PSYCHOPHYSIOLOGICAL DETERMINANTS OF REPEATED VENTILATOR WEANING FAILURE

by

Yu-Ju Chen

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SIGNED: ______Yu-Ju Chen_____________________
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DEDICATION

The dissertation is dedicated to my mother.
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ABSTRACT

**Background.** A significant gap in prior research in the area of mechanical ventilation (MV) weaning is the paucity of studies that have investigated the adverse psychophysiological impact of a failed weaning trial, as well as relationships that may exist among psychological and physiological factors on weaning outcomes.

**Purpose.** The purpose of this study is to test the psychophysiological ventilator weaning model (PVWM), which is theory based and empirically derived, to explain the repeated ventilator weaning failure.

**Methods.** This was a cross-sectional design study. A convenience sample (N = 102) of mechanically ventilated patients who had failed their first weaning trial were enrolled in the study. The data collection was a prospective design. Confirmatory factor analysis (CFA) and structure equation modeling (SEM) were used to test the goodness of fit of PVWM and hypotheses of this study.

**Results.** The results indicated that the originally specified measurement model was a misfit with the sample data. Accordingly, a modified measurement model was established by dropping four indicators for further structural model and hypothesis testing. Conditioned fear strongly affected state anxiety, but had no significant effects on respiratory function and weaning outcome. State anxiety presented non-significant effects on respiratory function and weaning outcome. Among the three psychophysiological factors in PVWM, respiratory function had the strongest effect on the length of MV. Based on the underpinning theoretical thinking, the alternative models were established by post hoc analysis and were confirmed by nested model comparison.
**Conclusion.** The resulting model indicates that patients who have a high acquired conditioned fear from the first ventilator weaning failure will have a high state anxiety during the second weaning trial. High state anxiety will cause compromised respiratory function during the weaning process and further cause prolonged mechanical ventilation in the subsequent weaning. The outcomes in the subsequent weaning trial will also be directly determined by MV patients’ state anxiety and respiratory function. Findings from the present study provide a different perspective, new insight, and a direction for health care providers to consider when managing the care of patients with repeated ventilator weaning failure.
CHAPTER ONE: INTRODUCTION

Background

Mechanical ventilation (MV) is commonly used to support the respiratory function of patients with life-threatening illnesses. Despite the therapeutic, and, at times, lifesaving nature of mechanical ventilatory support for patients with serious illness, mechanical ventilation is not an intervention without complications. Mechanical ventilation can be both physiologically and psychologically stressful (Rotondi et al., 2002). In fact, most patients describe being on a ventilator as a miserable experience (Logan & Jenny, 1997).

Weaning from mechanical ventilation is the procedure used to permit the patient to resume spontaneous breathing without the support of MV (Knebel et al., 1998). Most mechanically ventilated patients can be weaned from MV, usually within seven days following successful treatment of the underlying cause of respiratory failure, but 20% to 30% of mechanically ventilated patients are difficult to wean, experiencing repeated weaning failures and, as a result, need longer mechanical ventilation (Esteban et al., 1994; Seneff et al., 1996; Wu et al., 2000).

Patients experiencing repeated weaning failures need prolonged mechanical ventilation (PMV), which leads to extended stays in the intensive care unit (ICU) and hospital, and increased risk of mortality and morbidity (Burns et al., 1995; Dries, 1997; Mancebo, 1996). Prolonged mechanical ventilation incurs a high proportion of medical care costs and contributes to poorer quality of life for the patients and caregivers (Daly et al., 1991). Hence, facilitating the weaning process becomes a great challenge for health
care providers. Both physiological and psychological factors that might hinder the weaning process are garnering more attention from clinicians. Unfortunately, studies related to mechanical ventilation weaning are typically more focused on exploring physiological weaning predictors than psychological weaning predictors.

*Physiological Weaning Indices are Predominate in Contemporary Studies*

A large number of contemporary studies have been conducted in an attempt to determine the variables that might predict successful ventilator weaning. By determining objective predictors, researchers hope to shorten the duration of mechanical ventilation and to prevent complications or adverse effects rising from failed weaning or extubation trials.

Sahn and Lakshminarayan (1973) began to examine important physiological predictors of successful ventilator weaning four decades ago. The results of these studies show that physiological predictors can be assigned into two main categories: mechanical/neuromuscular ability to breathe and the adequate ability to oxygenate arterial blood. However, the predictive value of these criteria is controversial (Epstein, 2000).

In recent studies, researchers have examined the mechanisms of respiratory failure to develop a theoretical framework for ventilator weaning (Tobin & Alex, 1994; Vassilakopoulos et al., 1996). Gas exchange, neuromuscular competence of the respiratory system, and severity of respiratory workload are three of the most important factors predicting the outcomes of ventilator weaning in this theoretical framework.

Many authors have used this framework to propose indices that might represent each of these three factors and have examined the relationships among these indices and
the outcome of ventilator weaning (e.g., Tobin & Alex, 1994; Vassilakopoulos et al., 1996). However, most of these studies tried to find a superior index to predict the weaning outcome in all patient populations. Due to the differences in patient population, prevalence of weaning success, duration of mechanical ventilation prior to weaning, and the applied thresholds, it has been difficult to find one index that is superior to other indices.

A well-recognized limitation of using a single weaning predictor/index is that it produces a biased result from the inevitable measurement error and omission of other relevant indices inherent in such an approach. Accordingly, many integrated respiratory parameters have been proposed and are expected to have a better predictive effect than a single predictor. These integrated respiratory parameters include: (1) CROP, which integrates thoracic compliance, respiratory rate, arterial oxygenation, and maximal inspiratory pressure (Chen et al., 1994; Yang & Tobin, 1991); (2) the Weaning Index (WI), which is based on three components of ventilatory capacity: respiratory mechanics, gas exchange, and respiratory muscle strength and endurance (Burns et al., 1994; Chen et al., 1994; Jabour et al., 1991); and (3) the Burns Weaning Assessment Program (BWAP), which is based on a 26-factor bedside assessment checklist including general, pulmonary, and mechanical factors (Burns et al., 1994). Although integrated parameters are more complex to calculate, in comparison to single indicators they provide a more accurate prediction than maximum inspiratory pressure and minute ventilation. However, these integrated parameters have been found to be a less accurate prediction than the rapid shallow breathing index and tidal volume (Epstein, 2000). Hence, it appears that the
strongest predictors of ventilator weaning have yet to be identified.

From this perspective, the shortcoming of studies using only single indicators and integrated parameters approaches is that they all solely focused on physiological factors. That leaves a proportion of variance in unsuccessful weaning unexplainable, because it overlooks other potential aspects, such as psychological factors.

*Exploring Psychological Factors in Ventilator Weaning*

In response to the inadequacy of physiological indices to predict ventilator weaning, there is a growing number of nursing researchers who have proposed theoretical frameworks and conducted studies to identify subjective or psychological predictors of ventilator weaning failure. Most patients who had been mechanically ventilated described a high degree of anxiety, uncertainty, discomfort and fatigue during mechanical ventilation and the weaning process (Knebel, 1990; Wunderlich et al., 1999). Moreover, findings from a survey of clinical health care providers demonstrated that virtually all providers recognize the importance of incorporating both physiological and psychological parameters into the care of mechanically ventilated patients during the weaning process (Martensson & Fridlund, 2002; Clochesy et al., 1997). However, no detailed psychological consideration has been documented in the weaning assessment tool or weaning criteria in clinical settings.

Two nursing researchers, Knebel (1990) and Moody (1997), each developed theoretical models to describe the process of exploring psychological factors in ventilator weaning. Knebel’s (1990) model proposed a cyclical interaction between physiological and psychological factors that contribute to prolonged mechanical ventilation. In her
model, Knebel (1990) suggested that a physiological change occurs in conjunction with the direct and indirect emotional responses in mechanically ventilated patients. Moody et al. (1997) proposed a conceptual model related to psychophysiological predictors of weaning from mechanical ventilation in subjects with chronic bronchitis and emphysema (CBE), in which physiological and psychosocial variables were hypothesized to have direct and indirect correlations with each other. Although theoretically strong, the empirical evidence from the studies did not permit the authors to estimate correlations between psychological factors and weaning outcome adequately, due to small sample sizes and the use of a single predictor to measure the psychological factors.

Given the limitations and inadequacy of contemporary studies, it is important to conduct a well-designed study that examines the critical working hypotheses regarding relationships among underlying physiological and psychological problems and repeated ventilator weaning failure. The critical working hypotheses should be based on a theoretical framework driven by multiple theories and empirical evidence. Findings from such a study can help health care providers to implement the proper evidence-based interventions to efficiently resolve patients’ problems and further facilitate their weaning process.

Statement of Problems

According to clinical investigations, mechanically ventilated patients have higher in-hospital and after-hospital discharge mortality, morbidity, and poorer quality of life than patients who do not need MV support. In addition, these patients’ caregivers were found to have a poor quality of life. These problems are recognized to proportionally
increase with the length of mechanical ventilation. Similarly, a disproportionate number of medical care resources has been found to be spent on treating the associated problems of prolonged mechanical ventilation (Combes et al., 2003; Wagner, 1989).

**High Morbidity and Mortality in Mechanically Ventilated Patients**

Patients with mechanical ventilation have an in-hospital mortality rate of 23% to 44% (Burns et al., 2003; Douglas et al., 1997; Epstein & Vuong, 1999; Kollef, O’Brien, & Silver, 1997). One study reported that patients who required MV for more than 48 hours had 43% mortality within 2 months, and this mortality rate increased by 34% for each decade increase in patient’s age (Quality of life after mechanical ventilation in the aged study investigators, 2002). In addition, 35% of the 2-month survivors were at risk for clinical depression and 78% of these survivors required care by a caregiver (Im et al., 2004).

Several studies reported that complications of mechanical ventilation are generally related to the duration of ventilatory support. Fagon et al. (1989) found that about 30% of patients with mechanical ventilation would develop nosocomial pneumonia, which is associated with a more than two-fold increase in mortality. Further, the risk of developing nosocomial pneumonia increases about 1% per day for each day that patient requires mechanical ventilation. Gilmartin et al. (1999) reported that patients with prolonged ventilator weaning are more likely to have the following medical problems: sepsis, volume overload, tracheal bleeding, ileus, worsening renal failure, chest tube replacement, and seizures. In addition, the longer duration of ventilatory support increases the risk for other potential complications related to mechanical ventilation:
toxic effects of oxygen, endotracheal-tube complications, volume-induced alveolar injury, barotraumas, decreased cardiac output, and psychological problems (Fagon et al., 1989; Tobin & Alex, 1994).

Poor Quality of Life and Tremendous Burdens for Patients and Caregivers

Prolonged mechanical ventilation, which might be caused by repeated ventilator weaning failure, not only results in increased morbidity and mortality in patients, but also decreases quality of life for patients and their caregivers. Combes et al. (2003) conducted a study to evaluate the outcome and quality of life of ICU patients mechanically ventilated for at least 14 days. They reported that these patients had a poorer health-related quality of life (HRQL) as compared with other ICU patients. Douglas, Daly, Gordon, & Brennan (2002) found that short-term ventilator patients (continuous in-hospital mechanical ventilation of more than 24 hr but less than 96 hr) had a better overall quality of life at all points postdischarge than long-term ventilator patients (continuous in-hospital mechanical ventilation of over 96 hr).

These patients’ caregivers are vulnerable to psychological and physical burden: 33.9% of caregivers of patients placed on MV for 48 hours or more were at risk for developing clinical depression (Im et al., 2004), and their depression scores were even higher than other caregiver groups (Douglas & Daly, 2003). These caregivers significantly dropped their physical health scores from the time of the patients’ hospital discharge until 6 months after discharge, which was a statistically significant contribution to caregivers’ depression (Douglas & Daly, 2003).
Medical Care Costs and Resources

Although the direct costs of prolonged mechanical ventilation are insufficiently reported and poorly generalized, treatment of MV patients appears to incur disproportionately more medical care costs and greater use of resources. Ely et al. (2000), for example, used post-hoc analyses to investigate the cost of care in MV patients and reported that respiratory care (14% of total hospital costs), including ventilator costs, was the third largest category of hospital costs after beds (27% of total hospital costs) and pharmacy expenses (25% of total hospital costs). In addition, the cost to ensure long-term survival for patients with long-term mechanical ventilation was significantly greater than that for patients with short-term mechanical ventilation (Combes et al., 2003). Furthermore, patients with prolonged mechanical ventilation were not commonly discharged before their successful weaning. These patients accounted for a substantial proportion of total ICU bed days, contributing to overcrowding and limiting the availability of ICU beds (Andrulis, Kellermann, & Hintz, 1991; Melnick, Mann, & Golan, 1989).

Wagner (1989) reported that patients requiring mechanical ventilation for seven days or longer represented 6% of the total ICU population but accounted for 37% of all ICU costs. In addition, the medical cost after the seventh day for these patients comprised 21% of the total ICU cost. A study investigating the age- and sex-adjusted incidence of mechanical ventilation from 1992-2000 reported that the incidence of mechanical ventilation increased 2% from 1992 to 2000, but the number of mechanical ventilation days and inpatient days for ventilated patients increased 69%, and the proportion of total
bed days increased 30% (Needham, 2005). These findings demonstrated that PMV patients utilize a disproportionate number of technological and financial resources in the clinical setting.

Limitations in Contemporary Studies

To decrease the problems previously mentioned, many studies have been conducted to explore the underlying causes of ventilator weaning failure and to search for effective predictors for ventilator weaning. However, due to limitations of the contemporary studies, it is still unclear why 20-30% of patients remain on mechanical ventilation longer than physiologically necessary. Identified limitations in prior studies are as following: (1) use of a single predictor of the multifactorial nature of weaning outcomes; (2) omission of relevant psychological variables in studies related to physiological weaning predictors; (3) exploring relevant psychological factors by using a single indicator or measurement; (4) small sample size; and (5) no proven correlation between psychological factors and weaning outcome.

In view of these limitations, the results of the prior studies have done little to help these patients. Therefore, deriving sufficient research evidence to facilitate weaning of mechanically ventilated patients is a significant concern for health care providers, and drives this study.

Significance

The need for devising a study to overcome the limitations of prior studies and further helps to ameliorate patients’ problems from repeated weaning failures cannot be overstated. The present study was based on theories and empirical evidence to identify
the psychophysiological determinants in repeated ventilator weaning failure. This is pioneering work that approaches the patients’ psychophysiological problems related to ventilator weaning failure from the perspective of classical conditioning (Pavlov, 1928). The psychophysiological impacts from the first ventilator weaning failure were first approached from that viewpoint. Findings of this study will provide health care providers with comprehensive knowledge necessary to develop evidence-based interventions to care for patients who experience repeated ventilator weaning failure. Accordingly, the future evidence-based interventions related to care of these patients can increase quality of care and relieve patients and their caregivers’ physiological, psychological, and financial burdens, and, further, provide an efficient allocation of health care resources.

A Pavlovian-inspired Approach for Repeated Ventilator Weaning Failure

To overcome the limitations of contemporary studies, the present study will approach psychophysiological problems in patients with repeated ventilator weaning failure from the perspective of classical conditioning. Most studies try to empirically identify psychophysiological variables that exist in mechanically ventilated patients with weaning failure. Informed by several theories, the present study focused further on exploring relationships between the psychophysiological variables and repeated ventilator weaning failure.

Descriptive retrospective studies have identified acute psychological states, like fear and anxiety, in patients during mechanical ventilation and during the ventilator weaning process. Unfortunately, prior studies testing correlations among these empirically derived psychological factors and weaning outcomes fail to find significance
between these factors and weaning failure. In response, the model proposed in this study included classical conditioning theory, anxiety theory, mind-body connection theory, and medical weaning predicting models. These multiple theories provide a comprehensive description of how selected psychophysiological variables affect the weaning outcome and their interplay with the weaning outcome. This study was, then, driven by multiple working hypotheses, in which the important and relevant variables were included to avoid unnecessary error and bias. Psychological variables included conditioned fear and state anxiety. The physiological variable was represented by respiratory function. These psychological and physiological variables were treated as latent variables that can be measured by multiple indicators. Therefore, by diminishing the limitations of previous studies, these steps should produce less biased results, which in turn should provide more knowledge to assist in understanding repeated ventilator weaning failure.

**Evidence Based Interventions for Future Nursing Care**

The findings from the present study could not only help the clinician to better comprehend patients' repeated weaning failures, but also help health care providers to develop interventions to wean these patients more efficiently. Bonell (1999) indicated that high quality care linked with evidence-based practice would help to generate profound clinical decisions.

