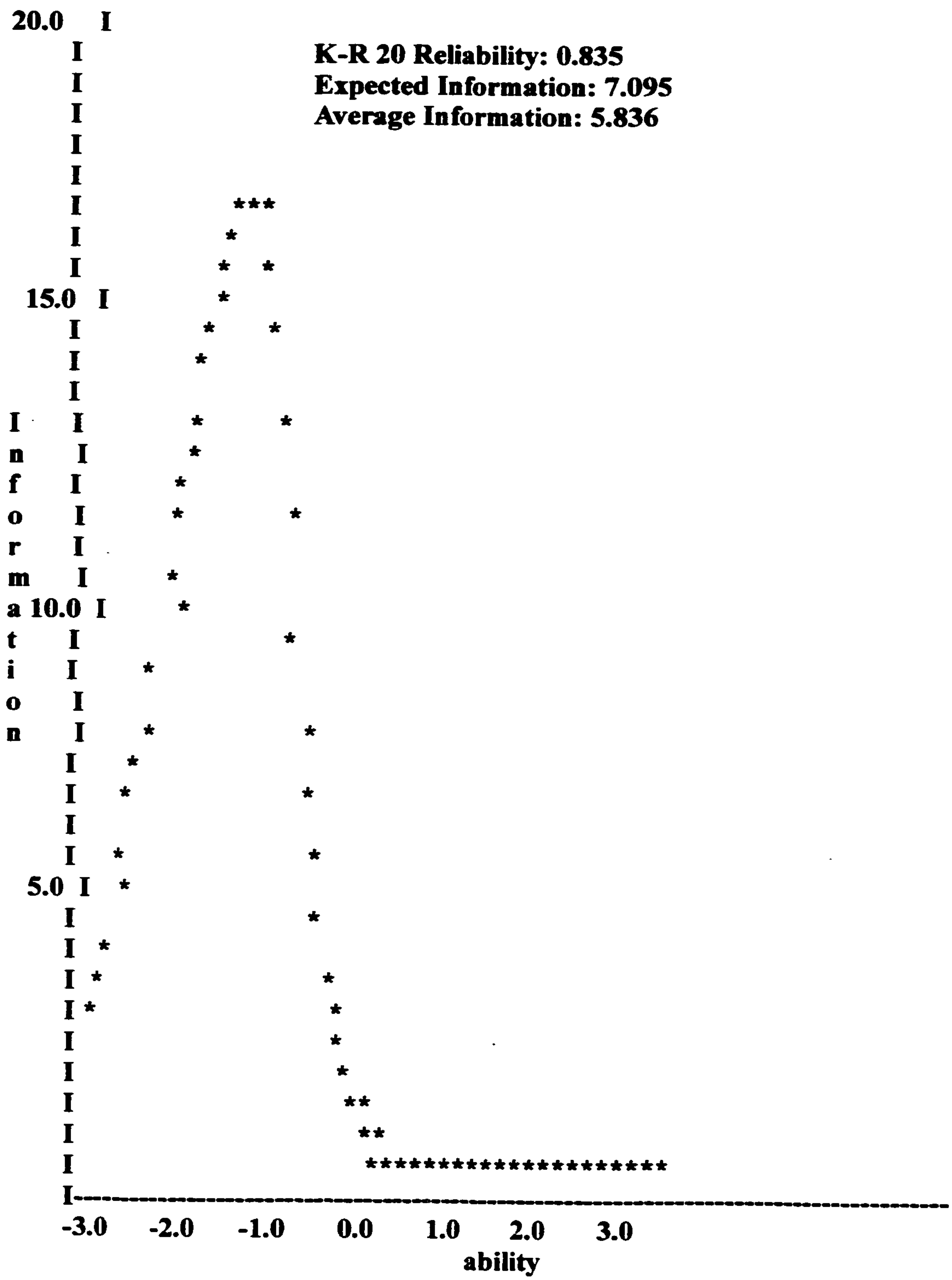


Figure 4.7 Test Information Curve of the 2PL Model from the 16-Item MMSE

that these items were easy items. At the ability level of (θ) = -1, the proportion of correct was .5. With an ability (θ) = 0, the proportion of correct responses increased to .90.

The test information curve is a visual display of test effectiveness at different levels of the latent trait. The information is the reciprocal of the precision with which a parameter can be estimated. It presents how well the test estimates ability over the whole range of the ability scores. The amount of information at a given ability level is the reciprocal of its variance. If the amount of information is large, it means that the subject's true ability at that level can be estimated with precision (Baker, 1985).

The maximum of the information occurred at an ability level corresponding to the value of the difficulty parameter. From Figure 4.7, the final test information curve peaked at ability (θ) = 0 ~ -1 and was above 10 for the ability range of $-2 <= \theta <= 0$. Within this range, ability is estimated with some precision. Outside this range the amount of information decreased rapidly and the corresponding ability levels were not estimated very well. Thus, the ability was estimated with some precision near the center of the ability scale. The cutoff point of the 16-item MMSE came from the item information curve. The information curve of the 16-item MMSE is not similar to an ideal curve. In a general-purpose test, the ideal information curve would be a horizontal line at some large value of information and all ability levels would be estimated with the same precision. But, it may not be the best for specific purpose (Baker, 1985). The shape of the desired test information curve depends on the purpose of the test. If we were to separate two groups, then the ideal one (horizontal line) may not be proper in this situation. On the contrary, the peaked information function is preferred to measure ability with considerable precision at levels used to separate these two groups. In this case, the best test information curve, like the test information curve for the 16-item MMSE, would have a peak at the cutoff score (Baker, 1985). When the final parameters of the16 items were used to calculate the information provided at different ability levels, the results showed that maximal information was provided when θ was set to -1 (Table C.3 in Appendix C). Outside this ability level, the amount of information decreased rapidly. From the test information curve (Fig. 4.7), the curve peaked at θ = -1 on the ability level. From the curve, the maximal amount of information provided is 16.5 at the ability level of -1. The standard error of estimate is .25 (SEM = $1/(16.5)^{1/2}$). This suggests 68% of the estimates of this ability level fall between -1.25 (-1 -0.25) and -.75 (-1 + 0.75). With a small range for this estimation for the final 16-item MMSE, it represents that the ability level is estimated with a moderate to high amount of precision. The internal consistency of the 16-item MMSE was .84. Compared to the original 30-item MMSE, when the items decreased, the value of internal consistency did not decrease much (.86 to .84). This suggests that the test was reliable.

The expected score for subjects with ability (θ) = -1 was 9.28 for the 16-item MMSE (Table C.4, Appendix C). Two by two tables were used to measure the agreement between the score on the 30-item MMSE at cutoff point 23/24 versus 9/10 and 10/11 for the 16-item MMSE. When a score of 10 was used as the cutoff point for the 16-item MMSE, 660 subjects had scores equal or higher than 10 and 141 subjects scored lower than 10. When comparing this result with the original assessment of the 30-item MMSE from the cutoff point of 24, 15 subjects were misclassified. The correct classification rate (measurement agreement, Kappa) was .938. When using 11 as the cutoff point, 17 subjects were misclassified. The correct classification rate (measurement agreement, Kappa) was .935. (Table 4.8). They were all statistically significant at the $p < .001$ level. Differences in sensitivity and specificity for these two cutoff points were also examined by employing the definition from Haynes (1981) and Fields, Fulop, Sachs, Strain, and Fillit (1991). The sensitivity is defined as the fraction of time a test makes a diagnosis when the disorder is present. It also equals to the fraction of the true positives to the sum of true positives and false negatives. When using 10 as the cutoff point, the sensitivity of the 16-item MMSE was 90.4% (141/(141+15)). When using 11 as the cutoff point, the sensitivity was 100% (156/(156+0)). The specificity is defined as the fraction of time a test makes a negative diagnosis when the disorder is absent. It also equals the fraction of true negatives to the sum of true negatives and the false positives. When using 10 as the cutoff point, the specificity was 100% (645/(645+0)) When using 11 as the cutoff point, the specificity was 97.4% (628/(628+17)).

Factor Analysis of the 16-Item MMSE

The total scores of the 16-item MMSE were significantly correlated with the total scores of the 30-itme MMSE at the .01 level (correlation coefficient $r = .98$). From the principal component analysis with Varimax rotation of the 16-item MMSE, four components were extracted (eigenvalue higher than 1) which explained 62.9% of the

Table 4.8 <u>The Correct Classification Rate of the 16-item MMSE with a Cutoff Point of 10 and 11 Compare to Original Cutoff Point of 24 (N=801)</u>

	Score <10	Score ≥10	Total	Score <11	Score ≥11	Total
Score < 24	141	15	156	156	0	156
Score ≥ 24	0	645	645	17	628	645
Total	141	660	801	173	628	801
Kappa	.938 $p < .001$			.935 $p < .001$		

variance (Table C.5 in Appendix C). The communalities ranged from .457- .821. With a cutoff point of .3 for inclusion of a variable in interpretation of a component, four items in this solution were complex and could be located in two components. Table 4.9 presented these four components and their correspondent items and loadings. Component 1 consisted of five items explaining 22.3% of the total variance. These five items are related to attention and calculation. Component 2 consisted of three items explaining 16.0% of the total variance. These three items are related to orientation to place. Component 3 consisted of five items explaining 15.1% of the total variance. These five items are related to orientation to time, language, and visual construction. Component 4 consisted of three items explaining 9.5% of the total variance. These three items are related to recall items. Table 4.10 showed the final retaining questions in the 16-item MMSE and its corresponding factor.

Summary

The RASCAL program, which generated difficulty levels to analyze the 1-parameter model, converged after seven loops. However, the chi-square values indicated the one-parameter model did not fit the data well for both the 30-item MMSE and the 16-item MMSE. The two-parameter model, which generated difficulty level and discrimination function, fits the data better. As a result of the item analysis, 14 items were deleted from the original 30-item MMSE. The remaining 16 items included measures of orientation, language, recall, attention and calculation, and visual construction that were located in four factors. These four factors explained 62.9% of

Table 4.9 Component Matrix of the 16-item MMSE

Item/loading	Component 1	Component 2	Component 3	Component 4
1			**.666**	
2		.474	**.596**	
3			**.657**	
17	.306		**.708**	
30	.434		**.514**	
8		**.743**		
9		**.825**		
10		**.820**		
22				**.692**
23				**.761**
24				**.577**
25	**.585**	.407		
26	**.745**			
27	**.826**			
28	**.853**			
29	**.842**			

Table 4.10 The Final Retaining Questions in the 16-Item MMSE

Original Item #	Factor	Maximal Score	Questions
			ORIENTATION TO TIME
1,2,3	III	(3)	What is the (year) (month) (date)?
			LANGUAGE
17	III	(1)	Read and obey the following: "Close your eyes.: (1 point)
			VISUAL CONSTRUCTION
30	III	(1)	Copy design (overlapping pentagons, 1 point)
			ORIENTATION TO PLACE
8-10	II	(3)	Where are we: (floor) (room) (bed)?
			RECALL*
22-24	IV	(3)	Ask for 3 objects repeated above. Give 1 point for each correct.
			ATTENTION AND CALCULATION
25-29	I	(5)	Serial 7s. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.
TOTAL		**(16)**	
			ORIENTATION TO TIME
4, 5	delete		What is the (day) (season)?
			ORIENTATION TO PLACE
6, 7	delete		Where are we: (town) (hospital)?
			REGISTRATION
11-13	delete		Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until the patient learns all 3. Count trials and record.
			LANGUAGE
14-15	delete		Name a pencil, and watch (2 points)
16	delete		Repeat the following "No ifs, ands, or buts.: (1 point)
18	delete		Write a sentence (1 point)
19-21	delete		Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor." (3 points)

* The questions about asking for naming 3 objects have been deleted.

the total variance. The total scores of the 16-item MMSE were significantly correlated with the total scores of the 30-itme MMSE. The internal consistency (KR-20) of the analysis is .86 and .84 for the 30-item and 16-item MMSE, respectively. Table 4.11 summarizes the information of the original 30-item MMSE and final 16-item MMSE for the 2PL model item response analysis.