Therefore, the anticipated contribution from this study is to provide health care providers with more knowledge about patients who experience repeated ventilator weaning failure that will aid in the development of more effective interventions for these patients. In the present study, the sample data supported the proposed model and partial
hypotheses, which would provide information to health care providers about effects of conditioned fear and its associated psychophysiological reactions on the weaning outcome. Conditioned fear acquired from the first ventilator weaning failure was found to indirectly affect the weaning outcome by mediating state anxiety and compromised respiratory function in subsequent weaning trials. Accordingly, health care providers may develop interventions based on counter-conditioning and/or operant conditioning to modify patients’ conditioned fear. These interventions might include biofeedback, relaxation, or systematic desensitization strategies (Hannich et al., 2004; Holliday & Hyers, 1990; Holliday & Lippman, 2003). Resolving patients’ conditioned fear may also resolve its cascade effects, like reactive anxiety and compromised respiratory function, and help patients out of the vicious cycle of repeated ventilator weaning failure.

Facilitating Efficient Allocation of Medical Care Resources

The high mortality and morbidity rate of patients with prolonged mechanical ventilation from repeated ventilator weaning failure incurs physiological and psychological burdens for patients and their caregivers. In addition, these patients require a disproportionately great number of medical care resources (Wagner, 1989). Therefore, if evidence-based interventions derived from the findings of the present study facilitate patients’ successful weaning from the mechanical ventilation and transfer out of ICU or discharge from the hospital, then substantial burdens on caregivers, hospitals, and medical care resources may be relieved (Needham, 2005). Therefore, the results from the present study could concurrently produce the following benefits for patients, caregivers, and the health care system: (1) developing cost-effective health care to relieve patients’
and their caregivers’ physiological and psychological burdens, and the financial burden on the medical care system; and (2) facilitating the efficient allocation of medical care resources.

Conceptual Framework

The conceptual framework for this study was derived from subjective and objective empirical evidence and contemporary theories including classical conditioning theory, anxiety theory, mind-body connection theory, and the medical weaning predicting model. The Psychophysiological Ventilator Weaning Model (PVWM) was proposed to explain the multifactorial nature of ventilator weaning in patients with repeated weaning failures (see Figure 1). In this model, the outcome of repeated ventilator weaning failure was strengthened by the interplay among selected psychological and physiological variables; the selected psychological factors were conditioned fear and state anxiety, and the selected physiological factor was the respiratory function.
Figure 1. Psychophysiological Ventilator Weaning Model (PVWM) in Repeated Ventilator Weaning Failure:
Conditioned fear acquired from the first ventilator weaning failure causes psychophysiological reactions and further affect the following weaning outcomes.

- Self-report State Anxiety
- Intensity of Anxiety
- Dyspnea
- Conditioned Fear
- State Anxiety
- Ventilator Weaning Outcomes: Length of MV
- Respiratory Function
- Respiratory Central Drive
- Respiratory Muscle Capacity
- Respiratory Muscle Workload
- Gas Exchange
- Hyperventilation
- Increased Heart Rate
- Rapid Shallow Breathing Pattern
- Emotional Fear
- Cognitive Fear

Rapid Shallow Breathing Pattern
Dyspnea
Conditioned Fear
State Anxiety
Ventilator Weaning Outcomes: Length of MV
Respiratory Function
Respiratory Central Drive
Respiratory Muscle Capacity
Respiratory Muscle Workload
Gas Exchange
Hyperventilation
Increased Heart Rate
Rapid Shallow Breathing Pattern
Emotional Fear
Cognitive Fear
Conditioned Fear Acquisition Defined

Conditioned fear is defined as the fear acquired by rapid learning from a conditioning process, in which contiguous pairings between a conditional stimulus (CS) and an unconditional stimulus (US) occur. A conditional stimulus is regarded as neutral and elicits little more than an orienting response, whereas an unconditional stimulus elicits an unconditional response (UR). Following Pavlov’s observations (Pavlov, 1928), after several pairings of CS and US, the previously neutral CS elicits a response, known as the conditional response (CR), which may appear similar to the unconditional response (UR). The acquisition of intense conditioned fear or fear of dyspnea can occur from a single pairing (Figure 2) (e.g., Campbell, Sanderson & Laverty, 1964; Mongeluzi et al., 1996).

In the clinical setting, a weaning trial, such as a T-piece weaning trial, begins after the clinician (respiratory therapist, nurse, or physician) talks to the patient about the weaning process and adjustment of the ventilatory support. The adjustment of the ventilatory support in a T-piece weaning trial is to disconnect the patient from the ventilator and allow him/her to breathe spontaneously through a T-tube circuit. During the T-piece weaning, the patient’s condition will be monitored throughout the process. The clinician will terminate the trial if the patient appears unable to tolerate the weaning or if weaning is successful. If the clinician terminates the trial because of intolerance, the condition is set for the patient to establish associations between relatively benign events (e.g., health care providers entering the room, adjusting the ventilatory support) and severe, frightening events (dyspnea, anxiety, fear). Hence, the presence of health care
providers and adjustment of the ventilatory support can be regarded as a conditional stimulus (CS). An imbalance of the respiratory supply and demand, such that respiratory support by an inappropriate ventilator adjustment is inadequate to meet patient’s respiratory needs, can be regarded as an unconditional stimulus (US). The unconditional response (UR), like dyspnea, anxiety, and possible fear of death elicited by the US in the first ventilator weaning failure, will be similarly evoked by CS in the second weaning trial (see Figure 3).

**Figure 2. Fear Conditioning Acquisition**

1st trial

\[
\text{CS (Conditional stimulus)} + \text{US (Unconditional stimulus)} \rightarrow \text{UR (Unconditional response)}
\]

2nd trial

\[
\text{CS (Conditional stimulus)} \rightarrow \text{CR (Conditional response)}
\]

**Figure 3. Conditioned Fear Acquired from Ventilator Weaning Failure**

1st weaning failure

\[
\begin{align*}
\text{CS (the presence of health care providers, adjustment to the ventilator)} \quad & \quad \quad \quad \quad \rightarrow \quad \text{UR} \\
+ \quad \text{US (imbalance of the respiratory supply and demand)} \quad & \quad \quad \quad \quad (\text{dyspnea, anxiety, & fear of death})
\end{align*}
\]

2nd weaning trial

\[
\text{CS (the presence of health care providers, adjustment to the ventilator)} \rightarrow \text{CR (fear, anxiety, & dyspnea)}
\]

Under these circumstances, the patient would be expected to establish conditioned emotional memories – memories which may be automatically elicited by the cues
associated with the beginning of a weaning trial. If this is true, then the entrance of a particular clinician and adjustment of the ventilatory support or the onset of subsequent T-piece weaning trials will evoke emotional memories (the learned fear and anxiety response) producing acute fear, anxiety, fatigue, and dyspnea (Blackwood, 1996). Therefore, conditioned fear acquired from the first weaning failure would not only directly affect the weaning outcome in the following trial, but would indirectly affect the weaning outcome by affecting the patient’s state anxiety and respiratory function.

**Representations of Conditioned Fear**

The failed ventilator weaning trial is considered a powerful conditioning process. In the subsequent presence of CS, conditioned fear will be evoked in individuals as a series of representations: self-reports of fear, increased heart rate, hyperventilation, and rapid shallow breathing pattern (Campbell et al., 1964; LeDoux, 1995; Ley, 1999) (Figure 4).

**Figure 4. The Representations of Conditioned Fear**

![Diagram of Conditioned Fear](image)

Self-reports of fear will be described as the emotion-cognitive dyad. LeDoux
(1993) asserted that emotional and cognitive processing of a stimulus fundamentally different. Emotional fear is defined as the subjective response to the presence of a stimulus, like the adjustment of the mechanical ventilator, based on whether the subject perceives the stimulus as threatening or not (LeDoux, 1995). In contrast, cognitive fear is defined in terms of the attention a subject pays to the stimulus in an apparent effort to determine whether the threatening stimulus is dangerous in one situation and not in another (LeDoux, 1995).

Taking a neural perspective on fear, the amygdala plays the core role in reacting to dangerous stimuli. Two primary inputs of a stimulus to the amygdala are from the thalamus and the cortex. The amygdala initially responds to crudely processed input from the thalamus, which reaches the amygdala after crossing a single synapse rapidly, when the input signals danger. On the other hand, inputs from the cortex, such as hippocampal formation, provide more highly processed and detailed information to the amygdala often and appropriately inhibiting its initial response. In other words, information arriving at the cortex is highly processed, involving neural structures that include simple processing by the thalamus, perceptual processing by the neocortex, spatial, contextual, and mnemonic processing by the hippocampus (LeDoux, 1993). During Pavlovian fear conditioning the amygdala is an important part of an aversive emotional memory system, whereas the hippocampus and cortex are parts of the system involved in contextualization and cognitive or declarative forms of memory. Because these systems are separable at the anatomical level, as well as at behavioral and cognitive levels (Lang et al, 1998), patients’ self-report of conditioned fear should be assessed in both emotional and cognitive
Increased Heart Rate

Increased heart rate is considered an important physiological response elicited by a fear-inducing stimulus. The conditioned fear response activates the autonomic nervous system, which can alter locomotor activity and cardiovascular function (Stiedl & Spiess, 1997; LeDoux, 1993). In several studies investigating the changes of cardiovascular function in conditioned fear (Stiedl et al., 1999; Stiedl & Spiess, 1997; Tovote et al., 2005), an instantaneous acceleration of heart rate to almost maximum physiological values was found in response to the conditional stimulus, but elevation of the mean arterial blood pressure (MAP) was a slow and delayed response. Therefore, the accelerated heart rate is regarded as a representation/indicator of acute conditioned fear.

Hyperventilation and Rapid Shallow Breathing Pattern

Ley (1999) indicated that there are several potential ventilatory changes present during the adaptive process of conditioning emotions: (1) increased minute ventilation that will be manifested in either increased tidal volume or increased respiration frequency, or both; (2) decreased end-tidal carbon-dioxide (PetCO2); and (3) increased respiratory cycle. Accordingly, hyperventilation and a rapid and shallow breathing pattern are regarded as two other representations of conditioned fear in patients who have experienced a ventilator weaning failure.

The present study was based on the assumption that the subjects had acquired conditioned fear of ventilator weaning from their first ventilator weaning failure. Accordingly, procedures that signal the beginning of subsequent weaning trials for the
patients would elicit conditioned psychological and physical responses. These might include patients’ self-reports of emotional and cognitive fear, increased heart rate, hyperventilation, and rapid shallow breathing pattern. These responses could interfere with the weaning process itself.

*State Anxiety*

Anxiety is regarded as a connotation of fear, which is caused by different degrees of fear and is temporarily separated from the object of fear. People who perceive fear in threatening situations will try to escape and avoid them. However, when they cannot successfully escape or avoid these threatening situations, fear will become anxiety (LeDoux, 1998). In this case, anxiety is described as unresolved fear. Accordingly, patients with conditioned fear, acquired from their first ventilator weaning failure, might perceive the second weaning trial as threatening or as an uncontrollable event. In the clinical settings, as patients’ physiological conditions indicate that they are ready to be weaned from the ventilator, the following weaning trial cannot be avoided. The inescapable conditioned fear will accompany the subsequent weaning trial and will further lead to anxiety. In other words, an inescapable or unavoidable conditioned fear in repeated ventilator weaning failure patients will lead to the development of state anxiety during the subsequent weaning process.

Spielberger’s (1966) state-trait anxiety theory proposes that a sequence of temporally perceived (cognitively appraised) threatening or dangerous events, initiated by external or internal stimulus conditions, culminate in the evocation of a state anxiety reaction. State anxiety (A-state) is a transitory emotion characterized by physiological
arousal and consciously perceived feelings of apprehension, dread, and tension (Spielberger, 1966). The intensity and duration of A-state are dependent upon the degree and persistence of threat confronting an individual; simply, the “person by situation” approach is hypothesized to assess the A-state response. From Beck’s (1993) cognitive schemata view of anxiety, states of anxiety are associated with automatic thoughts and images relevant to danger. These automatic thoughts and images might result from distorted information processing and trigger inappropriate motor, physiological, and affective components of the anxiety response.

Most descriptive studies report that anxiety is a patient’s chief complaint during mechanical ventilation and the ventilator weaning process (Lowry & Anderson, 1993; Pochard et al., 1995; Rotondi et al., 2002). In addition, researchers report that anxiety in mechanically ventilated patients leads to increased patients’ self-reports of dyspnea (Carriero-Kohlman et al., 1993; Gift et al., 1986). Therefore, self-reports of anxiety and dyspnea will be regarded as representations of state anxiety in the proposed model (Figure 5).

Figure 5. The Representations of State Anxiety
Representations of State Anxiety

Self-Reports of State Anxiety

State anxiety in patients with conditioned fear acquired from the first ventilator weaning failure is described as perceived feelings of apprehension, dread, and tension during the following weaning trial. Self-reports of state anxiety will allow subjects to describe how they feel at a particular moment in time. Anxiety is an emotion that is relatively easy to self-rate, and subjects who have experienced anxiety can accurately rate their own level of anxiety (Grinker, 1966). Therefore, self-reports of anxiety will be a useful means of assessing patients’ state anxiety.

Dyspnea

Patients’ intensity of anxiety may be represented by the intensity of dyspnea. Empirical data indicates that patients’ intensity of anxiety has a high correlation with their level of dyspnea during the weaning process (Knebel, 1994). Other research findings also show the subjective feeling of dyspnea is significantly correlated with the level of anxiety (Bailey, 2004; Carrieri-Kohlman et al., 1993; Gift et al., 1986). Anxiety is suggested as a predictor of the subjective experience of dyspnea. Patients who acquired conditioned fear from previous ventilator weaning failure might have experienced dyspnea during the first weaning failure. Therefore, this hypothesized model proposed that these patients’ anticipated anxiety of dyspnea will further induce the feeling of dyspnea in the following weaning trial.

State anxiety correlates highly with physiological weaning predictors (e.g., Moody et al., 1997; Twibell, Siela, & Mahmoodi, 2003; Wunderlich, 2003). Therefore,
based on the postulation of contemporary theory, patients’ state anxiety will be affected by conditioned fear acquired from the first weaning failure. The state anxiety during the second weaning trial is proposed to (a) directly affect respiratory function and weaning outcomes, and (b) indirectly affect the weaning outcome through influences on MV patients’ respiratory function.

**Respiratory Function**

Ventilator weaning is the process of facilitating the patient to resume spontaneous breathing with the support of mechanical ventilation. Spontaneous breathing is an endurance task that depends upon the repeated generation of inspiratory muscle forces to overcome lung and chest wall elastic loads, as well as airway and tissue resistance. This task requires an adequate central drive to control the respiratory muscles, anatomical and functional nerve integrity, unimpaired neuromuscular transmission, an intact chest wall, and adequate respiratory muscle strength (Tobin & Alex, 1994). According to Tobin & Alex’s (1994) and Vassilakopoulos et al.’s (1996) models, gas exchange, respiratory central drive, respiratory muscle capacity, and respiratory muscle workload are the four most important indicators of respiratory function in determining patients’ ability to tolerate weaning from mechanical ventilation (Figure 6). In the PVWM, these four indicators represent patients’ respiratory function, which can directly affect weaning outcome. Further, PVWM predicts that psychological variables (conditioned fear and state anxiety) will affect respiratory function in patients who have experienced ventilator weaning failure during the second weaning trial.
Figure 6. The Representations of Respiratory Function

Respiratory Function

- Gas Exchange
- Respiratory Central Drive
- Respiratory Muscle Capacity
- Respiratory Muscle Workload

Representaions of Respiratory Function

The main function of the lung is pulmonary gas exchange to match O₂ uptake and elimination of CO₂ to the whole-body metabolic O₂ consumption and CO₂ production. Adequate levels of ventilation and perfusion of the alveoli are needed for gas exchange. Tobin et al. (1986) indicated that resumption of spontaneous breathing is associated with tidal volume decreasing and respiratory frequency increasing, which may not change the minute ventilation but, worse, may lead to ventilation-perfusion (V/Q) mismatching. In addition, a study found that resumption of spontaneous breathing would alter gas exchange, including an increase in arterial carbon dioxide tension (PaCO₂), a decrease in pH, and an increase in mixed venous oxygen tension (Torres et al., 1989). The simultaneous increase in cardiac output during resumption of spontaneous breathing may not decrease PaO₂. However, this ventilation-perfusion mismatching will cause hypoxemia or gas exchange failure in patients with preexisting cardiac dysfunction or will be further affected by patients’ psychophysiological reaction—rapid, shallow breathing during the weaning. Rapid, shallow breathing, which increases respiratory
frequency and decreases tidal volume, may cause hyperinflation, increase physiological
dead space, and reduce alveolar ventilation, thereby inducing inefficient gas-exchange
(Tobin et al., 1986).

**Respiratory Central Drive**

Respiratory central drive is described as the inspiratory neuronal activity. An indicator of respiratory central drive—airway occlusion pressure at .1 second (P0.1)—was found to be inappropriately increased in patients during an unsuccessful weaning trial (Jubran & Tobin, 1997). The major cause of the increase in respiratory central drive is severe alveolar hypoventilation from poor respiratory function (Mancebo, 1996). The respiratory central drive output would be modified or downregulated by a feedback mechanism that might be activated by mechanical and chemical inputs arising from contraction of respiratory muscles, ventilation (workload), or blood gas tensions. However, when respiratory function was compromised, the downregulation of the respiratory motor output was not common in patients who failed a weaning trial (Jubran & Tobin, 1997).

**Respiratory Muscle Capacity**

Breathing is an endurance task that depends upon the repeated generation of inspiratory muscle forces. Absolute endurance, which depends on the strength and endurance of respiratory muscles, is the ability of respiratory muscles to sustain contractions of a specific tension to resist ventilatory failure (Vassilakopoulos et al., 1996). There are several factors that affect the capacity of respiratory muscles: dynamic hyperinflation, asynchronous and paradoxical motion of the rib cage and abdomen,
decreased oxygen delivery, respiratory acidosis, mineral and electrolyte abnormalities, malnutrition, and respiratory muscle fatigue (Jubran & Tobin, 1997). Patients with weaning failures easily develop tachypnea, which results in a decreased expiratory time and leads to dynamic hyperinflation. Hyperinflation will further diminish the efficiency and capacity of respiratory muscles. Accordingly, the respiratory function will be represented by respiratory muscle capacity.

*Respiratory Muscle Workloads*

Increased ventilatory requirement and increased work required to breathe both increase the workload on the respiratory muscle pump. Due to increased CO₂ production and increased dead space ventilation from compromised respiratory function, patients will need an increased ventilatory requirement, and this will cause tachypnea and further hyperinflation. Severe hyperinflation in these patients might lead the tidal volumes to near total lung capacity, causing the compliance to decrease dramatically, which in turn increases elastic loads. The intrinsic positive end-expiratory pressure (PEEPi) caused by hyperinflation will increase threshold loads that prevent airflow into or out of the airways (Coussa, et al., 1993; Mancebo, 1996). In addition, the resistive loads can be increased by a decrease in lung volume and accumulation of secretions. Therefore, increase in any of these respiratory loads will increase the respiratory muscle workload.

In summary, respiratory function consisting of these four indicators has been extensively used to predict ventilator weaning outcome. In addition, respiratory function is considered related to physiological arousal, such as alternations in respiratory pattern and other sympathetic reactions, evoked by fear and anxiety (Harrigan, Wilson, &
Rosenthal, 2004). Therefore, respiratory function is proposed to be affected by the interplay of psychological factors (conditioned fear and anxiety) to affect ventilator weaning outcome in the PVWM.

Ventilator Weaning Outcome

The duration of the weaning process is the indicator of weaning outcome in PVWM. The duration of the weaning process will be defined as the length of mechanical ventilation (measured in days) required for ventilator weaning patients to successfully wean. The length of mechanical ventilation is an important index related to the morbidity, mortality, and quality of life in mechanically ventilated patients. Ventilator weaning is the procedure used to permit patients to resume spontaneous breathing with the support of mechanical ventilation. However, the duration of the weaning process was found to account for a large proportion (40%) of the total time of ventilatory support (Esteban et al., 1994).

Successfully weaned patients will be defined as patients who can sustain spontaneous breathing for 24 hours without ventilatory support. If patients present any signs or symptoms of intolerance during the weaning, the weaning trial will be terminated and patients will be returned to partial mechanical ventilation at a previously tolerated setting for at least 24 hours. Thus, the respiratory system can rest while on mechanical ventilation and get ready for the next weaning trial. The weaning process will be continued until the patient is successfully weaned; therefore, the duration of the entire weaning process can be regarded as the weaning outcome.
Purpose of Study

The major purpose of this study is to test how well the hypothesized Psychophysiological Ventilator Weaning Model (PVWM) fits the sample data. This model proposes that selected variables (conditioned fear, state anxiety, and respiratory function) and their interplay affect the weaning outcome in patients with repeated ventilator weaning failure.

Specific Aims:

1. Examine the direct and indirect effects of “conditioned fear,” defined as patients’ acute fear acquired from the first ventilator weaning failure, on the weaning outcome of their following weaning trial

2. Examine the relationships among conditioned fear, state anxiety, and respiratory function in the weaning trial of patients following the first ventilator weaning failure

3. Test the effects of state anxiety and respiratory function on weaning outcomes in mechanically ventilated patients who have one ventilator weaning failure

Research Hypotheses

In the hypothesized model for the present study, the PVWM is presented in Figure 7. It consists of three latent variables and one observed outcome variable. The three latent variables are contained conditioned fear, state anxiety, and respiratory function. The outcome variable is determined by how many days patients needed mechanical ventilation after the second T-piece weaning trial.
1. The PVWM is theory based and empirically derived. In this hypothesized model, the first ventilator weaning failure functions as a conditioning process, from which conditioned fear was acquired. Conditioned fear has both direct and indirect positive effects on weaning outcome of the weaning trial following the first ventilator weaning failure (Figure 1). The indirect effect of conditioned fear on the weaning outcome is mediated by state anxiety and respiratory function.

2. State anxiety derived from unresolved fear has both direct and indirect effects on the weaning outcome. The indirect effect of state anxiety on the weaning outcome is mediated by respiratory function.

3. The respiratory function itself, or as affected by conditioned fear and anxiety, has a direct effect on patients’ ventilator weaning outcomes.

Figure 7. Hypothesis Framework

Summary

Repeated ventilator weaning failure resulting in prolonged mechanical ventilation not only jeopardizes patients’ physiological and psychological status and elevates their
mortality and morbidity, but also causes tremendous burdens to their caregivers and the health care system. In spite of extensive studies focused on physiological weaning predictors, researchers have failed to predict successful weaning for patients with prior repeated ventilator weaning failure. The lack of concrete knowledge to support the hypothesized correlations among psychological and physiological factors and weaning outcomes represents a significant gap in contemporary research. For this reason, the primary task of this study is to develop and test a proper theoretical framework to untangle the psychophysiological myth related to ventilator weaning in patients with repeated ventilator weaning failure.
CHAPTER TWO: LITERATURE REVIEW

The literature review presented in this chapter is the result of an extensive search of the theoretical and empirical data related to the substantive area of the inquiry. This work was focused on: (a) ventilator weaning models, (b) psychological theories related to conditioned fear and state anxiety, and (c) findings from contemporary studies related to ventilator weaning. Gaps in contemporary knowledge related to repeated mechanical ventilator failures were further addressed.

Weaning Continuum Model

Ventilator weaning is defined as a process to withdraw mechanically ventilated patients from ventilatory support. Hall & Wood (1987) suggested replacing the term “weaning” from the ventilator with “liberate,” since most mechanically ventilated patients can withdraw from the machine after a brief trial of spontaneous breathing. In contrast, ventilator “weaning” implies the gradual withdrawal of mechanical ventilation, a term appropriate for the difficult to wean patients. The weaning continuum model, proposed by the American Association of Critical Care Nurses (AACN) in 1994, defined ventilator weaning as the “process” of facilitating the patient to resume spontaneous breathing with the support of mechanical ventilation, which consists of three stages: prewean, weaning, and outcomes (Knebel et al., 1994).

During the preweaning stage, clinicians assess the readiness of the patient to begin the weaning process and determine the appropriate weaning approach for the patient. Physiological stability determines when patients reach the readiness threshold. When this occurs clinicians may decide to start the weaning process stage. This model
postulated that several factors would influence the weaning outcomes: myocardiac function and oxygenation, state of the ventilatory muscles, ventilatory requirement and drive, nutritional and electrolyte balances, environmental factors, and the psychological outlook of the patients (Knebel et al., 1994). Under the influence of these factors, the model hypothesized that the weaning trajectory of patients would be characterized by peaks and valleys; the upward slope of the baseline would indicate progress toward a successful weaning outcome. In order to achieve a successful weaning outcome, clinicians would need to optimize the patients’ physiological stability and psychological status in the weaning process. Unfortunately, if the patients’ physiological status deteriorated below the readiness threshold, then the weaning ceased and the preweaning stage would be re-entered. Weaning outcomes are decided by two situations: (1) a complete process, defined as patients with spontaneous breathing for 24-48 hours without ventilatory support, and (2) an incomplete process, defined as patients who reach a plateau and progress no further. The difference between ventilator weaning and extubation were clearly laid out in this model. Weaning success was defined as spontaneous breathing without ventilatory support, with or without an artificial airway; extubation would be performed upon weaning success (Knebel et al., 1998). In summary, the weaning continuum model proposed that ventilator weaning is a continuous process with a possible cyclic loop, which includes preweaning, weaning, and outcome stages. The entire process will end when the complete or incomplete outcome is determined.

Weaning Predicting Models

Several theoretical frameworks and models focusing on mechanisms of weaning
from mechanical ventilation were proposed to explain the multifactorial nature of failure to wean. Interestingly, medical and nursing researchers approached the phenomenon of weaning failure differently: medical researches were oriented toward physiological problems and nurse researchers toward psychological problems interacting with physiological problems. Two different focused models of ventilator weaning will be approached in the following content.

**Medical Models Predicting Weaning**

Respiratory failure is the primary indication for mechanical ventilation (Tobin & Alex, 1994). Both Tobin & Alex (1994) and Vassilakopoulos et al. (1996) proposed a similar theoretical framework related to mechanisms of respiratory failure that could explain failure to wean from a ventilator.

*Tobin & Alex’s (1994) Pathophysiological Determinants of Weaning Outcome*

Tobin & Alex (1994) proposed that adequacy of pulmonary gas exchange and performance of the respiratory muscle pump are major pathophysiological factors to determine a patient’s ability to tolerate discontinuation of ventilator support.

Resumption of spontaneous breathing is associated with tidal volume decreasing and respiratory frequency increasing that might not change the minute ventilation but might worsen ventilation-perfusion (V/Q) mismatching (Tobin et al., 1986). Gas exchange at the time of discontinuing ventilator support was characterized by an increase in arterial carbon dioxide tension (PaCO₂), a decrease in pH, and an increase in mixed venous oxygen tension. There was no significant reduction of PaO₂ that was explained by a simultaneous increase in cardiac output (Torres et al., 1989; Tobin et al., 1986).
However, whether this worsening of V/Q mismatching can cause gas exchange failure and prevent successful discontinuation of ventilator support still needs further study.

Ventilatory pump failure is considered the common cause of failure to wean from mechanical ventilation. Either alone or in combination, decreased respiratory neuromuscular capacity and increased respiratory muscle pump load can lead to ventilatory pump failure. Possible causes of decreased respiratory neuromuscular capacity are: decreased respiratory central output, phrenic nerve dysfunction neuromuscular disorders, and decreased respiratory muscle strength and/or endurance.

Breathing is an endurance task that depends on the repeated generation of inspiratory muscle forces that are primarily determined by the respiratory workload. Absolute endurance, which depends on the strength and endurance of respiratory muscles, is the ability of respiratory muscles to sustain contractions of a specific tension to resist ventilatory failure. Patients with mechanical ventilation commonly have the following problems that may cause decreased respiratory muscle strength and/or endurance and lead to failure weaning: hyperinflation, malnutrition, decreased oxygen supply, respiratory acidosis, mineral and electrolyte abnormalities, renal failure, endocrinopathy, drug-induced abnormalities, disused muscle atrophy, and respiratory muscle fatigue.

Increased respiratory muscle pump load may result from increased ventilatory requirements and/or increased work of breathing. Increased CO₂ production, increased dead space ventilation, and an inappropriately elevated respiratory drive will cause increased ventilatory requirements. Increasing the central drive would not only increase the ventilatory requirement but also proportionally increase the respiratory workload. An
increase in airway resistance or a decrease in pulmonary compliance, such as hyperinflation, will increase the work of breathing, which is a major determinant of patients’ failure to resume and sustain spontaneous breathing. In addition to pulmonary gas exchange and performance of the respiratory muscle pump, Tobin & Alex (1994) also briefly mentioned that psychological factors may interfere with a patient's ability to tolerate discontinuation of ventilator support.

Vassilakopoulos et al.’s (1996) Mechanical Model

Compared to Tobin & Alex’s (1994) theoretical framework, Vassilakopoulos et al.’s (1996) mechanical model not only proposed factors contributing to the failure to wean from the ventilator, but further postulated the relationship among factors. The imbalance between ventilatory needs and neurocardiorespiratory capacity has been attributed either to an imbalance between the load faced by the respiratory muscles and their neuromuscular competence or to an imbalance between the energy supply and the energy demand of the muscles. In addition, these two “imbalances” are considered to be linked to each other. When taking a spontaneous breath under normal conditions, subjects should be able to maintain a balance between inspiratory load and neuromuscular competence without fatigue, which is called “endurance.” Endurance is determined by the balance between energy supplies and energy demand.

Neuromuscular competence of the respiratory system is determined by respiratory drive, neural and neuromuscular transmission, and muscle strength. The loads imposed on the respiratory system include elastic loads and resistive loads of lung and chest wall. If the loads on the respiratory system outweigh the competence, then the ventilatory
pump insufficiently inflates the lungs and chest wall.

The inspiratory muscle blood flow, the blood substrate concentration and arterial oxygen content, the muscle’s ability to extract and utilize energy sources, and the muscle’s energy stores will determine the energy supplies. Energy demands will proportionally increase with the following factors: the mean tidal pressure developed by the inspiratory muscles, expressed as the fraction of maximum inspiratory pressure (\(P_i/P_{i,max}\)); the minute ventilation; the inspiratory duty cycle (\(T_i/T_{tot}\)); and the mean inspiratory flow rate (\(V_t/T_i\)). However, the energy demands are inversely related to the efficiency of the respiratory muscles. The efficiency is defined as the ratio of the mechanical work rate to the oxygen cost of breathing that can be affected by the elastic and resistive load, velocity of shortening, muscle fiber composition, and intrinsic rate of adenosine triphosphate (ATP) hydrolysis.

In this model, Vassilakopoulos et al. (1996) use the oxygen cost of breathing (\(VO_{2,\text{resp}}\)) to represent the energy demand. The equation of \(VO_{2,\text{resp}}\) during breathing at a constant tidal volume is given by \(VO_{2,\text{resp}} = K_1A + K_2W + K_3TTI\). \(K_1, K_2,\) and \(K_3\) are constants. “\(A\)” is the heat of activation. “\(W\)” is work rate and represents the respiratory load. TTI is the tension-time index, which is an indicator for endurance time. The equation of \(VO_{2,\text{resp}}\) helps to explain the relationship between oxygen demand and respiratory load, and the relationship between oxygen demand and endurance time. However, the concept of “imbalance” between the load faced by the respiratory muscles and their neuromuscular competence or between oxygen supplies and demands is easy to understand qualitatively, but difficult to quantify. In addition, the imbalance is not easy to
Theoretical thinking suggests that these two medical models are similar, and both of them explain the mechanism of failure to wean in detail. Gas exchange, neuromuscular competence of respiratory system, and severity of respiratory workload, three of the most important factors in determining the outcomes of ventilator weaning, are integrated in these two models. In addition, they maintain that there are correlations among these factors.

Nursing Models Prediction Weaning

According to study findings and clinical experiences, there are a portion of patients on mechanical ventilation who became ventilator dependent even though their physiologic stability permits weaning trials. Therefore, nursing researchers are giving more attention to psychological considerations when weaning patients from prolonged mechanical ventilation.

Knebel’s (1990) Conceptual Framework of Weaning Failure

Knebel’s (1990) circular model proposes that interactions between physiological and psychological factors contribute to prolonged mechanical ventilation. Based on suggested clinical practice and Grossbach-Lindis’s (1980) conceptual model, Knebel (1990) proposed that a physiological change is directly and indirectly correlated with the emotional response in mechanically ventilated patients. Mechanically ventilated patients experience negative emotions such as anxiety, anger, fear and frustration during mechanical ventilation because of the intensive care unit (ICU) environment, communication difficulties, and dyspnea due to lung disease. In addition, the weaning
process itself may precipitate anxiety or fear. A negative emotion, such as anxiety, increases muscle tension, which can increase the work of breathing during weaning. This in turn increasing energy demand and can lead to dyspnea, which can further decrease patients’ ability to breathe spontaneously. Knebel (1990) assumed that these negative emotional responses were not only associated with, but also had a direct effect on, dyspnea in ventilated patients and thus may cause weaning failure.