Variations of Cognitive/Behavioral Changes during the Course of Delirium

To achieve purpose (3) to describe variations of cognitive/behavioral changes in general and in selected cognitive dimensions during the course of delirium, four assessments of mental status by the MMSE were used to understand the cognitive/behavioral changes among post-surgical elderly patients. The four assessments included admission assessment, onset of delirium, the third day of delirium, and the fifth day of delirium for delirious patients, as well as admission assessment, post surgical day one, day three and day five for non-delirious patients. Two parts are included in this section. The first part presents the description analysis of the subjects and their four scores of the MMSE. The second part presents the comparison of the cognitive/behavioral differences among patients who developed post-surgical delirium and those who did not.

Description of the Subjects and Their Cognitive Function

Univariate analysis on demographic variables of the 106 subjects showed the age ranged from 65-93 years with a mean of 73.9 and standard deviation (SD) of 6.5. The number of male and female subjects was almost equal (50.9% vs.49.1%). The majority of the subjects (79.2%) was literate. The average number of years of education was

Table 4.11 Summary Information of the Original and Final Test Information for the 2PL Model for the MMSE

	Original 30-item MMSE	**Final 16-item MMSE**
Item Number	30	16
KR-20 Reliability	.86	.84
Factors Extracted	9	4
Variance Explained	72.3%	62.9%
Cutoff Point	24	11
Discrimination Parameter(a)	1.34	1.37
Range of a	.56 -- 2.01	.55 -- 2.01
Standard Error of a	.063 -- .139	.063 -- .107
Difficulty Parameter(b)	-2.05	-1.33
Range of b	-.57--3.00	-.56--2.45
Standard Error of b	.037 -- .167	.038 -- .099
Probability of Correct Response	.66 --1.00	.66 -- .97
Item-Total Correlation	.03 -- .75	.28 -- .77
Standardized Residual	.44 -- 2.13	.36 -- 1.84

7.2 years (SD = 5.2). Most of the subjects (81.2%) had family members or hired attendants accompanying them 24 hours a day during the hospital stay. Most of the subjects (78.3%) received orthopaedic surgery. In these 106 subjects, 41 had delirium, 65 did not during the post-surgical period. For the four time points, the numbers for the delirious group maintain the same (N=41), except one missing on Time 4. For the non-delirious group, the number decreased suddenly from Time 3 to Time 4 (60 to 44). More subjects in this group were discharged and no data were available for the fourth assessment.

When inspecting the data set, there were 106 complete data sets for Time 1, 102 for Time 2, 101 for Time 3 and 84 for Time 4. The correct response rate for each item of the MMSE for the total group, the non-delirious group, and the delirious group were presented in Table D.1, D.2, and D.3 in Appendix D. For the total group, the items in orientation to place, registration and language were easy items. Subjects scored more than 90% correct to these items. In non-delirious subjects, the correct response rate did not change much across the four time points. Thirteen out of the 30 items had 100% correct response rate for the first assessment. Every subject answered these items correctly. On the contrary, the correct response rate decreased in every item of the MMSE for delirious subjects from the first assessment (admission assessment, Time 1) to the second assessment (assessment on onset of delirium, Time 2), then the rates gradually increased for Time 3 and Time 4. Items in the registration subscale and some items in the language subscale received the highest correct response rate. Subjects scored 98% or higher correct response rate for Time 1. Items related to calculation and visual construction had the lowest correct response rate across the four time points. The rates ranged from 40% to 48% in most of the items.

Table 4.12 showed the descriptive analysis of the four assessments of the total score and seven subscores of the MMSE among the total group, the delirious group and the non-delirious group. All the total scores and subscores for the non-delirious group were higher than the delirious group. For the total subjects, the mean MMSE score for Time 1 is 25.70 (SD = 5.11). The score decreased slightly (22.13 ± 9.26) for Time 2, than gradually increased for Time 3 and Time 4 but did not return to the same level as Time 1. This pattern was the same in the total score and in the seven subscores of the MMSE. The graph of this change was presented Figure D.10 in Appendix D. For the non-delirious group, the scores slightly changed over the four assessments. To graph the change of the subscores of the MMSE there was almost no change during the four times points except the subscale orientation to time which slightly decreased for Time 2 and Time 3 (Figure D.11 in Appendix D). For the delirious group, all the scores were lower than the non-delirious group. The graph of the changes for the seven subscales of the MMSE across these four assessments was presented in Figure 4.8. From the graph, the subscores from Time 1 to Time 2 made the largest change in every subscale of the MMSE. The scores decreased suddenly from Time 1 to Time 2, then, every subscale gradually increased at Time 3 and Time 4, but did not return to the same level as Time 1.

Table 4.12 Descriptive Analysis of the Four Assessments of the Total Score and Seven Subscores of the MMSE among the Total Group, Delirious Group, and Non-Delirious Group

Dimension	Number of Items	Time 1 Mean ± SD	Time 2 Mean ± SD	Time 3 Mean ± SD	Time 4 Mean ± SD
Total Group		**(N = 106)**	**(N = 102)**	**(N = 101)**	**(N = 84)**
Total score	30	25.70 ± 5.11	22.13 ± 9.26	24.20 ± 7.22	24.84 ± 6.24
Orientation to time	5	3.99 ± 1.46	3.16 ± 1.84	3.39 ± 1.73	3.56 ± 1.64
Orientation to place	5	4.70 ± 0.92	3.92 ± 1.77	4.41 ± 1.31	4.46 ± 1.16
Registration	3	2.97 ± 0.29	2.56 ± 1.07	2.79 ± 0.77	2.95 ± 0.34
Language	8	7.49 ± 0.86	6.71 ± 2.18	7.21 ± 1.56	7.35 ± 1.26
Recall	3	2.28 ± 0.95	2.04 ± 1.23	2.34 ± 1.02	2.43 ± 0.96
Calculation	5	3.60 ± 1.88	3.19 ± 2.14	3.47 ± 2.00	3.52 ± 2.05
Visual construction	1	0.69 ± 0.47	0.56 ± 0.50	0.60 ± 0.49	0.60 ± 0.49
Delirious Group		**(N = 41)**	**(N = 41)**	**(N = 41)**	**(N = 40)**
Total score	30	22.13 ± 5.99	13.63 ± 8.96	18.56 ± 8.02	20.88 ± 6.63
Orientation to time	5	3.08 ± 1.83	1.51 ± 1.55	2.02 ± 1.68	2.43 ± 1.60
Orientation to place	5	4.30 ± 1.36	2.46 ± 1.98	3.63 ± 1.73	3.95 ± 1.45
Registration	3	2.93 ± 0.47	1.90 ± 1.46	2.49 ± 1.14	2.90 ± 0.50
Language	8	7.00 ± 1.06	5.10 ± 2.68	6.34 ± 2.10	6.83 ± 1.59
Recall	3	1.88 ± 1.11	1.05 ± 1.24	1.68 ± 1.21	2.05 ± 1.11
Calculation	5	2.50 ± 2.15	1.41 ± 1.97	2.07 ± 2.10	2.38 ± 2.23
Visual construction	1	0.45 ± 0.50	0.20 ± 0.40	0.32 ± 0.47	0.35 ± 0.48
Non-Delirious Group		**(N = 65)**	**(N = 61)**	**(N = 60)**	**(N = 44)**
Total score	30	27.91 ± 2.77	27.84 ± 2.89	28.05 ± 2.76	28.41 ± 2.75
Orientation to time	5	4.55 ± 0.75	4.26 ± 1.00	4.32 ± 1.00	4.59 ± 0.76
Orientation to place	5	4.94 ± 0.30	4.90 ± 0.47	4.93 ± 0.41	4.93 ± 0.45
Registration	3	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00	3.00 ± 0.00
Language	8	7.78 ± 0.52	7.79 ± 0.52	7.80 ± 0.51	7.82 ± 0.54
Recall	3	2.52 ± 0.73	2.70 ± 0.61	2.78 ± 0.52	2.77 ± 0.64
Calculation	5	4.28 ± 1.30	4.38 ± 1.23	4.42 ± 1.23	4.58 ± 1.10
Visual construction	1	0.83 ± 0.38	0.80 ± 0.40	0.80 ± 0.40	0.84 ± 0.37

SD: standard deviation

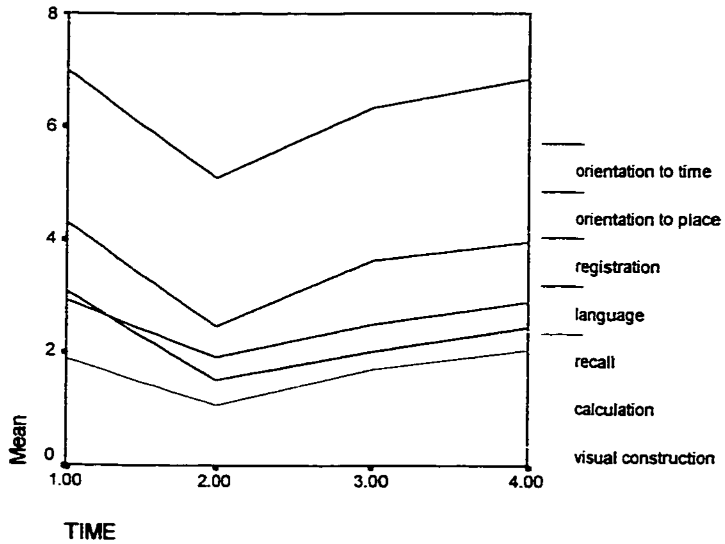


Figure 4.8 The Changes of the Subscores of the MMSE Overtime for Delirious Subjects.

Comparison of the Neurocognitive and Behavioral Differences

Repeated measure analysis of variance (ANOVA) was used to compare the four measures of the MMSE and its subscores. With repeated measures, the basic assumption about normal distribution of the dependent variables and the homogeneity of variance requirement should be met. There must be a correlation between the measures because they are from the same population. Table 4.13 listed the bivariate correlation of these four measures of the MMSE. These four measures were highly correlated to each other. The correlation coefficients ranged from .72 to .91. They were all significant at $p < .01$ level. For the assumption of the equal variance across measurement, the compound symmetry requirement must be met. If this is not met, the degree of freedom must be adjusted in the univariate approach to decrease the type I error rate. During the analysis process, while the variable had significant Mauchly's W (test for sphericity), meant the sphericity was not assumed. Then, the Greenhouse-Geisser Epsilon was used to adjust the degree of freedom. The epsilon was multiplied with the degree of freedom to get the new degree of freedom. The new degrees of freedom were used to test the F value while the assumption of sphericity was not assumed. It is a more conservative way to look at the result when the sphericity assumption is not assumed (Munro, 2001).