Moody’s (1997) Conceptual Model of Weaning from Mechanical Ventilation in Chronic Bronchitis and Emphysema

Moody et al. (1997) proposed a conceptual model related to psychophysiological predictors of weaning from mechanical ventilation in subjects with chronic bronchitis and emphysema (CBE). Moody et al. (1997) focused their model on mechanically ventilated patient responses, which contained psychosocial and physiologic weaning predictors. The physiologic variables were represented by CBE disease severity, rapid shallow breathing index (RSBI), age, and ability to speak. Mastery, hope, social support, and dyspnea were identified as important psychologic variables in patients’ recovery or coping with acute and chronic illness. These variables were also postulated to be important for weaning in long-term ventilator patients. These physiological and psychological variables were considered directly and indirectly correlated to each other. Moody et al. (1997) suggested that long-term mechanical ventilation represented the major external stressor for patients and the weaning outcome was determined by the interplay of the physiologic variables and the psychological variables.

Both Knebel’s (1990) and Moody et al.’s (1997) models are not well tested and
need to be further confirmed. However, these nursing prediction models can provide a different perspective for clinicians to identify risk factors other than physiological factors that potentially contribute to failure to wean patients from mechanical ventilation. Early interventions might improve psychological and physiological resilience in patients, reduce days on mechanical ventilation, and improve quality of life for the mechanically ventilated patients.

Classical Conditioning Theory

The Russian physiologist Ivan Pavlov (1928) observed that dogs salivated when a bell was rung, if the bell had been rung while the dog had a juicy morsel of meat placed in its mouth. Pavlov (1928) called the procedure Classical Conditioning, the bell a conditional stimulus (CS), the meat an unconditional stimulus (US), and the salivation elicited by the CS a conditional response (CR), which is similar to the unconditional response (UR) evoked by the US. A US is a natural trigger, but a CS is a learned trigger. The CR is not a learned response, but instead is a response elicited by an acquired trigger. Under some conditions, a conditional response might look like the unconditional response upon which it is based, but under others it might not. Hence procedurally classical conditioning consists of pairing two stimuli: a CS, which is neutral and elicits no response, and an US, which elicits a response. After several pairings of CS and US, the previously neutral CS may elicit a response similar to that elicited by the US (Rescorla, 1988). Pavlov’s intention was to study an example of an acquired reflex, salivation, and to apply the principles he discovered to all species. Ultimately, the purpose was to explain how such reflexes help animals adjust and survive in their environments (Rescorla, 2003).
Fear conditioning is one of the many phenomena discovered in the Pavlovian laboratory. Conditioned fear is regarded as a hypothetical construct used to explain the cluster of behavioral effects produced when an initially neutral stimulus is consistently paired with an aversive stimulus (Davis, 1992). Following pairings of a neutral conditional stimulus and an aversive unconditional stimulus, fear responses will occur when a learned triggering stimulus (the conditioned stimulus) is encountered. For example, fear of dyspnea/suffocation is acquired by rapid learning and can be conditioned in a single trial (Campbell, Sanderson & Laverty, 1964; Mongeluzi et al., 1996). After one pairing of CS (a tone) and US (respiratory paralysis), the subsequent presentations of CS could evoke a series of responses (CRs): increased respiration rate, heart rate, electrodermal conductivity, and self-reports of fear (Campbell, Sanderson & Laverty, 1964).

Fear conditioning is persistent, but repeated presentations of the CS in the absence of the US leads to “extinction” of the fear conditioning. It is important to note, however, that “extinction” of fear conditioning does not imply that the relationship between the CS and the US is altered. Fear responses spontaneously reappear with the passage of time, when the organism is distracted, when it receives noncontingent presentations of the US, or when CS and US pairing re-occurs (see Jacobs & Blackburn, 1996 for a review).

The Brain Pathway of Emotional Conditioning

External stimuli are first processed in the brain by the sensory equipment (e.g., retina, cochlea, etc.). This information is then passed to various nuclei in the thalamus. The amygdala, a structure in the limbic system which is critical for fear conditioning to
occur, receives information through a relatively direct pathway (one synapse) from the thalamus as well highly processed information by way of pathways from the thalamus to the cortex to the amygdala. The amygdala is a structure in which lateral nucleus input of fear-inducing sensory and autonomic information and its central nucleus output to behavioral response systems converge. Killcross, Tobbins, & Everitt (1997) reported that lateral nucleus of the amygdala is the site of convergence of neural pathways that carry information about conditioned stimuli (CSs) and unconditioned stimuli (USs)/aversive reinforcers; whereas this learned association in the lateral nucleus of the amygdala will connect to central nucleus of the amygdala mediated by neural connections. Efferents of the central nucleus of the amygdala and lateral bed nucleus of the stria terminalis travel down to the periaqueductal gray (PAG) to induce freezing, to the reticularis pontis caudalis (RPC) to potentiate startle, to the parabrachial nucleus (PB) to alter respiration rate, and to the lateral hypothalamus (LH), dorsal motor nucleus of vagus (DMN), and nucleus ambiguous (NA) to influence heart rate and blood pressure (Rosen & Schulkin, 1998).

The role of the bed nucleus of the stria terminalis is to control physiological activity of the hypothalamic-pituitary-adrenal axis in response to stress. Davis, Walker, & Lee (1997) indicated that differences in neuroanatomy of specific and nonspecific fear (fear vs. anxiety) can distinguish them; the central nucleus of the amygdala is critical for cue-specific fear, the bed nucleus of the stria terminalis is involved in nonspecific fear, and the basolateral nucleus of the amygdala in both types of fear.

The direct thalamo-amygdala path, which bypasses the cortex, is a short and fast
transmission route that allows organisms to avoid potentially dangerous stimuli before they fully know what the stimuli are (inputs from the cortical pathway). The cortical pathway provides detailed information about the stimuli, but takes a longer time for the information to reach the amygdala (LeDoux, 1998). In dangerous situations, the fast direct thalamo-amygdala path appears to have adaptive value. In the presence of stimuli that warn of danger transmitted to the amygdala, the central nucleus of the amygdala releases behavioral, autonomic, and endocrine responses, and modulates reflexes of conditioned fear (LeDoux, 1998). Besides input from sensory areas of the thalamus, the amygdala also receives inputs from cortical sensory processing systems to allow more complex aspects of stimulus processing.

During fear conditioning, the information regarding integrated stimuli from the cortex arrives in the hippocampus, which permits the organism to memorize the emotional context. This is then conveyed to the amygdala, which allows emotions to be triggered by such memories. Extinction, which is described as the repeated exposure to the CS without the US, appears to be due to inputs from the medial prefrontal cortex to the amygdala. It is as if the prefrontal cortex provides the rule “In this place, at this time, the CS no longer ‘means’ (predicts, triggers) the US will occur.” The knowledge of these physiological mechanisms in the brain helps to make predictions about functions that may contribute to emotional reaction under conditioning (LeDoux, 1998). In summary, during the process of fear-conditioning, the amygdala is a key structure for the rapid preattentive detection of threat-related stimuli as well as for elaborating the processing of emotional stimuli.
State-Trait Anxiety

Multifaceted definitions were proposed for the concept of anxiety by Spielberger in 1966, in which he distinguished between trait anxiety and state anxiety, which are unidimensional constructs (Endler & Kocovski, 1999). State anxiety (A-state) was defined as a transitory emotion characterized by physiological arousal and consciously perceived feelings of apprehension, dread, and tension. On the other hand, trait anxiety (A-trait) is an individual’s propensity to respond and the various degree of state anxiety that a person will experience in stressful situations (Spielberger, 1966). In Spielberger’s state-trait theory (1966), he proposed a sequence of temporally perceived (cognitively appraised) threatening or dangerous events, initiated by external or internal stimulus conditions, and culminated in the evocation of an A-state reaction.

The degree of perceived threat and the individual’s past experience in coping with such stimuli, which might be regarded as A-trait, will proportionally affect the intensity of A-state reaction. A-states vary in intensity and fluctuate over time as a function of the threat that impinges upon an individual; however, A-trait will remain constant. In addition, early childhood experience is considered to influence the development of individual differences in A-trait in Spielberger’s (1970) theory. High A-trait individuals might have greater A-state as they encounter threatening situations. However, Spielberger (1966) mentioned that the level of A-trait is not expected to elicit response in an A-state, especially if the stimulus is extremely small or large. Shedletsky & Endler (1974) concluded that the core of state-trait theory is that the intensity and duration of A-state fractions are dependent upon the degree and persistence of threat confronting an
individual; simply, “person by situation” approach is hypothesized to assess the A-state response. Spielberger (1966) further indicated that A-state is a signal that initiates a behavior sequence leading to avoiding or dealing directly with the danger situation.

Based on Spielberger’s definitions of state and trait anxiety, Endler & Edwards (1985) proposed an interaction model to evaluate state and trait anxiety as multidimensional constructs. The interaction model suggested that state anxiety is a function of the interaction between a specific facet of trait anxiety and a congruent situational threat. They postulated two facets of state anxiety: cognitive and emotional reactions. There are at least four facets of trait anxiety: social evaluation (interpersonal), physical danger, ambiguity, and daily routines (Endler & Edwards, 1985). Therefore, Endler & Edwards (1985) argued that high A-trait might not necessary reflect the high A-state in all types of threatening situations.

Harrigan, Wilson, & Rosenthal (2004) described the experience of anxiety as a perception of a threatening event, either physiologically or psychologically. This threatening event will lead to a physiological response and various attempts to cope with the arousing stimuli. In addition, they indicated that state anxiety is regarded as a transitory, situational response to anxiety—eliciting stimuli and the moment-to-moment change in emotion; whereas trait anxiety is defined as a stable feature of personality.

Physiological variables, such as heart rate, respiratory rate, and systolic blood pressure, were significantly correlated to A-state but only slightly correlated to A-trait (Spielberger, 1966). The findings from more recent studies indicated that individuals with higher A-trait experience and higher A-state present demonstrate more illness behavior
than those with lower A-trait. In evaluating state and trait anxiety in patients with Huntington’s disease undergoing PET scans, Boivin, Giordani, & Betley (1991) found that those having higher trait anxiety scores also had significantly higher state anxiety measures. The similar results were also found in general rheumatoid arthritis (RA) patients (VanDyke, Parker, & Smarr, 2004). In summary, the level of A-state may correlate to the level of A-trait; however, the A-trait may not directly correlate to the physiological responses elicited by the high level of A-state.

The Spielberger State-Trait Anxiety Inventory (STAI) was developed for self-reporting both A-state and A-trait in how people presently feel and how they feel in general, respectively (Spielberger, Gorsuch & Lushene, 1970). In order to overcome the barrier of patients’ inability to complete lengthy scales, Marteau & Bekker (1992) developed a six-item short form of the state scale of the Spielberger State-Trait Anxiety Inventory. They found that the six-item scale had a high correlation (r = .95) with the full-form STAI and had an acceptable reliability coefficient (α = .82). The validity of the six-item short form STAI was proven by showing no significant difference between the mean full-form STAI score and the means prorated from the short-form score. Researchers concluded that this briefer six-item short form will more likely maximize response rates and minimize the number of response errors and unanswered items. However, Marteau & Bekker’s (1992) short-form STAI only exhibited a moderate internal consistency coefficient alpha in two studies (Chlan, 1998; Wong, Lopez-Naha, & Molassiotis, 2001) when used to measure anxiety among mechanically ventilated patients in two studies; .67 and .72, respectively. Chlan, Saves, & Weinert (2003) also developed a shortened state
anxiety scale from the Spielberger STAI for patients receiving mechanical ventilatory support. They reported that this six-item shortened scale had a Cronbach’s alpha of .78 and a correlation of .92 to the 20-item full-form of STAI. However, due to the different sample population used to develop these two short-form STAI, only one item remained the same in both of these short-form scales.

Concept Analysis of Fear and Anxiety

In the literature, the concepts of anxiety and fear were vaguely used to describe patients’ aversive emotions. However, anxiety and fear are two distinct concepts that are caused by and result in different situations. It is important to distinguish between these two concepts for clinical providers.

Fisher (1970) defined fear as relating to a definite feared object, but he also mentioned that Freud’s neurotic anxiety refers to a painful experience based upon a dangerous situation in the external world. Epstein (1967) distinguished fear from anxiety by whether or not the arousal evoked by threatening circumstance is channeled into appropriate purposive action. In his view, fear is an avoidance motive in which a high level of arousal is directed into flight, whereas anxiety is viewed as a state of unresolved fear in which the arousal that occurs following the perception of threat persists and becomes diffuse because the individual is unable to direct it into purposive behavior. Goodwin (1986) described anxiety as a vague diffuse uneasiness, without a definite object being perceived as dangerous. Whitley (1997) indicated that anxiety can be differentiated from fear in that the cause and nature are not identifiable with the anxiety. In other words, the stimulus for anxiety is more likely to be internal, less specific or
clearly defined; in contrast, the stimulus for fear is usually specific, identifiable, and external and the danger is approaching (American Psychiatric Association, 1994).

**Characteristics**

Taylor-Loughran et al. (1989) conducted a study to define characteristics of anxiety and fear. They reported that apprehension, worry, and facial tension were characteristics that occurred most frequently in anxiety. The characteristics of fear were the feelings of being scared and apprehensive, with the ability to identify the object of fear. In Whitley’s (1997) study, they reported that there are two characteristics shared between fear and anxiety based on nurse expert validation, apprehension and cardiovascular excitation (caused by sympathetic stimulation). However, cardiovascular excitation is regarded as an attribute of fear that may reflect the body’s preparation for a defensive response (Bay & Algase, 1999), whereas during anxiety, it may be more subjective and chronically elevated over days or weeks.

**Neurobiological underpinnings of fear and anxiety**

Fear circuit involves the dorsolateral periaqueductal gray and superior colliculus that mediates more active defensive behaviors. The amygdala is the center of a defense system involved in both the expression and acquisition of conditioned fear. The sensory information will enter the amygdala through its lateral and basolateral nuclei and further project to the central nucleus of the amygdala. Subsequently, the central nucleus will project the sensory information to a variety of hypothalamic sites, the central gray, and brainstem target areas that directly mediate specific signs of fear and anxiety (Lang, Davis, & Öhman, 2000). This pathway starts at the preconscious level and results in a
neurochemical release, autonomic nervous system responses, or behavioral changes.

The anxiety circuit involves the bed nucleus of stria terminalis, which is so-called extended amygdala and is highly similar to the central nucleus of the amygdala in terms of its transmitter content, cell morphology and efferent connections (Lee & Davis, 1997). The bed nucleus of stria terminalis involve the elevations of startle that are more long-lasting than explicit cue conditioning. Anxiety is evoked by a response to threat and punishment or non-reward and mismatch among multi-modal sensory information, which communicates with the motor programming system involving the prefrontal cortex, the nucleus accumbens, and caudate motor system.

Corticotropin-releasing hormone (CRH) is released during the period of fear and anxiety. Some of CRH may come from the neurons in the central nucleus of the amygdala that project to or act on receptors in the bed nucleus of the stria terminalis (Lee & Davis, 1997). Therefore, phasic (fear) activation of the amygdala by certain stressors could lead to long-term activation (anxiety) of the bed nucleus of the stria terminalis via corticotrophin-releasing hormone. On the other hand, the similar efferent connections to various hypothalamic and brainstem target areas in both the bed nucleus of the stria terminalis and the central nucleus of the amygdala will lead to the specific signs and symptoms of fear and anxiety (Lang, Davis, & Öhman, 2000).

**Antecedents**

Antecedents to anxiety are having either the “perception of threat” or the feeling of “impending change,” which is caused by the nonspecific internal states of mismatch. Anxiety arises in response to a vague, nonspecific threat and is not directly linked to an
external source, whereas fear is a result of disruption by a perceived source that is identified as threatening (Bay & Algase, 1999). Therefore, antecedents of fear are having the feeling/emotion and a stimulus to provoke fear (Bay & Algase, 1999). Bay & Algase (1999) also indicated that a threat to more basic biological needs (i.e., exposure to suffocation, closed spaces, or near death) would result in fear, whereas perceived threat to biological homeostasis (i.e., financial security) would yield anxiety.

**Consequences**

Whitley (1997) indicated that consequences of both fear and anxiety can be either positive or negative depending on the person’s response to the situation. In spite of these commonalities, Bay & Algase (1999) indicated that the transition period (neurobiological reaction) of the outcomes is clearly different.