Two repeated measures ANOVA were run for the four assessments of the total MMSE score. The first one had one between-subjects factor, *delirium*, with two levels (with delirium and without delirium), and one within-subjects factor, *time*, with four levels representing four different time points of measurement. Forty subjects were in

Table 4.13 Bivariate Correlation of the Four Assessments of the Total MMSE Score

	Time 1 MMSE	Time 2 MMSE	Time 3 MMSE	Time 4 MMSE
Time 1 MMSE	1.00 (N=106)			
Time 2 MMSE	.718** (N=102)	1.00 (N=102)		
Time 3 MMSE	.782** (N=101)	.783** (N=101)	1.00 (N=101)	
Time 4 MMSE	.910** (N=84)	.743** (N=84)	.872** (N=84)	1.00 (N=84)

**$p < .01$.

the delirious group and 44 subjects were in the non-delirious group. There were significant differences between scores of the MMSE and its subscores at these four time points ($p < .01$). Table 4.14 presented the mean squares and F values for these four assessments of the total scores and the subscores. There were also significant differences between scores of the total MMSE and its subscores between the delirious and non-delirious groups ($p < .01$). The non-delirious group had higher mean total scores of the MMSE and for every subscore than the delirious group. Pairwise comparisons showed the scores for Time 1 and Time 2 were significantly different for the total MMSE score and for every subscore of the MMSE. Scores for Time 1 and Time 3 had significantly different in the total score, and three subscores of the MMSE. Scores for Time 2 and Time 3 had significantly different in the total score and six subscores of the MMSE. Scores for Time 2 and Time 4 had significantly different in the total score and every subscore of the MMSE. These were the major differences for the MMSE total score and subscores among the four time points for these 94 subjects.

Table 4.14 Comparison of the MMSE Total Scores and Subscores Overtime for Total Subjects.

Dimensions of the MMSE	Source	Mean Square	F	Significant Level (p)	Pairwise Comparison
Total Subjects					
Total MMSE score	Within Group	447.15	75.55	0.00**	T1, T2**, T1, T3* T2, T3**, T2, T4** T3, T4*
	Between Group	6663.3	75.88	0.00**	
Orientation to time	Within Group	11.58	16.74	0.00**	T1, T2**, T1, T3* T1, T4*, T2, T4**
	Between Group	398.26	77.18	0.00**	
Orientation to place	Within Group	19.71	17.22	0.00**	T1, T2**, T2, T3** T2, T4**
	Between Group	126.49	41.27	0.00**	
Registration	Within Group	8.07	13.44	0.00**	T1, T2**, T2, T3* T2, T4**
	Between Group	13.92	19.70	0.00**	
Language	Within Group	25.30	12.97	0.00**	T1, T2**, T2, T3** T2, T4**
	Between Group	165.77	43.48	0.00**	
Recall	Within Group	5.58	10.60	0.00**	T1, T2*, T2, T3* T2, T4**
	Between Group	75.03	34.05	0.00**	
Calculation	Within Group	6.34	8.16	0.00**	T1, T2**, T2, T3* T2, T4**
	Between Group	427.19	42.94	0.00**	
Visual construction	Within Group	0.32	8.06	0.00**	T1, T2*, T1, T3* T2, T3**, T2, T4**
	Between Group	21.25	34.22	0.00**	

*p < .05, **p< .01.

To look at the changes for these two group, a second repeated ANOVA was run on the four scores of the MMSE and its subscores for the delirious and the non-delirious groups. There were four within-subjects factors representing four time points of assessment. No between-subjects factor was in this analysis. Table 4.15 presented the mean squares and F values for these four assessments, both for the total MMSE scores and subscores. For the non-delirious group, the total score and the subscores were not statistically significant across these four time points except the recall subscale. The major difference came from Time 1 and Time 3 ($p < .05$). From Table 4.12, the mean score of the recall subscale for Time 3 (2.78 ± .52) was significantly higher than for Time 1 (2.52 ± .73).

For the delirious group, the total scores of the MMSE and its seven subscales were all significantly different across these four time points. The results revealed that the subjects had a significant decrease in their total scores of the MMSE and its subscores over the course of their hospital stays. Besides the calculation subscale, which was significantly different at the $p < .05$ level, the other subscales were all significantly different at the $p < .01$ level. All of the total scores and subscores decreased suddenly for Time 2 (onset of delirium), then gradually increased at the following two assessments but did not return to the level for Time 1. Pairwise comparison was used to understand the major sources of differences among these four time points. The results were presented in Table 4.15. Scores for Time 1 and Time 2 had significantly different in the total score and in every subscores of the MMSE for the delirious group. Scores

Table 4.15 Comparison of the MMSE Total Scores and Subscores for the Delirious Group and Non-Delirious Group.

Dimensions of the MMSE	Mean Square	F	Significant Level (p)	Pairwise Comparison
Delirious Group				
Total MMSE score	841.5	23.97	0.00**	T1, T2**, T1, T3* T2, T3**, T2, T4**
Orientation to time	17.67	14.59	0.00**	T1, T2**, T1, T3** T1, T4**, T2, T4*
Orientation to place	35.02	14.77	0.00**	T1, T2**, T2, T3**, T2, T4**
Registration	15.23	11.89	0.00**	T1, T2**, T2, T4**
Language	47.04	11.29	0.00**	T1, T2**, T2, T3* T2, T4**
Recall	8.74	9.52	0.00**	T1, T2**, T2, T3* T2, T4**
Calculation	8.36	3.87	0.02*	T1, T2**
Visual construction	0.52	6.91	0.00**	T1, T2**
Non-Delirious Group				
Total MMSE score	2.83	2.04	0.11	
Orientation to time	0.57	2.32	0.08	
Orientation to place	0.04	0.82	0.45	
Registration	0.00	--	--	
Language	0.01	0.66	0.58	
Recall	1.22	5.30	0.00**	T1, T3*
Calculation	0.79	2.57	0.07	
Visual construction	0.02	1.00	0.40	

--: all subjects had full score, no variance in that variable

*p < .05, **p < .01.

for Time 1 and Time 3 had significantly different in the total score and 1 subscore of the MMSE. Scores for Time 2 and Time 3 had significantly different in the total score and four subscores of the MMSE. Scores for Time 2 and Time 4 had significantly different in the total score and five subscores of the MMSE. These were the major differences for the 40 delirious subjects across these four time points. Scores were all significant at the $p < .01$ level.

To compare the correct response rate among the seven subscales of the MMSE, the scores in each subscale were summed and divided by their item numbers to get the correct response rates. Table 4.16 presented the correct response rates in each subscale of the MMSE among these four time points for the delirious group and the non-delirious group. For the non-delirious group, the correct response rates for the total scale and the seven subscales maintained similar over the four assessments. For the delirious group, the rates changed over the four assessments. For Time 1 (admission assessment), the correct response rates ranged from 98% (registration) to 45% (visual construction). For Time 2 (onset of delirium), the correct response rates ranged from 64% (language) to 20% (visual construction). For Time 3 (delirium day three), the correct response rates ranged from 83% (registration) to 32% (visual construction). For Time 4 (delirium day five), the correct response rates ranged from 97% (registration) to 35% (visual construction). Figure 4.9 shows the changes of the correct response rates in the seven subscales of the MMSE across the four assessments for the delirious group. From the figure, the subscales orientation to time, orientation to place, registration and recall had the largest correct response rates changes from Time 1 to Time 2. For Time 4

Table 4.16 Correct Response Rate in each Subscale of the MMSE among Four Assessments for the Delirious Group and Non-Delirious Group.

Group and Subscales	Time 1 %	Time 2 %	Time 3 %	Time 4 %
Delirious Group	**N=41**	**N=41**	**N=41**	**N=40**
Total MMSE score	74	45	62	70
Orientation to time	62	30	40	49
Orientation to place	86	49	73	79
Registration	98	63	83	97
Language	88	64	79	85
Recall	63	35	56	68
Calculation	50	28	41	48
Visual construction	45	20	32	35
Non-Delirious Group	**N=65**	**N=61**	**N=60**	**N=44**
Total MMSE score	93	93	94	95
Orientation to time	91	85	86	92
Orientation to place	99	98	99	99
Registration	100	100	100	100
Language	97	97	98	98
Recall	84	90	93	93
Calculation	86	88	88	92
Visual construction	83	80	80	84

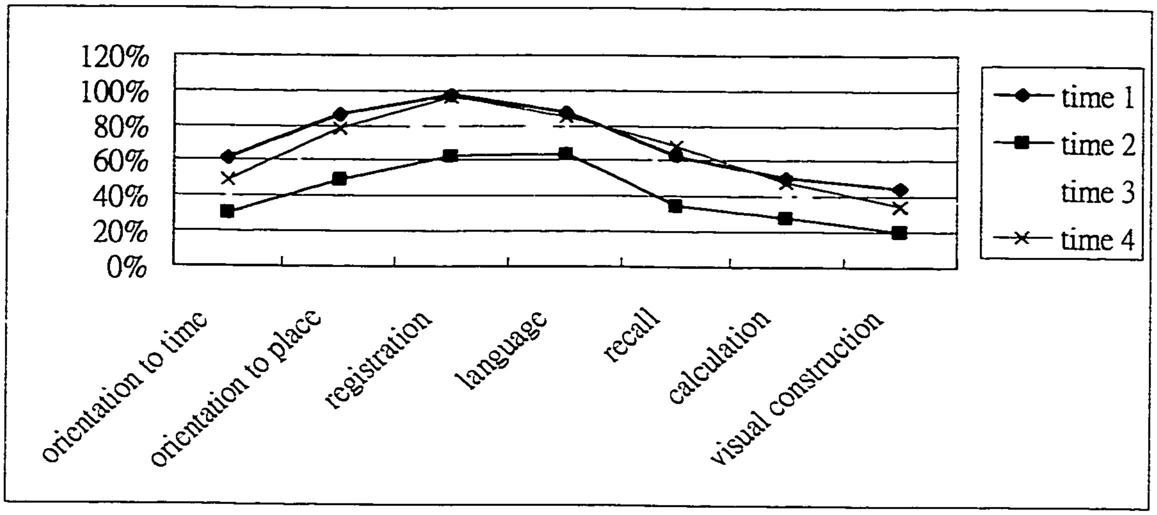


Figure 4.9 The Changes of the Correct Response Rate in Subscales of the MMSE Overtime for the Delirious Group.

assessment, five out of the seven subscales' correct response rates returned near the Time 1 level, except the orientation to time and orientation to place subscales.

Summary

One hundred and six subjects assessed four times by the MMSE were included in the analysis to understand the neurocognitive/behavior change during the course of delirium. Repeated measure ANOVA was used to analyze the within-subjects difference across these four time points and between-subjects differences between the delirious and the non-delirious groups. The results showed that the scores on delirious group and non-delirious group had significant differences with each other ($p < .01$). The scores on delirious group also had significant difference across these four assessments ($p < .01$) within the group. The subscales of orientation to time, orientation to place, registration and recall were the major changes from Time 1 (admission assessment) to Time 2 (onset of delirium) for the delirious subjects. When compared the scores for Time 4 to Time 1, the subscales of orientation to time and orientation to place had the least improvement among other subscales at Time 4.

Summary of Results

Three result sections were presented in this chapter. The first part was related to testing a theoretical model about post-surgical cognitive disturbance. Through path analysis, four major variables were retained in the final reduced model. They were age, physical function, cognitive function and physiological stability. These predicting variables accounted for 67% of the variance in post-surgical cognitive disturbance. The second part identified the most efficient items of the MMSE. Using the two-parameter item response theory model, the 30 items on the MMSE were reduced to 16 items. These 16 items were located in four factors that accounted for 63% of the total variance. The third part was related to neurocognitive/behavior change during the course of delirium. The delirious group had significantly lower scores than the non-delirious group. The scores for the delirious group also differed significantly across these four assessments ($p < .01$). The subscales of orientation to time, orientation to place, registration, and recall were the major changes from Time 1 (admission assessment) to Time 2 (onset of delirium) for the delirious subjects.

CHAPTER V

INTERPRETATION OF FINDINGS AND DISCUSSION

This chapter includes six parts: interpretation of findings according to the three research purposes, theoretical and methodological issues, implications for nursing, and strengths and limitations of this study.

Testing a Model of Post-Surgical Cognitive Disturbance

As hypothesized, the subjects' physical function and cognitive function had direct effects on post-surgical cognitive disturbance. Physical function and cognitive function also had indirect effects on post-surgical cognitive disturbance through physiological stability. These findings are supported from the literature such as the works of Williams (1985), Gustafson et al. (1988), Francis et al. (1990), Schor et al. (1992) Pompei et al. (1994), Marcantonio et al. (1994), McDougall (1995), and Dai et al. (2000).

In this study, physiological stability was a significant predictor for post-surgical cognitive disturbance. The items for physiological stability in this study were blood sodium, blood potassium, blood urea nitrogen, blood glucose, body temperature and dehydration index. This finding was also supported by the literature. From the literature, electrolyte imbalance and metabolic disturbances have been identified as major precipitating factors for delirium (Elmstahl et al., 1995; Foreman & Zane, 1996; Foreman, 1989; Francis et al., 1990; Koizumi et al., 1988; Marcantonio et al., 1994a; Seymour et al., 1980). These disturbances included abnormal sodium, potassium or glucose levels, elevated BUN and blood creatinine. Besides the electrolyte imbalance and metabolic imbalance, some reports suggested that fever, infection and dehydration can induce delirium (Cosgray et al., 1993; Inouye & Charpentier, 1996; Inouye et al., 1993; Mentes et al., 1999).

Most of the studies recorded these physiological indicators as background information and tested them as risk factors for delirium. These physiological variables were significantly associated with the onset of delirium, but it is impossible to conclude whether these variables are causes, effects or just simply correlates of delirium. Among the researchers, Marcantonio et al. (1994) indicated the admission biochemistry data significantly predicted further delirium for surgical patients. From the literature, it is indicated that either admission biochemistry data or random biochemistry data during the hospital stay correlated to the development of delirium. In the current study, the records of blood sodium, blood potassium, blood urea nitrogen and creatinine and glucose were selected from the literature as the most important physiological indicators for delirium. They were recorded from subjects' medical records. Some of the biochemistry data were not available in the data set. This missing data represents the complex nature of everyday practice. During the model testing in this study, use of either the pre-surgery biochemistry or the most recent available data post-surgery showed significant effects on the post-surgical cognitive disturbance. The findings support previous research results.

The physiological change of aging and the research results support that these electrolyte and biochemical indicators are important variables to monitor for delirium patients. A careful and systematic assessment of the patient's condition at the time of admission is important. It is necessary to monitor and correct these variables in admission or before surgery to prevent or reduce the potential for the post-surgical cognitive disturbance. It is also necessary to monitor these variables during the hospital stay to help distinguish the etiology of delirium. In each case, knowing when confusion is more likely to occur can provide more appropriate and effective efforts at detection, thereby reducing the consequences associated with confusion.

Psychoactive medication used and surgical stress did not have a significant effect on post-surgical cognitive disturbance. Psychoactive medications or multiple medication has been reported as a major predictor for cognitive disturbance (Dai et al., 2000; Foreman, 1989; Francis et al., 1990; Gustafson et al., 1988; Inouye & Charpentier, 1996; Martin et al., 2000; Rudberg et al., 1997; Schor et al., 1992). In the current study, a total of 26 medications were analyzed. In the literature these medications were thought to be significantly related to delirium. In data analysis, the medications were categorized into five types. They were recorded as "yes" indicating that the subjects used this type of medication and "no" indicating that the subjects did not use this type of medication. There was no prescription dosage or duration information available for the analysis. Whether subjects used a small amount or large amount, or one dose or 10 doses of a medication did not matter; medication in any amount was given the same value. This variability may be the reason that psychoactive medication did not show a significant effect on post-surgical cognitive disturbance. Some studies (Mach et al., 1995; Miller et al., 1988) transformed the serum anticholinergic level of the medication into atropine-equivalent level. This might be a better strategy to measure the medication effects.

In the current study, three items were combined to the variable of "surgical stress": type of anesthesia, type of surgery, and blood transfusion. Other indicators about surgical stress were not available for this secondary data analysis. Since only three items were used in this analysis, it may have been an unstable variable. Also, from the literature, different types of anesthesia may be an important factor for post-surgical cognitive disturbance. However, this is still uncertain. Some possible explanations of why the anesthesia had no effect were raised. These explanations included the postoperative cognitive decline, the existed pre-surgery undiagnosed neuropsychiatric disorders that continue to follow their course post-surgery; pre-operative physical condition; alteration in cerebral blood flow and metabolism due to factors other than anesthesia; and the medication given in conjunction with anesthesia (Ritchie et al., 1997). From the current study, the majority of subjects received spinal anesthesia (72%), had orthopaedic surgery (81%), and had a blood transfusion (90%). It was a relatively homogeneous group. By combining these indicators, the variations of the scores for this variable may decrease due to the similar treatment that they received during surgery. This may be one of the reasons that surgical stress did not have a direct effect on post-surgical cognitive disturbance in the current study.

Identifying the Most Efficient Items from the MMSE

From the item analysis of the 30-item MMSE, the items on registration and language are the easiest items for subjects to answer. They had the highest correct response rates. Items on recall, calculation, and visual construction had the lowest correct response rates. These results are similar to the studies of Fillenbaum et al.

(1987), Abraham et al. (1994), and Hill and Backman (1995). Those items that had low cognitive demand had fewer errors from the subjects. Subjects frequently missed more cognitive demanding items, such as recall items. The item on visual construction (copying a design) had the lowest correct response rate in the current study. One reason for the low response rate for surgical patients may be due to the treatment. It was reported that the drawing activity in the MMSE was impractical for bedridden patients (Kramer et al., 1985; Tombaugh & McIntyre, 1992). For example, when patients had IV lines, had pain, or general weakness post-surgery, these created difficulties in performing copy a design in the MMSE assessment.

Using the item response analysis, the original 30-item MMSE was reduced to 16 items. For the 16-item MMSE, four factors were extracted. Factor 1 consisted of five items related to attention and calculation. Factor 2 consisted of three items related to orientation to place. Factor 3 consisted of five items related to orientation to time, language and visual construction. Factor 4 consisted of three items related to recall items. The major signs of delirium found in the DSM-IV criteria for delirium (APA, 1994) were items included in these four factors. These are (1) a disturbance in consciousness, with a reduced ability to focus, to sustain focus, or to shift attention, and (2) a change in cognition or the development of a perceptual disturbance that is not better accounted for by preexisting, established, or evolving dementia. The 16-item MMSE covered the DSM-IV criteria for delirium. When the factor structure of the 16-item MMSE was compared to the literature, inconclusive factor structures are found between studies but some similarities are found in the literature. Concentration, orientation, and memory (recall) were the most frequently identified factors from previous research. The factor related to concentration items was identified from the work of Filenbaum et al. (1987), Tinklenberg et al. (1990), Abraham et al. (1994). The factor related to memory items was identified from the work of Filenbaum et al. (1987), Braekhus et al. (1992), Abraham et al. (1994), Hill and Backman (1995), and De-Leon et al. (1998). The factor related to language items was identified from the work of Filenbaum et al. (1987), Abraham et al. (1994), and Hill and Backman (1995). The factor related to orientation items was identified from the work of Filenbaum et al. (1987), Braekhus et al. (1992). Other factors identified include general functioning (Tinklenberg et al., 1990), and spatial ability (Hill & Backman, 1995; De-Leon et al., 1998). The current study derives some consistent dimensions from the 16-item MMSE when compared with previous studies. It reveals that only a few factors are needed to describe the full MMSE items. But still, some differences existed across these studies.

The total scores of the 16-item MMSE are highly correlated with the total scores of the 30-item MMSE in the current study. The internal consistency (KR-20) did not decrease much (.86 to .84) from the 30-item MMSE to the 16-item MMSE. This indicates that the 16-item MMSE is reliable and similar to the 30-item MMSE in assessing the subject's cognitive function. Deleting some items does not change the original tool much. When compared to the 30-item MMSE, items related to language and registration are deleted for the 16-item MMSE. The deleted items were the easiest items for the subjects to answer in the current study. The correct response rates of these items were higher than 99%. They provided little variation for analysis. From the literature, it has been reported that the 30-item MMSE was mainly verbal and items measuring language were relatively easy and less utility for identifying cognitive disturbance (Broshek & Marcopulos, 1999). The registration questions were the easiest items. The reported correct response rate was 96.0% to 100.0% (Abraham et al., 1994; Fillenbaum, Hughes, Heyman, George, & Blazer, 1988; Hill & Backman, 1995). The current study has similar results. This indicates the various difficulty levels in the MMSE items. The 30-item MMSE covers a variety of cognitive dimensions. But, maybe only a few factors are needed to describe the subject's cognitive status. Deleting the items with less variation makes this assessment tool short, but able to maintain validity as a cognitive function test.

From the item information curve, the expected score for the 16-item MMSE is 9.28. The correct classification rates from two cutoff points, 10 or 11, were all statistically significant when compared with the 30-item MMSE with a cutoff point of 24. But what is a proper cutoff point for the 16-item MMSE? When a score of 10 was used as the cutoff point for the 16-item MMSE, 15 subjects were misclassified when comparing results with the original assessment of the 30-item MMSE from the cutoff point of 24. These 15 subjects scored equal to or higher than 10 in the 16-item MMSE but lower than 24 in the 30-item MMSE. These 15 subjects were "false-negative" cases. When using 11 as the cutoff point, 17 subjects were misclassified. These 17 subjects scored lower than 11 in the 16-item MMSE but equal to or higher than 24 in the 30-item MMSE. These 17 subjects were "false-positive" cases. When 10 was used as the cutoff point, we may lose track of these 15 subjects because they were categorized as cognitively intact from the 16-item MMSE. When 11 was used as the cutoff point, we may pay more attention to these 17 subjects because they would be categorized as cognitively impaired by the 16-item MMSE. For the purpose of early detection and prevention from the onset of cognitive disturbance, we would rather over-identify people at risk for the attention they will need post surgery. So, a cutoff point of 11 will more appropriate than 10 in the 16-item MMSE.

Variations of Cognitive/Behavioral Changes during the Course of Delirium

The findings of the current study showed that total scores of the 30-item MMSE decreased slightly from Time 1 assessment to Time 2, but increased again through Time 3 and Time 4. But the scores for Time 4 still did not reach the same level as Time 1 for the total group. Same patterns of cognition change were found in the MMSE total scores, and memory subscores were reported by Milisen et al. (1998) and Stromberg et al. (1997). In addition to the total scores, the current study also had the same patterns of changes in every subscore of the MMSE. The results indicated that surgery is a stressful event to elderly patients. Surgical treatment alters the cognitive function of elderly patients. For less cognitively intact patients, surgery has a greater impact. This finding further supports the results from the model testing: cognitive function is a major predictor for post-surgical cognitive disturbance.