Fear will cause selected behaviors such as fight, flight, or freeze motoric behaviors, piloerection, defecation, autonomic changes, and adrenal hormone release. Fear memories are hard to extinguish and can lead to avoidance of those circumstances recalled to be threatening (Bay & Algase, 1999). Anxiety may result from the transformation of a set of subjective responses (mismatch) into a series of objective responses: vigilance, decline in short-term memory, confusion, as well as sympathetic responses.

**Conditioned Fear and Anxiety**

Leavitt (1953) proposed that if there is no specific conditioned fear to activate, a resulting perception of anxiety is unlikely. Anxiety is regarded as the other side of fear, it is caused by a different degree of fear and it temporarily is separated from the object of
fear. In other words, as the conditioned fear was acquired, it was memorized and put into the pre-conscious level. Before re-encountering the fear situation, an individual may recall the memory, then the consciously dominant perceived affect is anxiety (Leavitt, 1953). However, if an individual encountered the fear situation again, the fear pattern would be present. Salter (1961) incorporated Pavlovian conditioning in human adaptation with the concept of the fight/flight response. He suggested that anxiety is anticipatory in nature and possesses biological utility for living organisms. The adaptive motivation to deal with possible traumatic events in advance of their actual occurrence could help them to avoid harm. By this view, which Pavlov himself accepted, classical conditioning critically links the emotional anxiety accompanying cognitive anticipation of a threatening event with behavioral preparation to defend oneself (e.g., fight, flee, or freeze) from the threatening event.

Davis, Walker, & Lee (1997) indicated that differences in the neuroanatomy of fear and anxiety (specific vs. nonspecific fear) can be used to distinguish them; the central nucleus of the amygdala is critical for cue-specific fear, whereas the bed nucleus of the stria terminalis is involved in nonspecific fear. Rosen & Schulkin (1998) hypothesized that the amygdala and its connections play a core role in both normal fear and pathological anxiety. The stimulation of the amygdala will increase vigilance, arousal, and attentiveness. The hyperexcitability of fear circuits is caused by a process of neural sensitization or kindling in which psychosocial stressors will lead to heightened awareness and response to subsequent threat and danger. In addition, under fear stimuli the release of neuroendocrine hormones will increase, which leads to excitability of fear
circuits (amygdala and extended amygdala). Accordingly, Rosen & Schulkin (1998) postulated that the strong, repetitive fear elicitation results in reduced thresholds for activation and hyperexcitability in fear circuits. This enhances hypervigilance and increased behavioral responsivity, which in turn leads to pathological anxiety. Barlow (2002) explained that pathological anxiety is described primarily as high negative affect associated with a sense of uncontrollability and characterized by hypervigilance suggesting a readiness to respond to danger or negative events. Fear is one of the major normal precursors for the development of pathological anxiety disorders.

Bishop, Duncan, & Lawrence (2004) conducted a study to extensively test their hypothesis that amygdala responsivity not only to attended threat-related stimuli but also to unattended ones, and that it varied with individual differences in state anxiety. The results supported their hypotheses and indicated that highly anxious participants showed an increased amygdala response to fearful versus neutral stimuli when both stimuli were attended to, and when they occurred outside the current focus of spatial attention. However, less-anxious individuals showed an increased amygdala response only to attended fearful stimuli. They concluded that anxiety acts to influence a pre-attentive threat evaluation system and sensitization of the amygdala response to threat-related stimuli, which plays a role in anxiety. In addition, they posited that anxiety might have an additive effect on the top-down and bottom-up mechanism, in which the control processes can modulate the amygdala response, determining the appropriate allocation of attention to threat-related stimuli. Individuals with low-anxiety have greater modulation of the amygdala response to fearful stimuli by attention focus than highly anxious
individuals.

State Anxiety & Dyspnea

Luce & Luce (2001) mentioned that the term “dyspnea” is derived from the Greek; “dys” means difficult and “pneuma” means breath. The American Thoracic Society (ATS) (1999) generally defined dyspnea as the subjective experiences of difficult, labored, uncomfortable breathing and that it sometimes might mix with physical signs and symptoms. However, observed changes in either rate or depth of respiration might not be necessary to cause the subjective experiences of breathlessness/dyspnea (Gift, 1990). These experiences are caused by interactions among multiple physiological, psychological, social, and environmental factors, and may lead to physiological and behavioral responses (ATS, 1999). The mechanism of dyspnea may originate from central and peripheral chemoreceptors in response to increases in PaCO2 and decreases in PaO2, or may result from the mismatch between the afferent information from respiratory receptors and respiratory motor activity (Luce & Luce, 2001).

Dyspnea is regarded as the major symptom present in the acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Gift et al. (1986) conducted a study to determine the psychologic and physiologic factors related to dyspnea in COPD patients. The results indicated that the level of dyspnea is significantly correlated with the use of accessory muscles of respiration and the level of anxiety. Bailey (2004) conducted a narrative research to explore the affective component of dyspnea/anxiety in AECOPD. Patients and caregivers reported that inability to avoid and effectively manage experienced breathlessness made them feel a sense of disability or vulnerability in
emotional function. They felt fearful and scary during an episode of acute dyspnea in which the seriousness of future dyspneic events would be the biggest fear for them. In addition, they indicated that the relationship between emotional functioning and breathlessness is both circular and complex. Participants believed that emotional dysfunction was a result of both chronic breathlessness and increased physical or emotional activity. Accordingly, Bailey (2004) concluded that patient-reported anxiety can provide an important and potential measurable sign of invisible dyspnea for COPD patients in acute respiratory distress. Therefore, health care providers cannot assume that the dyspnea is caused by patients’ anxiety, but anxiety is a marker of breathlessness.

In contrast to Bailey’s (2004) statements, there are several studies indicating that effectiveness of psychotropic medications (Argyropoulou et al., 1993; Papp et al., 1995; Smoller et al., 1998) and cognitive-behavioral approaches (Eiser et al., 1997; Gift, Moore, & Soeken, 1992) in COPD patients could reduce depressive or anxiety symptoms or dyspnea, and further improve exercise tolerance and pulmonary function. Several research studies (Agle, Baum, Chester, & Wendt, 1973; Levin, Weiser, & Gillen, 1986; Belman, Brooks, & Ross, 1991) tested the physiologic and psychological dimensions of dyspnea and found that repeated exposure to higher than usual dyspnea in a safe environment will facilitate patients in tolerating more activities at home. These researchers suggested that desensitization to the fear and anxiety associated with dyspnea resulted in an increase in patients’ activity. In other words, a decrease in the sense of the fear and anxiety will lead to a decrease in the dyspnea intensity.

In addition, Carrièri-Kohlman et al. (1993) conceptualized the relationship
between anxiety and dyspnea as “anxiety-dyspnea-anxiety cycle” and posited that patients’ emotional reaction to a sense of breathlessness exacerbates their perception of breathlessness. Dale, Spitzer, Schechter, & Suissa (1989) conducted a study to test the association between psychological status and the reporting of respiratory symptoms. They found that those with more psychological symptoms, especially anxiety, were more likely to report respiratory symptoms (including dyspnea). They concluded that the result was consistent with the known influence of psychological disorders on somatic complaints seen in clinical practice (Dale, Spitzer, Schechter, & Suissa, 1989). In Carrieri-Kohlman et al.’s (1996) other study, they found that patients with COPD can distinguish between dyspnea and their anxiety about that symptom. Based on this result, Carrieri-Kohlman et al. (1996) suggested that recognizing a patient’s ability to perceive the affective dimension of dyspnea may improve medical practitioners’ ability to select medical treatment for individuals. Treatments used to reduce fear, anxiety, or distress should be most effective for patients who have significant emotional responses to dyspnea, but may be ineffective for individuals without these affective reactions to the symptom. Accordingly, these results would support the postulation of anxiety as a predictor of pulmonary deterioration and subjective breathlessness rather than a sign of them.

Further, there were many studies conducted to test the correlation between feelings of control and the level of dyspnea (Moody, McCormick, & Williams, 1990; Thompson, 1981). The results indicated that if patients believe they have cognitive or behavioral control of a feared event, the event may change from unendurable to
endurable and, subsequently, the patients feel less anxious and tolerate the shortness of breath more easily. In Knebel et al.’s study (1994), they found that dyspnea was highly correlated to anxiety during the ventilator weaning process, as measured by visual analogue scales. Accordingly, these results would support the postulation of anxiety as a predictor of pulmonary deterioration and subjective breathlessness rather than a sign of them.

Respiration, Emotion, and Cognition

Ley (1999) suggested that Pavlovian conditioning provides a theoretical framework for integrating emotion, cognition, and instrumentally conditioned behavior to comprehend the psychophysiology of and psychopathology related to breathing. Furthermore, Ley (1999) suggested that a modern interpretation of Pavlovian conditioning includes the adaptive process associated with it. Based on research findings, there are several potential ventilatory changes presented during the adaptive process of conditioning emotions: (1) increased minute ventilation (hyperventilation) that will be manifested as either increased tidal volume or increased respiration frequency, or both; (2) decreased end-tidal carbon dioxide (PetCO₂); (3) increase in the length of the respiratory cycle that is presented by an increased apnea pause following the inspiratory phase; and (4) increased total respiratory resistance (Ley, 1999). Accordingly, it is clear that emotional arousal gives rise to changes in ventilation. Hyperventilation is regarded as breathing a volume of air that exceeds metabolic demand for O₂ (Ley, 1999). In addition, hyperventilation is typically represented by low PCO₂.

On the other hand, the magnitude of these respiratory changes represents the
strength of conditioned fear, which is a direct function of the intensity of the US (Kalish, 1954). Mongeluzzi et al. (1996; 2003) conducted an animal study and found that the magnitude of the CR (fear) was directly affected by the intensity of the US (different concentration of CO₂: 0%, 5%, 35%, 100%) which evoked dyspnea and caused fear of suffocation (UR). In addition, they found that a higher degree of severity of the initial US would cause a greater resistance to extinction of CR. Forsyth & Eifert (1998) examined the relation between the intensity of CO₂-induced (20% vs. 14%) psychophysiological responses and content-specific fear conditioning (fear-relevant vs. fear-irrelevant) in humans. They found that conditioned responses, represented by several physiological measures (electrodermal and cardiac responses), were greater and more resistant to extinction when associated with fear-relevant stimuli compared with fear-irrelevant stimuli. In addition, the effect of fear-relevance was stronger to the more intense CO₂-enriched air. Based on the findings from conditioning studies, there is a bi-directional relationship between emotions and breathing.

The relationship between cognition and breathing can be demonstrated by the polygraphic lie-detector test and the think test. In a polygraphic lie-detector test, increased respiratory rate and depth, or changed breathing pattern from diaphragmatic to thoracic, accompanied by increased electrodermal response and blood pressure in response to the presentation of salient information, can be regarded as the evidence that subjects are trying to conceal the truth (Podlesny & Raskin, 1980). The think test is based on the effects of emotion-eliciting thoughts on breathing, which is represented by the changing of PetCO₂, to diagnose psychosomatic disorders (Nixon, Freeman, & King,
Based on Pavlovian conditioning, Ley (1987, 1989) developed a dyspnea/suffocation theory of panic disorder. This theory suggests that an encounter with a prolonged stressful event can produce a sudden unexpected sense of strained breathing with uncontrollable dyspnea that is considered a primary panic attack. Subsequently, if the events evoke an anticipatory response (e.g., fear or anxiety for strained breathing with uncontrollable dyspnea) that signals the occurrence of an attack similar to the ones they previously experienced, then secondary anticipatory panic attacks can occur. Echoing Ley’s theory, Klein’s (1993) suffocation alarm theory puts respiratory abnormalities, especially hyperventilation, at the core of panic disorder. In addition, Barlow (1989) proposed that a sense of uncontrollability over negative life events is a critical psychological mechanism in the production of anxiety and fear, and perhaps in the development of panic disorder. Based on these theories, the expectancy effect in the production of panic attack and the fear response with uncontrollable dyspnea clearly suggests that Pavlovian conditioning unites emotion, cognition, and conditioned emotional responding.

Research Findings of Physiological Weaning Problems

There are a tremendous number of studies related to mechanical ventilation use and ventilator weaning. Due to the growing MV related problems and medical cost for prolonged mechanically ventilated patients, this review focuses on weaning predictors that have been tested. Five categories of physiological predictors were commonly tested among contemporary studies and will be reviewed here: gas exchange, respiratory drive,
competence of inspiratory muscles, respiratory workload, and integrated weaning indices.

**Gas Exchange**

Gas exchange failure is a major indication for intubation and mechanical ventilation. Therefore, several studies used indices of gas exchange, such as the arterial blood gas value, the alveolar-arterial oxygen gradient (PAO$_2$-PaO$_2$), the arterial alveolar oxygen ratio (PaO$_2$/PAO$_2$), and the ratio of arterial oxygen partial pressure to fractional inspired oxygen concentration (the PaO$_2$/FiO$_2$ ratio), to predict the weaning outcomes (Bouachour et al., 1996; Epstein et al., 1997; Gandia & Blano, 1992; Krieger et al., 1997; 1989; Tobin et al., 1986; Torres, 1989). However, the changes of PaCO$_2$ and pH were the only predictors that distinguished failed weaning trials from successful weaning trials (Krieger et al., 1997; 1989; Tobin et al., 1986; Torres, 1989). Tobin et al. (1986) found that the significant increase in PaCO$_2$ and decrease in pH in the failed weaning group were due to the development of rapid, shallow breathing with consequent inefficient gas exchange during the weaning process. Simultaneously cardiac output increased as a result of augmentation of venous return with reduced pleural pressure during resumption of spontaneous breathing, which did not cause change in PaO$_2$.

Even though studies found that ventilation-perfusion (VA/Q) inequality deteriorated during weaning, the results did not show that VA/Q inequality would affect the weaning outcomes (Ferrer et al., 2002; Rodriguez-Roisin, 1994; Torres et al., 1989). Researchers explained that VA/Q inequality is not the only factor to affect pulmonary gas exchange, which might be influenced by other factors such as cardiac output, minute ventilation, or oxygen consumption. In addition, adequate oxygenation is necessary for a
weaning trial, which also explains why the indices of gas exchange are poor predictors of weaning outcomes (Epstein, 2000).

Respiratory Central Drive

Before inspiration, negative pressure is generated by contraction of the inspiratory muscles against an occluded airway, which is directly driven by a central neural stimulus. The measurement of this negative pressure .1 second from the onset of inspiration, known as airway occlusion pressure (P0.1), is a useful index of respiratory center motor output or drive (Conti et al., 1996; Tobin & Alex, 1994). Faced with an increased mechanical load in acute respiratory failure patients, increased inspiratory neuromuscular activity is needed to maintain adequate alveolar ventilation, and these patients should show a high P0.1 (Capdevila et al., 1995; Murciano et al., 1988; Sassoon et al., 1987). In addition, the high P0.1 is regarded as a valid index to detect the possibility of respiratory muscle fatigue and as an accurate predictor for weaning failure in COPD and acute respiratory failure patients (Capdevila et al., 1995; Conti et al., 1992; Murcoano et al., 1988; Purro et al., 2000; Sassoon et al., 1987). Conti et al. (1996) found that a value of P0.1 lower than 4.5 cmH2O during the first phase of a high-pressure support trial can predict successful weaning in COPD patients. Purro et al. (2000) found coupling of high P0.1 and low tidal volume (VT) in ventilator-dependent patients and concluded that low VT was caused by a poor transformation of that high central drive into the ventilatory output.

The measurement of P0.1 is influenced by lung volume, chest configuration, and respiratory muscle strength (Epstein, 2000). Muscle exhaustion or intrinsic PEEP
secondary to hyperinflation can falsely cause a low P0.1 value (Conti et al., 1996; Fernandez et al., 1990; Whitelaw & Derenne, 1993). In order to correct the value of P0.1 affected by respiratory muscles, Capdevila et al. (1995) and Gandia & Blanco (1992) both used P0.1/MIP to predict the weaning outcome in prolonged mechanical ventilation patients, and they found a high specificity (1.0 & .83) and sensitivity (.98 & .82).

The mean inspiratory flow rate (VT/Ti), as the ratio of tidal volume to inspiratory time, is another index of respiratory drive (Tobin et al., 1986). Van den Aardweg & Karemaker (2002) found that coherent oscillation in PetCO2 and Vi/Ti, where Vi/Ti was delayed .20 cycles per breath, was interpreted as a manifestation of chemoreflex activity. The positive predictive value of VT/Ti to predict the respiratory drive was 71% to 79% in patients with chronic obstructive pulmonary diseases (COPD) and restrictive lung diseases (Tobin et al, 1986). A relatively higher VT/Ti accompanied by a higher PaCO2 was found in patients who failed the weaning trial (Tobin et al., 1986), as would be expected.