The current study found that the most common clinical features of acute confusion were reduced orientation to time, orientation to place, registration, and recall abilities. These four clinical features changed most from Time 1 (admission) to Time 2 (onset of delirium) for the delirious group. Calculation and attention, language and visual construction abilities had the lowest response rates for Time 1 and changed least from Time 1 to Time 2 for the delirious group. The literature partially supported these ideas that disorientation and cognitive disturbances occurred in the highest frequencies. This finding is consistent with the DSM-IV criteria for delirium (Meagher & Trzepacz, 1998). Elmstahl et al. (1995) reported the most common clinical features of acute confusion were reduced attention, memory impairment and disorientation. Others reported memory and psychomotor changes (Milisen et al., 1997), and concentration and attention to stimuli changes (Foreman, 1990). Calculation and attention ability were not revealed as major behavior changes from Time 1 to Time 2 for the delirious group in the current study. This may be due to the fact that the correct response rate for the calculation and attention items was the second lowest in difficulty. The rate did not have the capacity to decrease further. The 16-item MMSE includes the items for detecting the changes of orientation, calculation and attention, and recall abilities, but not for registration ability. Items for registration ability have been deleted from the 30-item MMSE because registration had the highest correct response rate in the admission assessment. That seems deleting items from the MMSE by single assessment in the current study leads to the risk of missing some features of changes, such as registration ability in the course of delirium.

From the literature, most of the studies used a single assessment to identify factor structures of the MMSE (Abraham et al., 1994; Braekhus et al., 1992; De-Leon et al., 1998; Hill & Backman, 1995). Only Tinklenberg et al. (1990) repeatedly assessed patients by the MMSE for 1.5 years to find out the static and dynamic changes of cognitive functions for dementia patients. They reported that the factor related to concentration was the only factor that existed consistently over time. But the 16-item MMSE identified from the current study does include items relating the major changes of behavior during the course of delirium.

Reasons for the inconclusive findings may be due to the fact that delirium has no single pattern. Rudbert et al. (1997) reported that there is no single pattern of delirium for patients experiencing delirium on multiple days. Different delirium subtypes may be associated with specific disruption of the brain physiology. For example, Meagher et al. (Meagher, O'Hanlon, O'Mahony, Casey, & Trzepacz, 1998; Meagher & Trzepacz, 1998) reported that delirium subjects related to a drug-related etiologic group had significantly higher scores for changes in sleep-wake cycle and fluctuation of symptoms than the infectious/electrolyte etiologic and anti-cholinergic etiologic groups. The drug-related etiologic group also had higher scores than the anti-cholinergic group for perceptual changes, delusions, psychomotor disturbance, and mood lability. They concluded that the underlying cause of delirium might influence symptom patterns of delirium. The other reason is that the MMSE was not developed for delirium assessment but for general cognitive assessment. Although all the delirium subjects were confirmed by a neurologist through DSM-IV criteria, to use only the MMSE for delirium assessment, the MMSE may not be a comprehensive delirium assessment. Some of the major attributes in DSM-IV criteria, such as the transient nature of delirium, and the physiological bases are not included in the MMSE assessment. More differentiation of neurocognitive functioning over time is needed for guiding a more targeted selection of nursing activities for elderly patients.

Theoretical and Methodological Issues

Mitchell, Gallucci, and Fought (1991) indicated the importance of viewing human responses from multi-perspectives: physiologic regulatory responses, pathophysiologic responses, experiential responses and behavioral responses. In the current study, only selective physiological and pathophysiological indicators were tested in the model. For delirium development, it is important to know whether the changes over time and the variability among subjects relate to baseline physiology, the inciting events and compensatory mechanisms, associated investigations and medications, and the environmental factors such as sensory input. Further theory testing, including all of the four response perspectives about cognitive disturbance, will help to build the knowledge base for delirium care.

The secondary data analysis limits the selection of the variables for analysis. Some of the variables such as physiological stability, surgical stress, and psychoactive medication used are summed from several items. Although each item was significant to delirium development, it may be problematic to exclude other indicators. There were no existing instruments or criteria that measured these three variables in the data set. This resulted in Stage III variables that were not stable. Non-significant results were found for surgical stress and psychoactive medications used for this model. Further research to develop valid and reliable instruments to measure Stage III variables may be options for further model testing.

In this study, the post-surgical cognitive function was assessed every other day from post-surgical day one to post-surgical day five. What is the appropriate assessment frequency and duration? From the literature, there was no consensus for the frequency and timing for cognitive assessment. Most of the assessments were on a daily basis (Foreman, 1989; Gustafson et al., 1988; Pompei et al., 1994; Rockwood, 1989; Schor et al., 1992; Williams et al., 1985a; Williams-Russo et al., 1992). Jagmin (1998) assessed the patient at admission and twice (morning, 6-8 a.m. and afternoon, 4-7 p.m.) from post-surgical day one to day five to see the time effect of delirium development. It was concluded that the time of day was not significant in development of delirium. Three studies assessed patients at admission and every other day of the hospital stay (Francis et al., 1990; Inouye & Charpentier, 1996; Milisen et al., 1998). The reported incidence rates were not lower than other reports that used daily or twice daily assessments. Milisen et al. assessed patients at admission and on the first, third and fifth postoperative days with the MMSE. They reported that 73% of hip fracture patients showed cognitive disturbance post surgery. Based on previous research, it seems both daily or every other day assessments could provide similar results for cognitive measurement. But daily assessment may also induce high refusal rate (25%) because of the repeated questions asked every day or refusal due to pain and weakness in the post-surgical period (Dai et al., 2000). For objective delirium assessments, assessing patients every other day is appropriate.

The duration of assessment of the current study lasted to the fifth post-surgical day. From the literature, the duration of assessment for surgical patients ranged from five post-surgical days (Jagmin, 1998; Milisen et al., 1998; Williams et al., 1985b) to two weeks (Schor et al., 1992). For medical patients, the range of assessment was from nine days (Inouye & Charpentier, 1996) to discharge (Francis et al., 1990). Foreman (1989) reported that 70% of medical patients developed confusion by the second day of hospitalization. No new cases of confusion were detected after the sixth day of hospitalization. Post-surgical delirium has been noted to occur two to five days after surgery (Lipowski, 1990). It seems that the duration of assessment for five post-surgical days in the current study is feasible.

The current study assessed cognitive function by multiple measurements, such as daily nursing observations, interviews with nurses and medical record reviews. Use of multiple measurements helped identify all the cases of delirium. Delirium is a clinical diagnosis, based on bedside observations and information from collateral sources (families, caregivers). Its etiology is multidimensional. Using direct bedside observation during practice and information provided from the caregiver are the most efficient ways to understand the patient's cognitive status. Non-psychiatrists can make an accurate diagnosis as shown by several studies that have compared their diagnoses to the "gold standard" of a psychiatrist's interview (Francis, 1992b). Scales or questionnaires are used as supplements to understand the patient's cognitive change.

From the literature, most studies used multiple methods to determine delirium as well as direct observation and assessment of patients. Other information used to determine delirium includes chart review (Francis et al., 1990; Inouye & Charpentier, 1996; Jagmin, 1998; Marcantonio et al., 1994a; Pompei et al., 1994), nursing assessment (Francis et al., 1990; Marcantonio et al., 1994a; Pompei et al., 1994), an interview with the primary nurse (Inouye & Charpentier, 1996; Pompei et al., 1994), and an interview with family members (Francis et al., 1990). In spite of prior work showing the success of once daily or every other day assessments in identifying delirium, using measurement triangulation, the reported incidence for delirium is more reliable because the fluctuating nature of delirium limits the sensitivity of daily or every other day assessments. In summary, the timing, duration, and methods for cognitive assessment will be trade-offs in considering the patient's condition and time and cost of the research. With multiple measurements, the current study assessed patients every other day until the fifth post-surgical day. This current study has a sound research design for delirium detection.

Relatively homogeneous populations, such as the sample in the current study, can lead to conclusions about delirium that are much different from those based on heterogeneous groups. The study subjects were all relatively healthy elderly patients with little or no cognitive disturbance who underwent urological or orthopaedic surgery. The findings of this study should not be generalized to other populations.

Implications

Implications for Nursing Education

The study suggests that knowledge and assessment skills should be included in the nursing curriculum. From a previous study of nurses' experiences of caring for delirious patients (Lou, 2001), nurses indicated that there is no consensus in terms of assessment tools used for patients, and no consensus for signs and symptoms of delirium. Nurses indicated that they used items from the Glasgow Coma Scale, JOMAC (judgement, orientation, memory, abstract thinking and calculation), orientation to time and orientation to place to assess the patient's cognitive function. These assessment tools were developed for neurological or neurosurgical patients to check consciousness, but not for delirious patients.

When asked about the kinds of topics related to delirium that were taught during their undergraduate study, the answers varied. Students mentioned that topics related to delirium were discussed in psychiatric nursing class, medical-surgical nursing class, gerontological nursing; there is no content about delirium care included in the curricula. It is necessary to integrate the knowledge and skill for delirium care into the psychogeriatric care curricula. In the situation involving revisions of nursing curricula reduction, care should be taken to maintain content on delirium.

Implications for Nursing Practice

For early detection and prevention of further damage, cognitive assessment and physical assessment should be included as a routine procedure. Acquiring baseline data about mental status at the time of admission by means of standardized assessment instruments is relevant and should be included in nursing care plans of elderly patients. Patients at risk should also be closely monitored for clinical features of cognitive disturbance to make it possible for early detection and management. Besides early detection, nursing interventions, such as noise reduction and provision of orienting objects, should be included to treat cognitive disturbance. Early detection and management procedures can be taught during in-service nursing education. The results can also be used for in-service nursing education to stress the importance of mental state examination, physical function assessment and the biochemistry indicators during the patient's admission and hospital stay.

Implications for Future Research

The findings of this study show that physical and cognitive functions at admission are important variables for post-surgical cognitive disturbance. Some of the biochemistry indicators are also important predictors for post-surgical cognitive disturbance. Surgical stress and use of psychoactive medication are not significant predictors for post-surgical cognitive disturbance. It is important to test what other factor influence the post-surgical cognitive function. The followings are recommendations for future research:

(1) Re-testing the model with different populations such as patients who had impaired sensory function, different diseases or social economic backgrounds, and with different protective factors.

(2) Designing a study that includes different predicting variables such as other indices for physiological stability, disease severity, and other medication dosage, to test the outcome variable.

(3) Designing longitudinal research to understand the long-term consequences of cognitive disturbance on patients.

(4) Replication of this study with a larger sample size and additional measurement postoperatively is needed to confirm these findings and identify neurocognitive variations in general and in specific neurocognitive dimensions.

(5) Evaluating how the symptoms of delirium interact with each other over time.

(6) Testing the consistency of the 16-item MMSE from other cognitive assessment instruments.

(7) Testing the sensitivity and specificity of the 16-item MMSE in identifying delirium during the course of delirium.

(8) Designing intervention studies to prevent or treat post-surgical cognitive disturbance.

Since research related to delirium and cognitive disturbance is a new area of study in Taiwan, it is necessary to develop a program of study. This program would start with qualitative research such as perception of nurses caring for the delirious patient, the patient's experience during a delirium episode, to quantitative research with correlational and causal research design to further understand the phenomena of delirium in the Chinese social context. Designing targeted intervention will be necessary to understand the effectiveness of the treatment. Collaborated research with other disciplines will foster the understanding of the complexity of delirium.

Strength and Limitations of the Study

The secondary data analysis may limit the comprehensiveness of the theoretical model because of the limited selection of variables for study. Other variables, which are important to the post-surgical cognitive disturbance, cannot be included in this model including environmental factors and medication usage. The sample of this study was limited to subjects that were elderly with normal vision, hearing, and speech ability. All subjects had someone accompanying them 24 hours during hospitalization. The findings apply only to this specific population and limits generalization of the research findings to non-Chinese samples. Small sample size also limits the analysis of subgroups regarding different demographic characteristics of the sample.

The strength of the theoretical model is that there is a clear temporal order of the variables. The selected variables in the model, which included cognitive function, physical function and some biochemistry and vital signs, can be easily assessed through simple tests or through medical records. It also represents features of everyday nursing practice. This assessment can be incorporated into routine nursing care and will increase the quality of nursing care. The second strength of the study is the longitudinal design and repeated measures to determine the most significant variable that influences post-surgical cognitive disturbance as well as the changes of behavior during post-surgical period. A longitudinal research design is a sound research design to determine causality. The findings of this study indicated that mental status and physical function assessments on admission to identify patients at risk for cognitive disturbance post-surgery is necessary.

The number of data sets (801) is a high enough number on which to do an item response analysis. This study reduced the MMSE to 16 items. Also, the major neurocognitive changes during delirium are identified in this study. This will help nurses to determine the right course of action sooner and save nursing hours.

Conclusion

Acute confusion or delirium is an indicator of cognitive disturbance and is a significant health problem for the hospitalized elderly. The purposes of the current study are: (1) to test a theoretical model to understand the influences of age, cognitive function, physical function, physiological stability, surgical stress and psychoactive medication used on the severity of post-surgical cognitive disturbance; (2) to identify the most efficient items from the MMSE for assessment of cognitive function; and (3) to describe variations of cognitive/behavioral changes during the course of delirium. Secondary data analysis with subgroup analysis are used to achieve the study purposes. Data for this study comes from a prospective cohort study entitled "Confusion in the hospitalized elderly patient" (Dai et al., 1996). The data were collected in a medical center in Taiwan from 1995 to1997. Sample sizes varied in the analysis in achieving the three study purposes. For the first purpose, 93 subjects' data were included in the analysis. The findings showed that age, physical function, cognitive function, and physiological stability were the four major variables to predict post-surgical cognitive disturbance. These four variables accounted 67% of the total variance of post-surgical cognitive disturbance. Two variables, surgical stress and psychoactive medication used, did not have significant effects on the outcome variable. Both instrumentation and theoretical considerations were discussed for these two insignificant paths.

The second purpose was to include 801 subjects' data in the analysis. By using item response analysis, the original 30-item MMSE was reduced to 16 items. The 16-item MMSE is significantly correlated with the 30-item MMSE. For the 16-item MMSE, four factors were extracted. These 16 items were related to orientation to time, orientation to place, language, attention and calculation, recall and visual construction. The 16-item MMSE covers the major signs of the DSM-IV criteria for delirium. The proposed new cutoff point for the 16-item MMSE was 11. This new cutoff point was determined for the purpose of over-identifying patients at risk in order to ensure early detection of and prevention from the onset of cognitive disturbance.

For the third purpose, 106 subjects' data were included in the analysis. The findings showed that surgery was a stressful event to the elderly patient, especially for those less cognitively intact. Subjects who experienced delirium had significantly lower MMSE scores and significantly lower scores on every other measure than the non-delirious subjects in every stage of hospitalization. Besides this, the delirious subjects' scores of the MMSE significantly changed at the onset of delirium. The major changes of behavior were noted in orientation, registration, and recall abilities. These behavior changes were inconclusive from the literature. These changes may relate to different delirium subtypes that are associated with a specific disruption of the brain physiology.

The findings from the current study suggest that mental status and physical functioning assessments on admission are necessary to identify patients at risk for post-surgical cognitive disturbance. These findings can be incorporated into routine nursing care that will increase the efficiency of nursing.

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Appendix A

Human Subjects Approval Letter

Permission Email From Principal Investigator of the Original Research

Form HS EX-1 (rev 4-95)

UNIVERSITY OF WASHINGTON
Grant and Contract Services, Human Subjects Division

* PLEASE TYPE *

CERTIFICATION OF EXEMPTION

University procedures provide for departmental review of research involving human subjects exempt under federal, state, and university regulations. The exempt categories and exceptions are described on the back of this form. Exempt research may be approved by the department chair, director, or dean provided it is in accord with the general principles stated in the UW Handbook, Vol. IV, Part II, Ch. 2, Sect. 1 (see exempt doc). This form, properly endorsed, certifies that the research described here qualifies for exemption, and should be forwarded to Grant and Contract Services, Human Subjects Division, Box 355752.

PRINCIPAL INVESTIGATOR: MEEI-FANG LOU   ACADEMIC TITLE: DOCTORAL STUDENT

DEPARTMENT/DIVISION: BIOBEHAVIORAL NURSING & HEALTH SYSTEMS   MAIL BOX: 357260   TELEPHONE: 206-221-7738

PROJECT TITLE: COGNITIVE IMPAIRMENT AMONG TAIWANESE ELDERLY PATIENTS AFTER ELECTIVE SURGERY

STARTING DATE: MARCH 26, 2001   ANTICIPATED TERMINATION DATE: AUGUST 31, 2001

FACULTY SPONSOR (IF PRINCIPAL INVESTIGATOR IS A STUDENT): MARGARET F. DIMOND, RN, PHD, FAAN

GRANT TITLE (IF DIFFERENT FROM PROJECT TITLE): SAME AS ABOVE

PRINCIPAL INVESTIGATOR ON GRANT (IF DIFFERENT FROM PI LISTED ABOVE): SAME AS ABOVE

FUNDING AGENCY AND APPLICATION DUE DATE (IF APPLICABLE): NONE

I. Check category(ies) under which this research qualifies for exemption (see back of sheet for description of exempt categories): ___ 1 ___ 2 ___ 3 X 4 ___ 5 ___ 6

II. ABSTRACT: State briefly a) the purpose(s) of the research, b) what subjects will do (if applicable), c) the nature of the data to be obtained, and d) how anonymity or confidentiality will be maintained. Add sheets if necessary.

The purpose of this proposed study are:

1. To understand the influences of age, cognitive function, physical function, physiological stability, surgical risk index and psychoactive medication use on the cognitive impairment in Taiwanese elderly person after elective surgery.
2. To identify valid, reliable and efficient items from the MMSE for assessment of cognitive function in Taiwanese elderly, and
3. To describe variations of cognitive/behavioral change in general and in selected cognitive dimensions during the course of delirium in Taiwanese elderly person after elective surgery.

Secondary data analysis with subgroup analysis will be used to achieve the study purposes. Data for this study comes from a prospective cohort study entitled "Confusion in the hospitalized elderly patient". The data were collected in a medical center in Taiwan from 1995 to1997. The specific grants for the data collected was funded by the National Science Council of the Republic of China. To use of this data set for secondary analysis, permission was obtained from the principal investigator of the original research. See attached e-mail from Dr. Yu-Tzu Dai for permission to use this data set. All the data have been entered into the SPSS data file with no identifiers on the notes. The data set has been anonymized with a code number for each patient. There are no patients' names on the data file. The code numbers have been transformed. There is no way to connect the code numbers to the original questionnaires. Both descriptive and influential statistics will be used to analyze the data.

III. HUMAN SUBJECTS	YES	NO
Are any subjects under 18 years of age?		x
Are any subjects confined in a correctional or detention facility?		x
Is pregnancy a prerequisite for serving as a subject?		x
Are fetuses in utero subjects in this research?		x
Are all subjects presumed to be legally competent?	x	
Are personal records (medical, academic, etc.) used without written consent?		x
Are data from subjects (responses, information, specimens) directly or indirectly identifiable?		x
Are data damaging to subjects' financial standing, employability or reputation?		x
Is material obtained at autopsy used in the research?		x
Are facilities, staff, or patients from CHMC involved?		x

IV. PRINCIPAL INVESTIGATOR: I certify that the information provided above is correct and that, to the best of my ability to judge, this research qualifies for exemption and will be conducted in accord with the general principles stated in the UW Handbook, Vol. IV, Part II, Ch. 2, Sect. 1.

PRINCIPAL INVESTIGATOR'S SIGNATURE: Meei-Fang Lou   DATE: March 13, 2001

V. CHAIR, DIRECTOR, OR DEAN: I certify that this research is exempt from federal regulations and that it is in accord with the general principles stated in the UW handbook, Vol. IV, Part II, Ch. 2, Sect. 1.

SIGNATURE: [illegible]   TITLE: [illegible]   DATE: [illegible]

* VALID FOR FIVE YEARS AS LONG AS APPROVED PROCEDURES ARE FOLLOWED *

Date: Wed, 21 Apr 1999 11:26:34 +0800

From: Yu-Tzu Dai <yutzu@ha.mc.ntu.edu.tw>

To: Meei-Fang Lou <mfalou@u.washington.edu>

Subject: Re: NSC data

Dear Meei-Fang:

I am so glad to hear from you. I am sure you can use the data of our confusional study. I will be very proud of you if you finally create a dissertation from this data.

Looking forward to hearing from you. Yu-Tzu.