Respiratory Muscle Capacity

Maximum inspiratory pressure (MIP) is defined as peak negative pressure on maximum inspiration (Krieger et al., 1989); it gives information about the ability of the inspiratory muscles to generate force at a particular volume and is regarded as an indicator of neuromuscular competence (Bruton, 2002; Tobin & Alex, 1994; Vassilakopoulos et al., 1996). Sahn and Lakshminarayan (1973) indicated that if MIP values were < -30 cm H2O, this led to a successful weaning outcome; but if MIP values were > -20, this would likely lead to weaning failure. Krieger et al. (1989) also reported
that MIP was significantly lower among patients over 70-years-old in the unsuccessfully weaned group. However, MIP was found to have low specificity in predicting the weaning outcomes in several studies and lacked a clear cutoff point to distinguish successful weaning from weaning failure (Burns et al., 1994; Capdevila et al., 1995; 1998; Clochesy et al., 1997; Yang & Tobin, 1991). The high variation and low reproducibility of the MIP measurement may explain its poor performance in predicting the weaning outcomes. MIP values were highly affected by the patients’ motivation and visualization of the effort (Capdevila et al., 1995). They also strongly varied by administering investigators and day of trial (Multz et al., 1990). However, Truwit and Marini (1992) argued that if $P_{0.1}$ was greater than 2 cm H2O prior to the MIP maneuver, the value of MIP was not significantly different between coached and uncoached MIP maneuvers. Moreover, a sufficient respiratory drive is important for attaining reliable MIP measurements.

The concept of tension-time index (TTI), which is the product of the respiratory duty cycle ($Ti/T_{tot}$) and the ratio of the mean transdiaphragmatic pressure to the maximal transdiaphragmatic pressure ($P_{di}/P_{di,max}$), was first applied to test the endurance characteristics of the diaphragm by Bellemare and Grassino (1982). TTI is related to the endurance time; if TTI is greater than .15 that means the breathing task can not be sustained for long and will result in a diaphragmatic fatigue (Bellemare & Grassino, 1982).

Vassilakopoulos et al. (1996) indicated that endurance is determined by the balance between energy supplies and energy demand and also the balance between
inspiratory load and neuromuscular competence. Bellemare and Grassino (1982) argued that TTI is a better indicator than transdiaphragmatic pressure (Pdi) to predict the endurance time of the diaphragm, because TTI also take into account the blood flow of diaphragm that is considered to relate to Ti/Ttot. During the inspiratory period, the intramuscular vessels are compressed by the contracting respiratory muscles and thus limit the blood flow. In addition, the blood flow of the diaphragm will determine the energy supplied. Pdi/Pdi,max, that is the other part of TTI, represents the balance between the elastic and resistive loads imposed on the diaphragm and the neuromuscular competence.

McCool et al. (1986) reported that an increase in inspiratory flow rate, which is related to increased velocity of shortening of the inspiratory muscles and increased rate of muscle energy consumption, could have reduced the endurance of the inspiratory muscles and reduced the critical value of Pdi/ Pdi,max among their study population. Clanton and colleagues (1990) tested the influence of changes in inspiratory flow, tidal volume, and duty cycle on sustainable/endurance inspiratory pressure development in 6 normal subjects. They found that the sustainable dynamic pressures remained predictable fractions of initial dynamic pressure under a constant Ti/Ttot. However, increases in duty cycle led to proportional decreases in the sustainable fraction of initial maximum dynamic pressure.

Milic-Emili (1986) mentioned that the concept of the tension time index (TTI) should be applicable not only to the diaphragm, but to the global respiratory muscles (TTmus). TTmus = Pi/ Pimax X Ti/Ttot; Pi is mean pressure developed by the inspiratory
pressure at functional residual capacity (FRC) generated at the mouth. Ramonatxo et al. (1995) indicated that TTmus is a valid means of evaluating potential inspiratory muscle fatigue in patients with COPD, because of the change in the pattern of ventilatory muscle recruitment in COPD from diaphragmatic predominance to rib cage inspiratory muscle predominance. Thus, the rib cage muscles can be fatigued independent of diaphragmatic fatigue. Further, Capdevila et al. (1998) measured the TTmus to detect fatigue of the global respiratory muscle in MV patients and found a high TTmus appeared in the failed weaning group (Capdevila et al., 1998; Vassilakopoulos et al., 1998). Vassilakopoulos et al. (1998) found that TTI is a major pathophysiologic determinant of weaning failure or success and emphasized that it could predict that task failure would ensue within a limited time period; this is inversely related to the TTI value.

Respiratory Muscle Workload

Based on Tobin et al.’s (1986) finding of rapid shallow breathing in the unsuccessfully weaned group, Yang and Tobin (1991) developed a new index to predict weaning outcomes: the ratio of respiratory frequency (f) to tidal volume (VT), known as the rapid shallow breathing index (RSBI). They found that f/VT of 105 breath/min/L or more could accurately predict a failed weaning trial with high sensitivity (.97), specificity (.64), and receiver operating characteristic (ROC) (.89). However, Purro et al. (2000) also found that a high f/VT ratio (>100 breath/min/L) was highly predictive of weaning failure in COPD patients, but a low f/VT (<80 breath/min/L) was not always associated with a successful weaning. The latter might be due to ineffective inspiratory efforts caused by hyperinflation. Capdevila et al’s study (1995) also indicated that the cutoff value of 100
breath/min/L for f/VT had a high sensitivity (.97) but low specificity (.3) in predicting weaning failure and weaning success respectively.

Vassilakopoulos et al. (1998) defined that f/VT as a major pathophysiologic determinant underlying the transition from weaning failure to weaning success, but, similar to Yang and Tobin (1991), they had difficulty finding what was responsible for f/VT. They believed that if the f/VT represented only a response to loading, it should be strongly correlated with the indices of activity of the respiratory muscles (such as TTI). However, the evidence showed that f/VT ratio and TTI were not correlated during weaning failure (Vassilakopoulos et al., 1998). Based on theoretical considerations and Holliday & Hyers’s (1990) findings, Vassilakopoulos et al. (1998) proposed that the rapid, shallow breathing pattern is a response of the respiratory center to the anxiety that occurred during the weaning trial. Yang and Tobin (1991) suspected that an elevated f/VT ratio is a stress response reflecting an imbalance between respiratory neuromuscular reserve and respiratory demands.

During breathing, the respiratory muscles contract mostly during inspiration, but relax during expiration. The respiratory duty cycle (Ti/Ttot) can be described as that portion of the respiratory cycle at the time when the inspiratory muscles are active (Tobin et al., 1986). Capdevila et al. (1998) found that patients in the early weaning stage had a decrease in the value of Ti/Ttot to compensate for the increased high inspiratory pressure. Compared to the successful weaning group, the Ti/Ttot increased over the entire weaning period in the failed weaning group, which indicated that the patients lost the ability to minimize the impact of the inspiratory load. Accordingly, increase in the Ti/Ttot indicated
a decrease in the respiratory muscle performance and also an increase in the respiratory workload at the end of weaning stage.

Intrinsic positive end-expiratory pressure (PEEPi) is positive pressure present in the alveoli at the end of expiration; normally, this pressure should equal zero. In the instance where PEEPi exists, this would lead the inspiratory muscles to develop an equal amount of pressure to initiate the next inspiration, which would increase the elastic threshold load (Zakynthinos, Vassilakopoulos, & Roussos, 1995). The high PEEPi resulting in excessive respiratory load was found as the major determinant of ventilator-dependence and weaning failure in COPD patients (Appendini et al., 1996; Capdevilla et al., 1998; Purro et al., 2000). Researchers concluded that PEEPi caused the high workload that consequently reduced pressure generating capacity of the inspiratory muscles and caused weaning failure.

The respiratory muscle work of breathing (WOB) estimates the work required to inflate the lung and overcome airway resistance. However, in ventilated patients, it also includes the additional work needed to overcome the ventilatory system (Petrini, Evans, Wall, & Norman, 1998). The total work of breathing includes the resistive and elastic work of breathing. The WOB can be determined by transpulmonary pressure-volume changes and is usually reported in Joules, normalized either by volume (J/L) or by time (J/minute).

Increases in WOB can result from increased elastic and resistive loading (Banner, Kirby, Gabrielli, Blanch, & Layon, 1994), which were found highly correlated with ventilator dependence and weaning failure (DeHaven et al., 1996; Fiastro, Habib, & Shon,
An increase in elastic loading is considered secondary to decreased total compliance (lung and chest wall). In addition, increases in resistive loading result from an increase in total resistance, which includes physiologic airway resistance and the imposed resistance of the breathing apparatus. Accordingly, increases in elastic and resistive loading will lead to an increase in the elastic and resistive work of breathing, respectively (Banner, Kirby, Gabrielli, Blanch, & Layon, 1994). On the other hand, based on previous studies Levy, Miyasaki, & Langston (1995) used the threshold value of WOB of < .75 J/L to predict successful extubation, but failed to find it a better predictor of weaning than other standard weaning predictors. These researchers concluded that the predictor value of respiratory work as an index of weaning outcomes needs to be further defined based on the different patient population. However, Epstein (2000) indicated that the measurement of WOB is still valuable for health care providers to explore the cause for weaning failure and identify pathophysiologic process that further facilitate the development of therapeutic intervention.

**Integrated Weaning Indices**

Many integrated respiratory parameters have been proposed and are expected to have a better predictive effect than individual parameters. Yang & Tobin (1991) developed the “CROP” that represented and integrated thoracic compliance, respiratory rate, arterial oxygenation, and maximal inspiratory pressure. It reflected pulmonary gas exchange and the balance between respiratory demands and respiratory-muscle reserve. The study showed that the CROP was better than the conventional weaning parameters, but was less predictive than f/VT (Chen et al., 1994; Yang & Tobin, 1991).
The Weaning Index (WI) was developed by Jabour et al. (1991), and was based on three components of ventilatory capacity: respiratory mechanics, gas exchange, and respiratory muscle strength and endurance. Jabour et al. (1991) reported that the WI could successfully predict the weaning outcome with high sensitivity (.96), specificity (.95), positive predictive value (.96), and negative predictive value (.95) in MICU patients (MV $\geq$ 3 days) (Jabour et al., 1991). However, the WI did not accurately predict the weaning outcomes in SICU or PMV patients (MV $\geq$ 7 days) (Chen et al., 1994; Burns et al., 1994), and it also was regarded as a difficult calculation for clinical settings (Chen et al., 1994; Burns et al., 1994).

Burns et al. (1994) integrated general, pulmonary, and mechanical factors to develop a Burns Weaning Assessment Program (BWAP), which is a 26-factor bedside assessment checklist. Comparing the BWAP with WI, f/VT, CROP, and negative inspiratory pressure to predict weaning outcomes in ICU patients (MV $\geq$ 7 days), the results showed that none of these weaning indices have strong predictive power related to weaning outcome (Burns et al., 1994). However, Burns et al. (1994) indicated that the slightly progressive upward trend of the BWAP score measured before and during weaning was considered the best tool to track trends in the weaning progress specifically for difficult-to-wean patients.

Research Findings of Psychological Weaning Problems

Compared to the extensive studies that have tested the physiological weaning predictors for weaning, there are only a few studies conducted to test the psychological factors to predict weaning outcome. Due to the patients’ illness, weakness and difficulty
in communicating with an endotracheal tube, it is really difficult to get comprehensive and accurate subjective psychological data from mechanically ventilated patients. Therefore, most of these studies used a retrospective design to explore these patients’ experiences while being on mechanical ventilation and during their weaning process. Few prospective studies were conducted to test the correlation between weaning outcome and psychological distress, which were more focused on anxiety and dyspnea intensity.

Patients’ Perception of Being on Mechanical Ventilation and Weaning

In Logan & Jenny’s (1997) qualitative study, patients recalled their mechanical ventilation experience and weaning process as a mixed experience, though most of the time it was described as miserable. Lack of energy, confusion about their situation, pain, altered levels of consciousness, lack of information, and difficulty in communicating were negative factors reported by these mechanically ventilated patients. Logan & Jenny (1997) indicated these negative factors would affect patients’ efforts to adjust and recover from mechanical ventilation. Similar results were found in Rotondi et al.’s (2002) study, where one hundred ICU patients who had more than 48 hours of mechanical ventilation recalled their experiences. Pain, fear, anxiety, lack of sleep, feeling tense, inability to speak/communicate, lack of control, nightmares, and loneliness were indicated as being moderately to extremely bothersome during mechanical ventilation.

Nineteen successfully weaned patients described feeling highly uncertain and stressed while on mechanical ventilation and during the weaning process (Wunderlich et al., 1999). These patients reported that more information relating to their needs associated with the weaning process would have minimized their stress. In addition, pulmonary
patients perceived a higher degree of uncertainty and stress during the weaning process than nonpulmonary patients in this study group. Higgins (1998) conducted a prospective study to explore the perception of fatigue and its associated factors, such as nutritional status, depression, and sleep-rest in chronically, critically ill patients receiving long-term ventilatory assistance (LTMV) for more than 7 days (n=20). The results demonstrated that patients who underwent LTMV were undernourished and experienced fatigue, a depressed mood state, and disruptions in their sleep-rest patterns. Only fatigue was strongly correlated with depression, but was not correlated with sleep-rest or nutritional status.

According to reports from patients, psychological distress obviously occurs in patients while on mechanical ventilation and during weaning trials. However, Lowry & Anderson (1993) found that the subjects’ level of fear and anxiety from mechanical ventilation decreased as days on ventilation increased. The ventilator was internalized and apparently became an extension of the patient self. Lowry & Anderson (1993) interpreted this phenomenon as the construct-created-environment in Neuman systems model, which is a self-help phenomenon in response to stressors that can be temporary or long-term, unconsciously serving to shield the client against the true reality. In other words, when mechanical ventilation was prolonged, the patient may unconsciously come to regard the ventilator not as a stressor, but instead as part of the client’s created-environment, and hence, a comfort rather than a stressor. However, they also found that hope increased as time passed following successful weaning, and hopelessness predominated for patients who continued to require mechanical ventilation. Lowry and
Anderson’s (1993) finding should be taken into account by clinicians when they try to wean patients from prolonged mechanical ventilation.

Pochard et al. (1995) evaluated the psychological status among ICU survivors who needed mechanical ventilation (n = 43). A 32-item questionnaire was filled out by the patients 48-96 hours after weaning from mechanical ventilation. The results indicated that patients experienced poor psychological status, including an inability to communicate, sleep disorders, diffuse anxiety, depression, and fear of abandonment by staff. However, the poor psychological status was not specifically focused on the weaning process, but related to general MV experience.

A review of qualitative studies (Cook, Meade, & Perry, 2001) related to patient’s experiences of weaning from mechanical ventilation indicated that frustration, uncertainty, hopelessness, fear, and lack of mastery were defined as important experiences of patients during their weaning from mechanical ventilation. They indicated that all researchers assumed if clinicians comprehend MV patients’ experiences, they will more appreciate patients’ needs during the weaning process. However, it is hard to conclude that these patients’ experiences would determine the consequences of weaning failure.

**Correlational Test between Psychological Factors and Weaning Outcome**

Based on the suggestions of the mind-body connection in psychoneuroimmunology (Maier, Watkins, & Fleshner, 1994), psychological events and mood states may dys-regulate the pituitary-adrenal system by way of the hypothalamus. Accordingly, the dys-regulation of the immune system influenced by the emotional states could further affect the outcome of weaning. Using the mind-body approach as a guide,
Connelly, Gunzerath, and Knebel (2000) conducted a pilot study to explore the preweaning mood state and dyspnea in mechanically ventilated patients and the extent to which mood state might distinguish a positive weaning outcome. Twenty-one adult ICU patients with more than 3 days mechanical ventilation were interviewed using the short form of the Profile of Mood States (sPOMS) and a visual analogue scale (VAS) for dyspnea. Results indicated that successfully weaned patients experienced greater mood disturbance and lower preweaning vigor than unsuccessfully weaned patients. In addition, dyspnea intensity and total scores or subscores of mood disturbance did not show a significant correlation with each other or on weaning outcomes. The findings were not consistent with their theoretical thinking. However, the finding from Lowry & Anderson’s (1993) study suggests that the lower intensity of mood disturbance may result from longer days on the ventilator when it becomes a part of patient’s safety zone. In this situation weaning from the ventilator may become a stressor for the patient who feel less mood disturbance in preweaning, and that may cause failure to wean.