Appendix B

Figures Related to Testing a Model of Post-Surgical Cognitive Disturbance

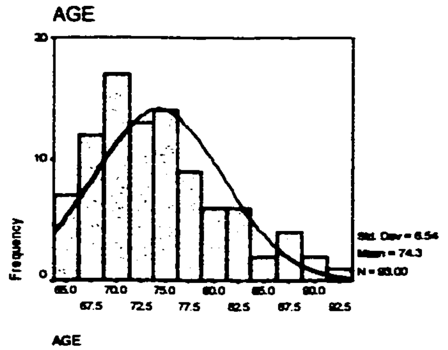

Figure B.1 Histogram and Distribution of Age

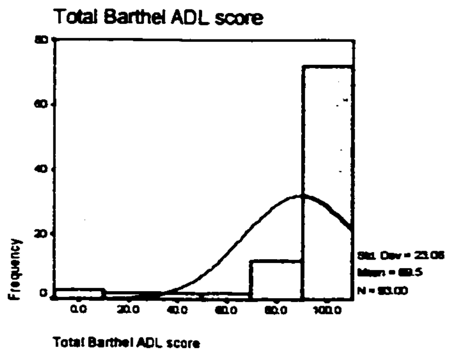

Figure B.2 Histogram and Distribution of Physical Function

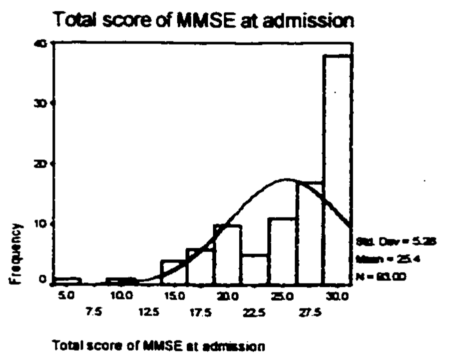

Figure B.3 Histogram and Distribution of Cognitive Function

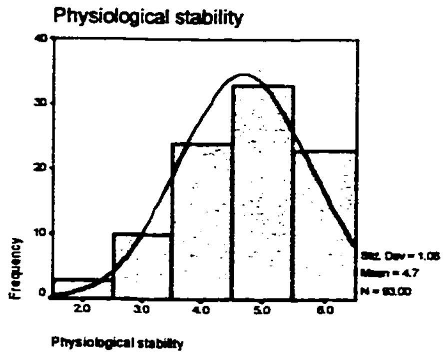

Figure B.4 Histogram and Distribution of Physiological Stability

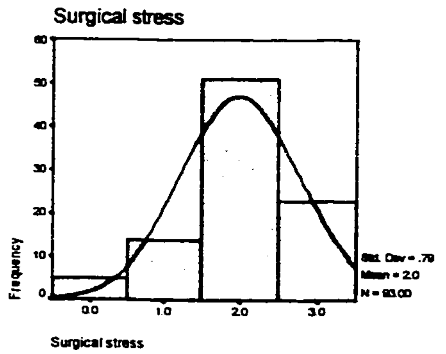

Figure B.5 Histogram and Distribution of Surgical Stress

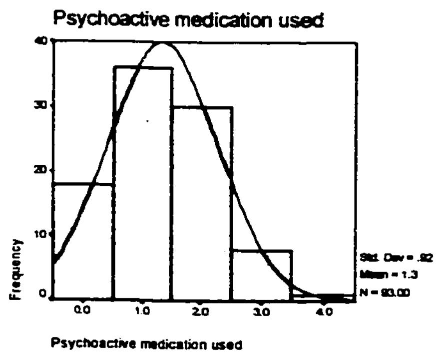

Figure B.6 Histogram and Distribution of Psychoactive Medication Used

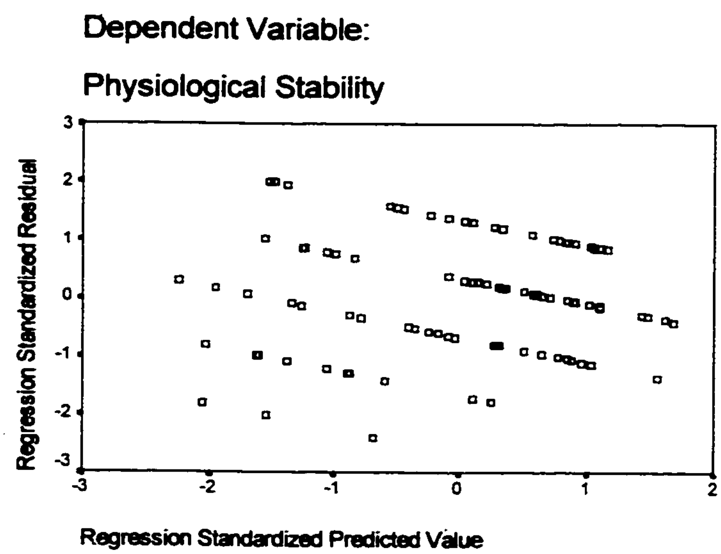

Figure B.7 Scatterplot of Predicated Values of Physiological Stability against Residuals from the Original Empirical Model for Predicting Severity of Post-Surgical Cognitive Disturbance (N=93).

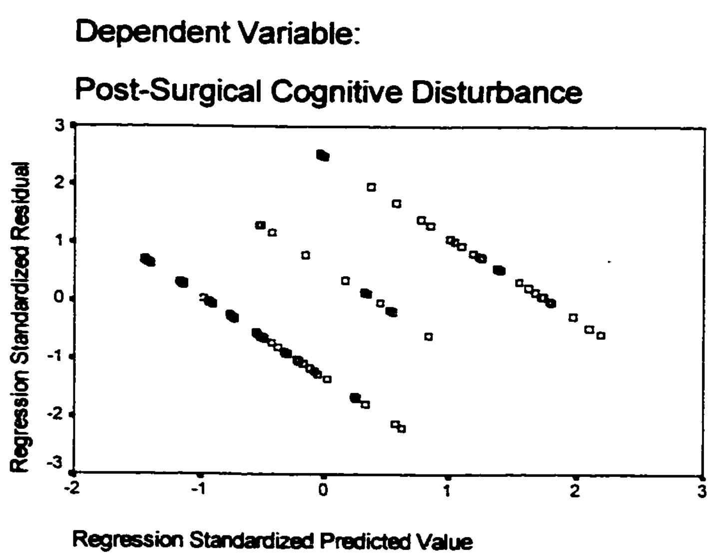

Figure B.8 Scatterplot of Predicated Values of Post-Surgical Cognitive Disturbance against Residuals from the Original Empirical Model for Predicting Severity of Post-Surgical Cognitive Disturbance (N=93).

Appendix C

Tables Related to Identifying the Most Efficient Items from the MMSE

Table C.1 Factors Extracted from Principal Components Analysis of the 30-Item MMSE

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loading		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	7.102	23.673	23.673	7.102	23.673	23.673	4.044	13.481	13.481
2	3.822	12.740	36.413	3.822	12.740	36.413	3.689	12.298	25.780
3	2.323	7.743	44.155	2.323	7.743	44.155	2.371	7.902	33.682
4	1.976	6.588	50.743	1.976	6.588	50.743	2.316	7.719	41.401
5	1.570	5.233	55.976	1.570	5.233	55.976	2.153	7.178	48.579
6	1.452	4.840	60.816	1.452	4.840	60.816	2.152	7.175	55.754
7	1.332	4.439	65.255	1.332	4.439	65.255	1.862	6.208	61.962
8	1.106	3.688	68.943	1.106	3.688	68.943	1.565	5.215	67.177
9	1.022	3.405	72.348	1.022	3.405	72.348	1.551	5.171	72.348
10	0.783	2.609	74.957						
11	0.755	2.517	77.474						
12	0.707	2.355	79.829						
13	0.650	2.168	81.998						
14	0.614	2.047	84.044						
15	0.571	1.902	85.946						
16	0.525	1.748	87.694						
17	0.476	1.586	89.280						
18	0.443	1.477	90.757						
19	0.405	1.351	92.107						
20	0.380	1.268	93.375						
21	0.327	1.091	96.466						
22	0.297	0.988	95.455						
23	0.281	0.937	96.392						
24	0.273	0.911	97.302						
25	0.246	0.821	98.124						
26	0.201	0.671	98.795						
27	0.189	0.629	99.423						
28	0.173	0.577	100.000						
29	0.000	0.000	100.000						
30	0.000	0.000	100.000						

Extraction Method: Principal Component Analysis

Table C.2 Final Parameter Estimates for the Initial 2PL Model from the 30-Item MMSE

Item	Lnk	Flg	a	b	c	Resid	PC	PBs	PBt
1			1.57	-1.24	0.00	1.19	0.82	0.67	0.59
2			1.52	-1.69	0.00	1.51	0.89	0.63	0.52
3			1.03	-1.14	0.00	1.76	0.76	0.54	0.51
4		R	1.04	-1.97	0.00	2.11	0.89	0.46	0.39
5			1.41	-2.90	0.00	1.59	0.98	0.41	0.28
6		P	1.57	-3.00	0.00	0.56	0.99	0.40	0.26
7		P	1.46	-3.00	0.00	0.44	0.99	0.31	0.23
8			1.64	-2.46	0.00	0.60	0.97	0.52	0.39
9			1.44	-1.85	0.00	1.79	0.91	0.58	0.48
10			1.60	-1.84	0.00	1.33	0.91	0.61	0.50
11		P	1.61	-3.00	0.00	0.57	1.00	0.23	0.15
12		P	1.61	-3.00	0.00	0.57	1.00	0.23	0.15
13		P	1.61	-3.00	0.00	0.57	1.00	0.23	0.15
14		P	1.57	-3.00	0.00	0.58	1.00	0.11	0.08
15		P	1.55	-3.00	0.00	0.57	1.00	0.24	0.16
16		P	1.54	-3.00	0.00	0.47	1.00	0.22	0.15
17			1.02	-0.77	0.00	0.77	0.69	0.55	0.58
18		P	0.96	-1.96	0.00	2.13	0.88	0.43	0.40
19		P	0.88	-3.00	0.00	1.34	0.99	0.02	0.03
20		P	0.83	-3.00	0.00	1.30	0.99	0.06	0.07
21		P	0.76	-3.00	0.00	1.13	0.98	0.08	0.09
22			0.62	-1.77	0.00	1.71	0.80	0.34	0.29
23			0.58	-1.68	0.00	1.73	0.78	0.32	0.28
24			0.56	-1.51	0.00	1.68	0.75	0.32	0.29
25			1.57	-1.93	0.00	1.18	0.92	0.58	0.49
26			1.70	-0.77	0.00	0.97	0.73	0.66	0.69
27			1.88	-0.93	0.00	0.67	0.77	0.73	0.71
28			2.01	-0.88	0.00	1.48	0.76	0.76	0.74
29			1.90	-0.67	0.00	1.32	0.70	0.73	0.75
30			1.24	-0.57	0.00	0.73	0.66	0.62	0.65

P: potential problematic
R: revised

Table C.3 The Information Provided at Different Ability Level by the Final 2PL Model from the 16-Item MMSE

θ	θ-b	-a(θ-b)	$e^{-a(\theta-b)}$	P(θ)	Q(θ)	a^2	I(θ)
-3	-1.67	2.29	9.87	0.092	0.908	1.88	0.16
-2	-0.67	0.92	2.51	0.28	0.72	1.88	0.38
-1	0.33	-0.45	0.64	0.61	0.39	1.88	0.45
-0.5	0.83	-1.14	0.32	0.76	0.24	1.88	0.34
0	1.33	-1.82	0.16	0.86	0.14	1.88	0.23
1	2.33	-3.19	0.04	0.96	0.04	1.88	0.07
2	3.33	-4.56	0.01	0.99	0.01	1.88	0.02
3	4.33	-5.93	0.003	0.997	0.003	1.88	0.006

a = 1.37, b = -1.33

Under a 2PL model, the item information function is defined as $I_i(\theta) = a_i^2 P_i(\theta)Q_i(\theta)$

a_i is the discrimination parameter for item i

$P_i(\theta) = 1/[1 + EXP(-a_i(\theta-b_i))]$

$Q_i(\theta) = 1- P_i(\theta)$

θ is the ability level of interest

From Baker, F.B. (1985). The Basics of Item Response Theory (p. 85). New Hampshire: Heinemann.

Table C.4 The Expected Score of $\theta = -1$ for the 16-Item MMSE

item number	a	b	$-a(\theta-b)$	$e^{-a(\theta-b)}$	$1+e^{-a(\theta-b)}$	$1/[1+e^{-a(\theta-b)}]$
1	1.54	-1.21	-0.32	0.73	1.73	0.58
2	1.53	-1.65	-0.99	0.37	1.37	0.73
3	1.02	-1.11	-0.11	0.90	1.90	0.53
8	1.59	-2.45	-2.31	0.10	1.10	0.91
9	1.47	-1.80	-1.18	0.31	1.31	0.76
10	1.62	-1.80	-1.30	0.27	1.27	0.79
17	1.03	-0.74	0.27	1.31	2.31	0.43
22	0.61	-1.79	-0.48	0.62	1.62	0.62
23	0.56	-1.69	-0.39	0.68	1.68	0.60
24	0.55	-1.51	-0.28	0.76	1.76	0.57
25	1.56	-1.90	-1.40	0.25	1.25	0.80
26	1.79	-0.74	0.47	1.60	2.60	0.38
27	1.88	-0.90	0.19	1.21	2.21	0.45
28	2.01	-0.86	0.28	1.32	2.32	0.43
29	1.93	-0.64	0.69	1.99	2.99	0.33
30	1.20	-0.56	0.53	1.70	2.70	0.37
Expected Score						**9.28**

The equation for the 2PL logistic model is:

$P(\theta) = 1/[1+e^{-a(\theta-b)}]$ e is the constant 2.718, b is the difficulty parameter and a is the discrimination parameter.

The equation for an expected score for examinees with ability level θ_j is:

$$\text{Expected Score}_j = \sum_{1}^{N} P_i(\theta_j)$$

i denotes an item and $P_i(\theta_j)$ depends on the particular item characteristic curve model employed.

From Baker, F.B. (1985). The Basics of Item Response Theory (pp. 15 & 49). New Hampshire: Heinemann.