The effect of psychological factors associated with weaning outcomes is difficult to determine in PMV patients. Burns et al. (1995) indicated that symptoms such as anxiety, fear, discomfort, and dyspnea are difficult to quantify, and their causal relationships are also hard to explore. Knebel (1990) conducted a prospective study to determine relationships among dyspnea intensity, psychological distress, anxiety intensity, and inspiratory effort prior to and during weaning. There were 21 ICU patients with three or more days on mechanical ventilation who were recruited in for this study. Even though patients reported subjective feelings of fatigue and anxiety prior to weaning, these
feelings did not affect the dyspnea intensity, the anxiety intensity, or the inspiratory effort measured during the weaning trial. None of the values of these pre-weaning psychological variables could predict the weaning outcomes. During the weaning process, dyspnea intensity was correlated to anxiety intensity and inspiratory effort, and it was the only variable related to a successful weaning outcome.

Knebel’s (1990) study used intermittent mandatory ventilation (IMV) and pressure support ventilation (PSV) as the two weaning methods. Although subjects had lower inspiratory effort during PSV weaning than during IMV, there were no differences in dyspnea or anxiety intensities between these two weaning methods. However, the small sample size (n=21) lowers the effectiveness of detecting true relationships between the variables and the weaning outcomes, which may have resulted in non-significant results.

Moody et al. (1997) conducted a study to test the relationship between physiologic and psychological variables related to ventilator weaning. The physiologic variables were represented by CBE disease severity, rapid shallow breathing index (RSBI), age, and ability to speak. Mastery, hope, social support, and dyspnea were regarded as important psychologic variables for weaning in long-term ventilator patients; they were identified as important in patients’ recovery or coping with acute and chronic illnesses. Results indicated significant correlations between mastery and the variables of hope, dyspnea, and ability to speak. There were no statistically significant differences by gender on the measures of all variables. A significant direct correlation was found between mastery and hope and a significant indirect correlation between mastery and
dyspnea. In addition, analysis of the endpoint (weaned, death, or discharge) data indicated that mean dyspnea and mastery were the only two variables found to be statistically different between the success and failure groups. Mastery was significantly higher in the success group, and dyspnea was significantly higher in the failure group. However, results from logistic regression found mastery and RSBI were the only two variables predicting weaning outcomes (Moody et al., 1997). Unfortunately, Moody et al. (1997) did not report the results of these variables during the weaning process. This model still needs to be further tested on the psychophysiologic variables that influence successful weaning from mechanical ventilation.

Twibell, Siela, & Mahmoodi (2003) conducted a descriptive, correlation study to explore the subjective perceptions of dyspnea, fatigue, and self-efficacy and selected physiological variables in patients being weaned from mechanical ventilation. The subjective perceptions dyspnea, fatigue, and self-efficacy were measured by three visual analog scales (VAS), while physiological variables were measured by the Burns Assessment Program (BWAP) at the time prior to weaning trial. They found that PaCO2 and PaO2 were strongly correlated to weaning outcomes and participants reported perceived mild dyspnea, moderate fatigue, and high weaning self-efficacy. Patients’ subjective perceptions were significant correlated to physiological variables, but not correlated to the weaning outcomes. Twibell, Siela, & Mahmoodi (2003) concluded that subjective perceptions were not directly associated with weaning outcomes in this study, but their effect on physiological variables may influence weaning outcome indirectly.

According to Roy's Model of Adaptation which viewed humans as holistic
adaptive systems, Wunderlich (2003) proposed a theoretical framework that supports interplay between physiological and psychological components when a person is adapting to a threatening situation (i.e., weaning from mechanical ventilation). The purposes of her study were to explore the relationship between physiological and psychological variables and their ability to predict successful weaning from mechanical ventilation. The Psychological Observational Weaning Evaluation Rating Scale (POWERS) was developed to objectively measure patients’ general psychological status when they faced the weaning process. Physiological status was evaluated by weaning readiness assessment scale (WRAS). The results indicated moderate correlation between physiological and psychological variables ($r = .52$). Patients who scored lower on the POWERS and WRAS were more likely to wean successfully from mechanical ventilation, and POWERS was more effective to predict weaning outcomes than WRAS. However, Wunderlich (2003) found that her model was more effective when patients successfully weaned but appeared to be problematic in identifying possible failures.

*Intervention Test on Relieving Patients’ Psychological Distress while Being on Mechanical Ventilation and Weaning Process*

A prospective intervention study (Chang et al., 1994) found that patients’ levels of dyspnea and anxiety increased significantly during the weaning trial. In addition, implementing progressive muscle relaxing exercises significantly relieved subjects’ sensations of dyspnea and anxiety, and reduced respiratory rate, rapid-shallow index, and the frequent use of accessory muscles. Based on the study findings, there are recommendations that nurses’ or clinicians’ presence may help to relieve patients’
negative emotion (Jenny and Logan, 1994; 1996; Logan & Jenny’s, 1997; Wunderlich et al, 1999). However, the effectiveness of progressive muscular relaxing exercise on reducing the intensity of anxiety and dyspnea may have been contaminated because of the researcher’s presence during the patients’ entire weaning trial.

Wong et al. (2001) conducted a crossover repeated measures study to test the effectiveness of music therapy on decreasing anxiety in Chinese patients with ventilator dependence. Patients with mechanical ventilation had higher levels of anxiety than patients without mechanical ventilation in the ICU. They also found that anxiety was significantly decreased by music therapy compared to uninterrupted rest periods. Due to the short time of the crossover repeated measurement and the possible Hawthorne effect, the generalizability of this finding may be limited.

Based on its effects on pain control, anxiety relief, and stress symptom reduction, hypnotic technique was found to efficiently wean a patient from prolonged mechanical ventilation (Treggiari-Venzi et al., 2000). Researchers concluded that hypnosis is not simply relaxation, cognitive coping, or placebo, but also inhibits the excitatory neural impulses in the brain and the peripheral nervous system (Holroyd, 1996; Treggiari-Venzi et al., 2000).

Johnson et al. (1995) indicated that psychological depression could leave the MV patient anergic, apathetic, and with deficits in attention, thus making it difficult to wean. Unfortunately, this factor is too often overlooked for several reasons: (1) screening tools for depression or anxiety symptoms are not routinely used in clinical practice; (2) physical symptoms such as breathlessness and fatigue mask the symptoms of depression
and anxiety in COPD patients; (3) not all physicians are confident enough to pursue psychiatric assessment; (4) the stigma of mental illness prevents patients from seeking psychiatric help (Yohannes, Baldwin, & Connolly, 2000). Based on the psychiatric point of view, clinical observation and experience, Rothenhäusler, Ehrentraut, & Degenfeld (2000) used psychostimulants (methylphenidate) to treat depression in ICU patients difficult to wean from mechanical ventilation ($n = 7$). They found that patients had a marked or moderate improvement in mood and activity within 3 to 4 days, and successfully weaned within 8 to 14 days. However, these researchers recommended that it is important for a psychiatrist to clearly detect the causes of difficult ventilator weaning: severe anxiety of dyspnea, or depressed mood, or apathetic state secondary to depression (Johnson et al., 1995; Rothenhäusler et al., 2000). The reason for this is that the administration of methylphenidate might be counterproductive to anxious and agitated patients. High anxiety patients might not benefit from methylphenidate, but could well be treated with reassurance, benzodiazepines, or biofeedback (Johnson et al., 1995; Rothenhäusler et al., 2000).

The principle of biofeedback is to externalize physiological functions, which are mostly controlled by the autonomous nervous system, and to transform them into acoustic or visual signals that can be perceived by patients. Through these signals, patients can develop a cognitive effect such as passive concentration to counteract fearful thoughts and images and to further influence the physiological parameters (Hannich et al., 2004). Breath re-training and biofeedback can be used to reinforce progress in functional breathing with less mechanical ventilatory support. The results from several
contemporary case studies (Acosta, 1988; LaRiccia, et al., 1985; Jacavone et al., 1998) indicate that biofeedback and progressive relaxation decreases respiratory rate, increase tidal volume, and reduce the time on mechanical ventilation. Holliday & Hyers (1990) tested the effect of tidal volume and relaxation biofeedback on reducing the weaning time for the hard-to-wean patients. They found that relaxation biofeedback reduced the anxiety and improved the respiratory muscle electromyograph (EMG) efficiency during the weaning process, and also reduced time on mechanical ventilation. Holliday & Lippman (2003) conducted further studies to demonstrate the possible mechanisms for the effectiveness of biofeedback relaxation in reducing weaning time. They found that the respiratory relaxation feedback (RFB) could reduce anxiety and neural respiratory drive (NRD) during the breathing without the help of the ventilator. This facilitated successful weaning.

Gaps in Knowledge

Even though numerous studies related to ventilator weaning have been conducted over the past 3 decades, the relationship between psychological factors and weaning outcomes is still poorly understood and the mechanism of repeated weaning failure is still not well researched. Possible reasons for the lack of research regarding the psychological impact and the mechanism of repeated weaning failure are the following: a) difficulty interviewing these patients due to their limited ability to communicate and susceptibility to easily fatigue while on mechanical ventilation; b) the smaller the sample size, the lower the efficacy of detecting the significant relationship between the psychological variables and the weaning outcomes; c) without combining physiological variables and
psychological variables to predict the weaning outcome, the omission of strong relevant physiological variables will contribute a huge bias, rendering rejection of the hypothesized psychological model and the potential for type II error; and (d) the limitations of exploring relevant psychological factors with a single indicator or measurement. Therefore, an important issue for the present study is to design multiple working hypotheses in which physiological and psychological variables are combined and interplayed to explain the weaning difficulty among mechanically ventilated patients. A nested model comparison was used to identify the importance of psychological variables in determining weaning outcomes.
CHAPTER THREE: METHODOLOGY

This chapter will discuss the design of this study, including setting and sample, data collection, and measurements administered to the study subjects. The explanation of the method of data analysis as it relates to the study and hypotheses will be addressed. Further, the protection of human subjects will also be described.

Research Design

This was a cross-sectional design study. The data collection was a prospective design, which was used to test the proposed psychophysiological ventilator weaning model (PVWM) in patients with repeated ventilator weaning failure.

Research Setting

Subjects were recruited from the medical intensive care unit (MICU), surgical intensive care unit (SICU), and the respiratory care center (RCC) at a 1,200 bed medical center in Taipei, Taiwan.

Sample

Convenience sampling was used to recruit subjects for the present study. Enrolled were 102 subjects, who were mechanically ventilated and had failed their first T-Piece weaning; they met the target medical center’s weaning criteria and were ready to attempt the second weaning trial. The following three weaning criteria were used in the target medical center: (1) satisfactory gas exchange: PaO2/FiO2>150 & PEEP ≤ 5 cm H2O, (2) satisfactory resolution of patients’ underlying cause requiring MV, and (3) stable vital signs with only intermittent use of sedatives or low-dose dopamine. The first T-piece weaning failure was defined as patients who could not tolerate being disconnected from
the ventilator and breathing spontaneously through a T-tube circuit for 2-hours, who self-reported shortness of breath, and who needed to be completely or partially assisted by a ventilator after the weaning trial.

Inclusion Criteria

Those patients on mechanical ventilation aged 18 years or older, alert, cooperative, and who could understand, read or write Chinese were eligible to participate. In addition, the underlying causes for the need for acute mechanical ventilation needed to be satisfactorily resolved. Also, patients were hemodynamically stable, had no need of vasoactive agents, no hyperthermia ($\geq 38^\circ$C), no administration of respiratory depressant drugs, no important nutritional deficiencies (hemoglobin $\geq 10$ g/dl), no diet rich in carbohydrates, and had correction of arterial hypoxemia (PaO2$>60$mmHg) at inspired oxygen fraction (FIO2) $\leq .5$ & PEEP $\leq 5$ cmH2O.

Exclusion Criteria

Patients with uncontrolled pain who were ventilator dependent before hospital admission were not enrolled in this study. In addition, patients with contraindication to insertion of an esophageal catheter were excluded from this proposed study, such as recent esophageal or gastric surgery, active upper gastrointestinal bleeding, or history of esophageal perforation, cancer, varices, or strictures.

Sample Size

A sufficient sample size is important to accurately and reliably detect the effect of the proposed psychophysiological ventilator weaning model on patients with repeated ventilator weaning failure. A sample size that is too small makes it difficult to detect the
predicted relations and easy to commit type II error. In the present study, structural equation modeling was used to test the PVWM. The small sample size will easily cause falsely accepting the hypothesized model in structural equation modeling (SEM) (Kline, 2005). In contrast, a sample size that is too large will cause unnecessary expenditure of time, effort, and finance.

Bentler & Chou (1987) suggest that the minimum estimated ratio of a sample size to the number of estimated parameters be as low as 5:1 to test a structural equation model (SEM), if the data have a normal or elliptical (homogeneous shape) distribution. Parameters are the characteristics of the population, which are not known and must be estimated from the sample statistics (Kline, 1998). The number of parameters is the sum of the variances and covariances of exogenous variables, exogenous latent variables’ disturbances and measurement errors, and direct effects on endogenous variables that include endogenous latent variables and measurement variables (Kline, 1998). Parameters are usually referred to as fixed or free in SEM. Fixed parameters are not estimated, whereas free parameters, also known as estimated parameters, are estimated and calculated by analyzing the covariances of the various indicators (Kline, 1998). According to the principle of SEM testing, the variance of exogenous latent variables and endogenous latent variables’ disturbances are fixed to 1.0. In addition, the measurement errors of measurement variables are simultaneously known from the estimated direct effect loadings (path coefficient) on the measurement variables from the respective latent variable. Therefore, the measurement error is equal to 1 minus the path coefficient loading on the measurement variable. As a result, the total number of estimated
parameters includes the number of direct effects on the measurement variables and on the endogenous latent variables.

In the entire hypothesized PVWM model, there were a total of 18 estimated parameters (represented as asterisks in Figure 8), which included 12 direct effects from latent variables on the measurement variables, 6 direct effects on two endogenous latent variables and one outcome measurement variable. Therefore, using the rule of thumb of Bentler & Chou’s (1987) sample size estimation, 90 subjects with a ventilator weaning failure who were ready to attempt the second weaning trial were considered an adequate minimum sample size to test this model with 18 estimated parameters. However, Loehlin (1992) strongly recommended that the minimum sample size to operate the confirmatory factor analysis model/measurement model with 2 to 4 factors/latent variables is 100 subjects. Loehlin (1992) indicated that the rationale for obtaining a minimum sample size of 100 was to avoid the following problems caused by a small sample size such as: (1) convergence failure (the software cannot reach a satisfactory solution), (2) improper solutions (including negative error variance estimates for measured variable, (3) lowered accuracy of parameter estimates. Therefore, a sample size of 102 subjects met both Bentler & Chou’s (1987) and Loehlin’s (1992) rule of thumb and were considered sufficient to accurately and reliably test the proposed model.
Figure 8. The Proposed PVWM with Estimated Parameter (*)
Measurement of Variables and Instruments

Data collection included measures of selected manifest variables to represent the psychological variables (conditioned fear and anxiety), physiological variable (respiratory function), and the weaning outcome variable, as listed in Table 1. In addition, patients’ general information (i.e., age, gender, etiology for mechanical ventilation, and length of mechanical ventilation prior to the second weaning trial) was collected from chart reviews, which provided descriptive information for the sample population.

Table 1.
Selected Psychophysiological Variables and Their Respective Indicators and Measurements

<table>
<thead>
<tr>
<th>Selected Variables / Indicators</th>
<th>Measurements</th>
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<tbody>
<tr>
<td><strong>Conditioned Fear</strong></td>
<td></td>
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<tr>
<td>Emotional Fear</td>
<td>Numerical Rating Scale (NRS)-Emotional Fear</td>
</tr>
<tr>
<td>Cognitive Fear</td>
<td>NRS-Cognitive Fear</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>End-tidal CO₂ (PetCO₂)</td>
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<tr>
<td>Increased Heart Rate</td>
<td>Bedside EKG-Heart Rate</td>
</tr>
<tr>
<td>Rapid Shallow Breathing Pattern</td>
<td>Rapid Shallow Breathing Index (RSBI): f/VT</td>
</tr>
<tr>
<td><strong>State Anxiety</strong></td>
<td></td>
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<tr>
<td>Self-report of State Anxiety</td>
<td>Shortened State Anxiety Scale (SSAS)</td>
</tr>
<tr>
<td>Intensity of Anxiety</td>
<td>NRS-Anxiety</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>NRS-Dyspnea</td>
</tr>
<tr>
<td><strong>Respiratory Function</strong></td>
<td></td>
</tr>
<tr>
<td>Gas Exchange</td>
<td>PaO₂/FiO₂</td>
</tr>
<tr>
<td>Respiratory Central Drive</td>
<td>P0.1/MIP</td>
</tr>
<tr>
<td>Respiratory Muscle Capacity</td>
<td>TTI</td>
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<tr>
<td>Respiratory Muscle Workload</td>
<td>WOB</td>
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<tr>
<td><strong>Weaning Outcome</strong></td>
<td>The length of mechanical ventilation (LOMV) (in days)</td>
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<td></td>
<td>starting at the second weaning trial</td>
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</table>
To conduct a good quality study, all testing variables should be as free as possible from the biasing effects of measurement error. Therefore, clear definitions, validity, and reliability are necessary for all measurements, which will be described below.