Table C.5 Factors Extracted from Principal Components Analysis for the 16-item MMSE

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loading		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	5.811	36.321	36.321	5.811	36.321	36.321	3.573	22.329	22.329
2	1.657	10.358	46.679	1.657	10.358	46.679	2.568	16.048	38.377
3	1.412	8.826	55.505	1.412	8.826	55.505	2.409	10.055	54.433
4	1.186	7.409	62.914	1.186	7.407	62.914	1.517	9.482	62.914
5	0.893	5.583	68.498						
6	0.779	4.871	73.369						
7	0.709	4.433	77.802						
8	0.607	3.791	81.593						
9	0.567	3.542	85.135						
10	0.514	3.215	88.350						
11	0.440	2.750	91.100						
12	0.397	2.479	93.479						
13	0.331	2.071	95.651						
14	0.285	1.778	97.429						
15	0.230	1.434	98.863						
16	0.182	1.137	100.00						

Extration Method: Principal Component Analysis

Appendix D

Tables and Figures related to Variations of Cognitive/Behavioral Changes during the Course of Delirium

Table D.1 Correct Response Rate of Each Item for the Four Assessments of the MMSE for the Total Group

Item	Time 1 (N=106) %	Time 2 (N =102) %	Time 3 (N =101) %	Time 4 (N =84) %
Orientation to Time				
Item 1	74	67	69	70
Item 2	78	64	67	71
Item 3	70	40	44	46
Item 4	81	63	70	76
Item 5	96	82	88	92
Orientation to Place				
Item 6	97	85	92	95
Item 7	96	84	95	96
Item 8	97	78	89	92
Item 9	90	71	82	82
Item 10	89	74	82	81
Registration				
Item 11	99	85	93	99
Item 12	99	85	93	99
Item 13	99	85	93	98
Language				
Item 14	100	96	98	99
Item 15	99	93	97	98
Item 16	99	89	96	99
Item 17	70	63	67	70
Item 18	81	72	76	76
Item 19	100	86	96	98
Item 20	99	86	95	98
Item 21	100	85	95	98
Recall				
Item 22	79	73	82	88
Item 23	76	68	73	77
Item 24	72	64	78	77
Calculation				
Item 25	89	77	85	83
Item 26	72	64	69	71
Item 27	70	61	62	65
Item 28	68	60	66	65
Item 29	62	57	63	67
Visual Construction				
Item 30	69	56	60	60

Table D.2 Correct Response Rate of Each Item for the Four Assessments of the MMSE for the Delirious Group

Item	Time 1 (N=41) %	Time 2 (N =41) %	Time 3 (N =41) %	Time 4 (N =40) %
Orientation to Time				
Item 1	53	29	39	48
Item 2	58	24	32	43
Item 3	45	10	15	13
Item 4	63	32	46	58
Item 5	90	56	71	83
Orientation to Place				
Item 6	93	63	80	90
Item 7	90	63	88	93
Item 8	93	49	76	85
Item 9	78	32	61	65
Item 10	78	39	59	63
Registration				
Item 11	98	63	83	98
Item 12	98	63	83	98
Item 13	98	63	83	95
Language				
Item 14	100	90	95	98
Item 15	98	83	93	95
Item 16	98	73	90	98
Item 17	50	32	41	50
Item 18	58	37	49	58
Item 19	100	66	90	95
Item 20	98	66	88	95
Item 21	100	63	88	95
Recall				
Item 22	65	39	66	78
Item 23	58	29	41	63
Item 24	65	37	61	65
Calculation				
Item 25	75	44	63	68
Item 26	48	27	39	48
Item 27	45	24	34	40
Item 28	43	24	39	40
Item 29	40	22	32	43
Visual Construction				
Item 30	45	20	32	35

Table D.3 Correct Response Rate of Each Item for the Four Measurements of the MMSE for the Non-Delirious Group

Item	Time 1 (N=65) %	Time 2 (N =61) %	Time 3 (N =60) %	Time 4 (N =44) %
Orientation to Time				
Item 1	88	92	90	91
Item 2	91	90	92	98
Item 3	85	61	63	77
Item 4	92	84	87	93
Item 5	100	100	100	100
Orientation to Place				
Item 6	100	100	100	100
Item 7	100	98	100	100
Item 8	100	98	98	98
Item 9	98	97	97	98
Item 10	95	97	98	98
Registration				
Item 11	100	100	100	100
Item 12	100	100	100	100
Item 13	100	100	100	100
Language				
Item 14	100	100	100	100
Item 15	100	100	100	100
Item 16	100	100	100	100
Item 17	83	84	85	89
Item 18	95	95	95	93
Item 19	100	100	100	100
Item 20	100	100	100	100
Item 21	100	100	100	100
Recall				
Item 22	88	95	93	98
Item 23	88	93	95	91
Item 24	77	82	90	89
Calculation				
Item 25	97	100	100	98
Item 26	88	89	90	93
Item 27	85	85	82	88
Item 28	83	84	85	88
Item 29	75	80	85	91
Visual Construction				
Item 30	83	80	80	84

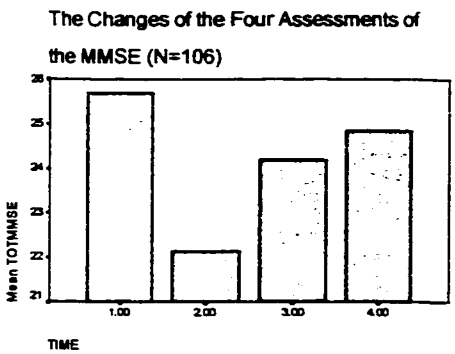

Figure D.1 The Changes of the Total Score of the MMSE in Four Time Points

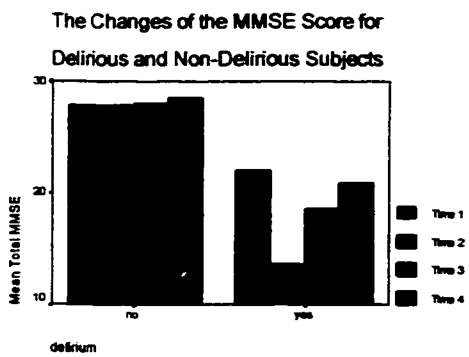

Figure D.2 The Changes of the MMSE Score for Delirious and Non-Delirious Subjects

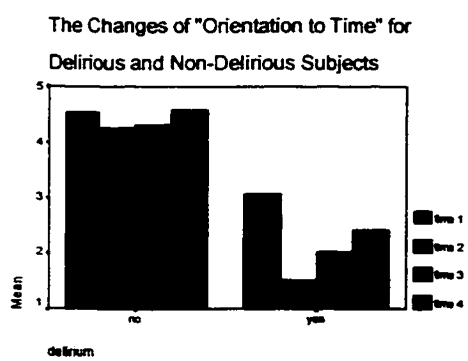

Figure D.3 The Changes of "Orientation to Time" for Delirious and Non-Delirious Subjects

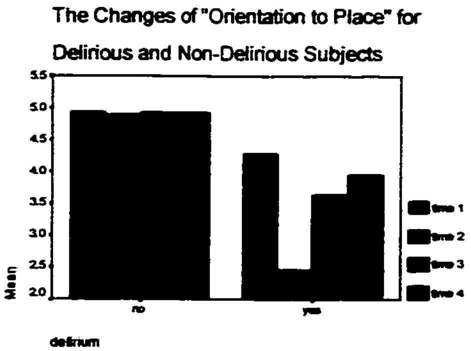

Figure D.4 The Changes of "Orientation to Place" for Delirious and Non-Delirious Subjects

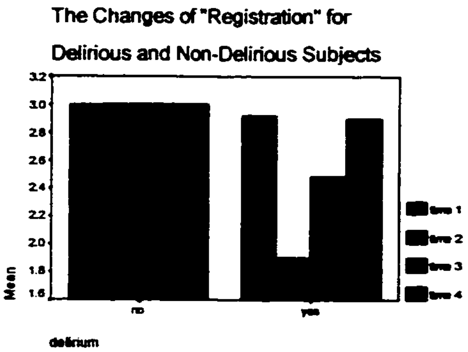

Figure D.5 The Changes of "Registration" for Delirious and Non-Delirious Subjects

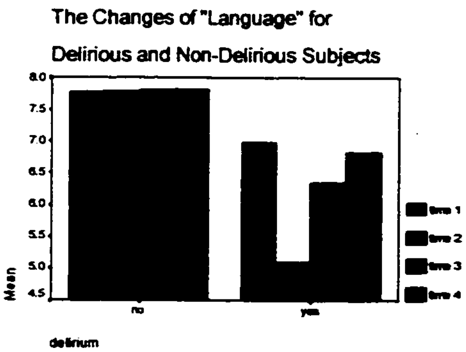

Figure D.6 The Changes of "Language" for Delirious and Non-Delirious Subjects

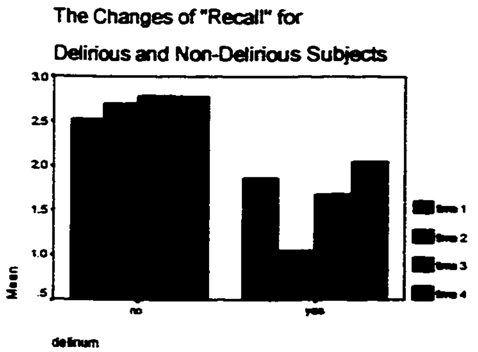

Figure D.7 The Changes of "Recall" for Delirious and Non-Delirious Subjects

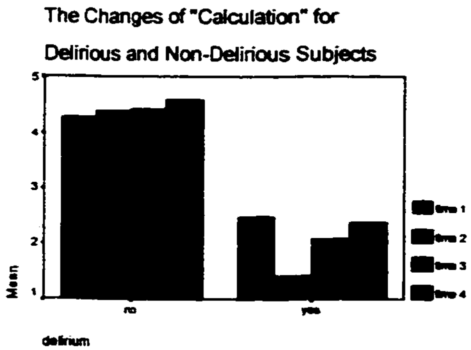

Figure D.8 The Changes of "Calculation" for Delirious and Non-Delirious Subjects

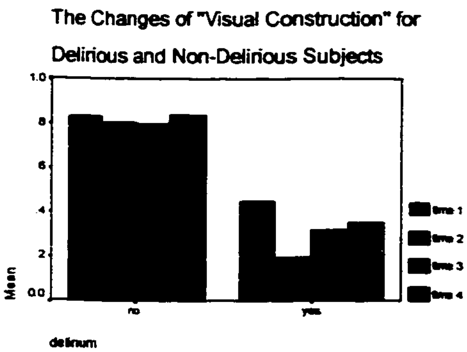

Figure D.9 The Changes of "Visual Construction" for Delirious and Non-Delirious Subjects

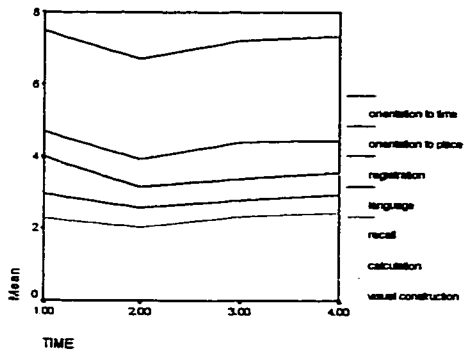

Figure D.10 The Changes of the Subscores of the MMSE Overtime for Total Subjects.

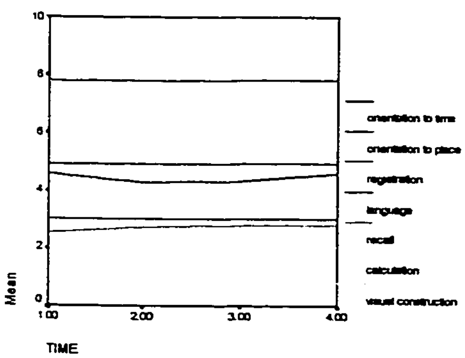

Figure D.11 The Changes of the Subscores of the MMSE Overtime for Non-Delirious Subjects.

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