**Measurements for Psychological Variables**

**Conditioned Fear**

Conditioned fear in the present study was represented by emotional fear, cognitive fear, increased heart rate, hyperventilation, and rapid shallow breathing pattern. Numerical Rating Scales (NRSs), which were unidimensional scales to quantify the intensity of measurement variables, were used to measure two subjective feelings of conditioned fear: emotional fear and cognitive fear. The changes in heart rate, end-tidal CO\(_2\) (PetCO\(_2\)), and rapid shallow breathing index (RSBI) during the second T-piece weaning trial were measurements of increasing heart rate, hyperventilation, and rapid shallow breathing pattern, respectively.

**NRS-emotional fear.** To determine subjects’ emotional fear, they were asked to place a number on an 11-point (0-10) numerical rating scale (Appendix B) in response to the question: “How frightened/afraid are you now of weaning from ventilatory support?” The high end of the scale (0 point) was labeled “no afraid at all”, and the low end (10 points) was “most afraid you can be.”

**NRS-cognitive fear.** The NRS-cognitive fear asked subjects to place a number on an 11-point (0-10) numerical rating scale (Appendix C) in response to the question: “What do you think is the chance that you will experience shortness of breath from ventilator weaning?” The high end of the scale (0 point) was labeled “None,” and the
low end (10 points) was “Extremely high chance”.

*Heart rate.* Heart rate was recorded from a bedside EKG monitor. To optimize the quality of the EKG signal, the research investigator practiced the following standards for instrumentation: (1) selected the best lead system to accurately detect ventricular rhythm, (2) checked the electrode sites for assuring attachment, (3) reduced the interference from the environment, and (4) checked the connection of the cable (Habet & Calvin, 1998).

*PetCO₂.* The change in PaCO₂ was the measurement variable of hyperventilation as a result of conditioned fear. The value of the change in PetCO₂ has been tested and found to have a high correlation with the change in PaCO₂ ($r = .67$ to $0.87$) (Morley et al., 1993). Therefore, the change in PetCO₂, measured by Nellcor N-1000, was used to estimate the change in PaCO₂ to avoid the extra arterial blood gases (ABGs) analyses. To increase the accuracy of PetCO₂ measurements, several techniques were implemented before the measurement: (1) removed secretions at patient airway (suction) to prevent blocking of the sensor window, (2) calibrated the monitoring system, (3) removed the water trapped in the sample line and adapter, and (4) checked the artificial airways to prevent kinking, displacement, or leaking (LaValle & Perry, 1995).

*RSBI*: $f/VT$. The rapid shallow breathing index (RSBI) is the ratio of respiratory frequency ($f$) to tidal volume (VT). A variable-orifice pneumotachograph connected to Bicore Monitor was used to measure the respiratory rate ($f$) and tidal volume (VT) during the resting ventilation. Due to a significant breath-by-breath variability in physiological variables, 3 repeated measurements was obtained for average calculation and used for
analysis. Measurements of the physiological variables will be separated by an interval of not fewer than 15 seconds.

*State Anxiety*

To decrease the subjects’ response burden, the research investigator read the SSAS to subject. Subjects responded to the investigator by “mouthing” or holding a certain number of fingers indicating the desired response.

*NRS-anxiety.* The NRS-anxiety asked subjects to place a number on an 11-point (0-10) numerical rating scale (Appendix D) in response to the question: “How anxious are you feeling right now?” The NRS-anxiety was anchored on the high end (0 points) with “not anxiety at all” and on the low end (10 points) with “most anxious you can be.”

*NRS-dyspnea.* The NRS-dyspnea asked subjects to place a number on an 11-point (0-10) numerical rating scale (Appendix E) in response to the question: “How short of breath are you right now?” The high end of scale (0 point) was labeled “no shortness of breath” and the low end (10 points) was “the worst possible shortness of breath.”

*Shortened State Anxiety Scale (SSAS).* Chlan et al’s (2003) 6-item shortened State Anxiety scale (SSAS) (Appendix F), which was developed from the 20-item Spielberger State Anxiety Inventory (SAI), includes 3 anxiety-present items and 3-anxiety-absent items. The Chinese version of SSAS was derived from the Chinese version of the Spielberger State inventory, and it was used to measure MV patients’ state anxiety in this proposed study. The subjects would respond to each of the 6 items on a 4-point Likert scale—“not at all, somewhat, moderately so, and very much so.”
Feasibility of NRSs

The target population of this study was mechanically ventilated patients who perceived mechanical ventilation and the weaning process as a miserable experience and physiologically and psychologically stressful (Logan & Jenny, 1997). Most patients with repeated ventilator weaning failure were weak and immobilized for several days. Accordingly, they easily got tired and usually had some visual and motor deficits that might cause difficulty for administering the lengthy inventory and paper-and-pencil instruments. From Chlan’s (1998) study experience, she indicated that MV patients had difficulty maintaining focused concentration and easily tired from responding to long scales. Therefore, the feasibility of the present study depended on quick and easy-to-administer instruments to gather psychological sensations and feelings from this population. The advantages of NRSs are that they are easy to respond to, do not require a high level of reading ability, or maintenance of motivation. Eleven-point numerical rating scales are easier to use and no motor skills are needed; even if the patients are weak, they are still able to hold up the number of fingers, “mouth” or point the number, or nod as the researcher points to the number (Powers & Bennett., 1999). Therefore, the numerical rating scales (Appendix B to E), assisted with printed large-digit cards, were used for measurement of patients’ emotional fear, cognitive fear, anxiety, and dyspnea in this study.

Validity and Reliability of 11-point Numerical Rating Scale

The utility of a verbally-administered anxiety rating, which is an 11-point (0-10) numerical rating scale (NRS), has been proven to have good validity and reliability in assessing patients’ state anxiety during interventional radiology procedures (Benotsch,
The results indicated that pre-procedure verbally-administered anxiety ratings were highly correlated with the Spielberger SAI ($r = .73$) and able to detect the difference between pre-procedure and post-procedure state anxiety rating. In addition, the test-retest reliability of this rating scale was also assessed, by examining the first four adjacent 15-minute anxiety ratings ($r = .66$), and it was found that its one-hour stability was similar to the measurement by Spielberger SAI. In Houtman & Bakker’s (1989) study, they examined validation and reproducible data for the 11-point numerical rating scale in assessing the state anxiety, before confrontation with an ego-threatening stressor—a written examination. The results indicated that the validity of this scale was fairly well correlated (.63 - .77) with that of Spielberger SAI. Its reliability was also fair, in which the test-retest reliability coefficients were .60 to .70.

The NRS of dyspnea has numbers that signify the degree of dyspnea. The test-retest reliability and the criterion validity of the numerical rating scale for dyspnea had been assessed and compared with four other dyspnea rating scales in patients receiving mechanical ventilation (Powers et al., 1999). The results indicated that the NRS had an acceptable test-retest reliability (30-minute repeated measurements), with intraclass correlation coefficient .85 and an acceptable criterion validity, which was represented by strong correlations with the visual analogue scale (VAS) at times 1 and 2 (Spearman $\rho$ .96 and .89). In addition, Powers et al. (1999) found that most patients (75%) preferred the NRS. The possible reasons for MV patients preferring the NRS were its ease of use and no motor skills were needed (Powers et al., 1999).

The 11-point NRSs were also used to detect subjects’ emotional state in several
In Bolton’s study (2004), the result indicated that the NRS could provide the best cutoffs with a balance between the highest sensitivity and highest specificity in detecting subjects’ biopsychosocial improvements, which included pain intensity, functional states, anxiety, depression levels, fear-avoidance behavior, and locus of control behavior, after a clinical intervention. Hollen et al. (2005) conducted a study to evaluate the convergence of ratings obtained with an 11-point Numerical Rating Scale (NRS) format to those obtained with a VAS format in lung cancer patients. They found that the scores obtained from the two scales format had an excellent agreement, with intraclass correlation coefficient (ICC) and Lin's concordance correlation coefficient (CCC) ≥ .90. Therefore, Hollen et al. (2005) concluded that the NRS format could be substituted for the VAS format. In addition, almost all patients (99%) indicated that the NRS was easy to complete.

Overall, the good feasibility, reliability, and validity of the 11-point numerical rating scales were used to measure MV patients’ emotional fear, cognitive fear, intensity of state anxiety and dyspnea in this study (see Appendix B1-E1). Since this study was conducted in Taiwan, all NRSs were translated into Chinese versions (see Appendix B2-E2). In order to help MV patients, who had communication impairments in responding to their feelings, a clipboard with printed large-digit cards was used to assist them for appropriate responses.

**Validity and Reliability of the Shortened State Anxiety Scale**

The Spielberger’s State Anxiety inventory (SAI) has been recognized as an excellent anxiety measure with excellent psychometric properties in patients admitted to
coronary care units after acute myocardial infarction, in patients with chronic obstructive pulmonary disease, and in patients undergoing a variety of surgical procedures (Lueders-Bolwerk, 1990; Steelman, 1991; Stice & Morhinweg, 1995; White, 1999). In addition, Spielberger State Anxiety Inventory (SAI) has been translated and used to assess the state anxiety in high school students in Taiwan, and reported test-retest reliability of .737 and internal consistency-Cronbach’s alpha coefficient of .898 (Chung & Long, 1984). Construct validity of the state anxiety scale was also evaluated by comparing the scores under the “exam condition” and “norm condition,” and the results showed a significant difference between the two conditions (Chung & Long, 1984). In addition, the concurrent validity of the Chinese version of SAI (C-SAI) was supported by a significant correlation with the test anxiety, general anxiety, and defensiveness in a Chinese version of the Autobiographical Survey (r = .30 – .43). The C-SAI had been used to test MV patients’ state anxiety in Taiwan and was found to have a high Cronbach’s alpha and split-half reliability, .95 and .82, respectively.

However, Chlan et al. (2003) indicated that there were many challenges to measuring anxiety with the SAI in mechanically ventilated patients, which included the length of the instrument, communication impairments, patient energy limitations, and the lack of relevance of certain items in these patients. These challenges were also found to limit the anxiety measure during the ventilator weaning in mechanically ventilated patients by a respiratory therapist in the target medical center. In order to overcome the challenges and limitations of existing anxiety measures in the mechanically ventilated patients, Chlan et al. (2003) conducted a study to develop a shortened scale from the 20-
item Spielberger SAI. In their study, exploratory factor analysis techniques were used to create a shortened, 6-item scale, which found a Cronbach’s alpha of .78 with a correlation of .92 to the 20-item SAI. Accordingly, Chlan et al.’s SSAS (Appendix F1), which includes 3 anxiety-present items and 3-anxiety-absent items, was substituted for the 20-item Spielberger SAI to measure MV patients’ state anxiety in this study. Based on the fair validity and reliability of the Chinese version of the Spielberbger State Anxiety Inventory (C-SAI) in measuring state anxiety in Taiwan, Chlan et al.’s shortened, 6-item SAI was translated from the C-SAI (see Appendix F2). SSAS presented good internal reliability to measure subjects’ state anxiety in the present study, Cronbach’s alpha was .77.

Measurements of Physiological Variables

Respiratory Function

In the proposed study, respiratory function was represented by measurements of gas exchange, respiratory central drive, respiratory muscle capacity, and respiratory muscle workload. The ratio of arterial oxygen partial pressure to fractional inspired oxygen concentration (the PaO₂/FiO₂ ratio) was the index used to measure gas exchange. The PaO₂/FiO₂ ratio was calculated by using the routine arterial blood gases (ABGs) analysis data and the recorded inspired oxygen concentration. The ratio of occlusion airway pressure to maximum inspiratory pressure (P0.1/MIP), tension-time index (TTI), and work of breathing (WOB) were the measurements of respiratory central drive, respiratory muscle capacity, and respiratory muscle workload, respectively. These three variables were measured and calculated by the Bicore CP-100 Pulmonary Monitor.
**PaO\textsubscript{2}/FiO\textsubscript{2} ratio.**  PaO\textsubscript{2}/FiO\textsubscript{2} (P/F) ratio is regarded as the best index to measure oxygenation (Zetterstrom, 1988). In addition, the P/F ratio is considered a stable and reliable index of abnormal gas exchange when the FiO\textsubscript{2} is $\geq .5$ and the PaO\textsubscript{2} is $\leq 100$ torr under usual clinical conditions (Gould et al., 1997; Gowda & Klocke, 1997). The PaO\textsubscript{2} was gathered from the patients’ routine ABGs measurements. FiO\textsubscript{2} was recorded from the patients’ inspired oxygen concentration at the time the ABGs were measured. The accuracy of ABGs measurements was ascertained by following standard procedures: (1) heparin used less than 10% of the blood sample volume, (2) air bubbles removed from the blood gas syringe, (3) no delay more than 20 minutes in analyzing the blood sample (Biswas, 1982; Hutchison et al., 1983; Woolley & Hickling, 2003). Another way to monitor the accuracy of the data is to re-examine measurements that have more than 5% difference between the oxygen saturation measured by pulse oxymetry (SpO\textsubscript{2}) and laboratory results from arterial blood sample (SaO\textsubscript{2}). According to Woolley & Hickling (2003), there is less than a 5% chance of this difference occurring.

**P0.1/MIP ratio.**  The airway occlusion pressure (P0.1) is the airway pressure generated at 100 ms after the airway is closed prior to conscious recognition of this occlusion. This reflects the neural drive that stimulates the force of diaphragmatic contraction. In the Bicore Monitoring System, the P0.1 was measured during the first 100 ms of inspiratory effort against the occluded valve as determined for the esophageal pressure tracing. The measurement of P0.1 is influenced by lung volume, chest configuration, and respiratory muscle strength (Epstein, 2000). In order to correct the value of P0.1 for differences in respiratory muscle strength, P0.1/ MIP, suggested by
Capdevila et al. (1995) and Gandia & Blanco (1992), were used in this study. Maximum inspiratory pressure (MIP) was represented by the maximal static inspiratory esophageal pressure (Pesmax), which is described in the following content.

**Tension-time index (TTI).** Tension-time index of the inspiratory muscles (TTI) is an index of endurance that reflects the capacity of the respiratory muscles. The TTI is estimated by the equation Ti/Ttot * Pes/Pesmax, where Pes is the mean inspiratory esophageal pressure, Pesmax is maximal static inspiratory esophageal pressure, Ti is inspiratory time, and Ttot is total duration of the breathing cycle. The mean esophageal pressure is calculated as the change in esophageal pressure from the X intercept of the chest wall compliance line (Point A) to the most negative point (Point B) on the esophageal pressure volume curve from the Campbell diagram (see figure 5). In addition, the Pesmax is the esophageal pressure corresponding to the X-coordinate of point B, as shown in the Campbell diagram.

**Work of breathing (WOB).** In mechanically ventilated patients, the work of breathing (WOB) estimates the work required to overcome airway resistance (resistive work), inflating the lung, and also the work needed to overcome the ventilatory system (elastic work). Under the Bicore Monitoring System, WOB is calculated by computer integration of the area (area ADBCA in Campbell diagram, see Figure 9) under the esophageal pressure and lung volume curve during respiration, which is the negative deflection of the esophageal pressure tracing (Blanch & Banner, 1994). The slope of the pressure-volume loop is lung compliance, whereas the chest wall compliance is calculated with the patients relaxed from the slope of the pressure-volume loop in a
counterclockwise direction. Therefore, the total work of breathing is the sum of the resistive (area ADBA) and elastic (area ABCA) work.

Figure 9. A modified Campbell diagram

\[\text{Figure 9. A modified Campbell diagram}\]

**Bicore Monitoring System.** The Bicore CP-100 Pulmonary Monitor was used to measure the P0.1, MIP, TTI, and WOB. This Monitoring System is used to measure pressures in the airways and the esophagus, and the airflow in the airways, with specially designed, self-calibrating catheters (Blanch & Banner, 1994).

Airway pressure, volume, and flow were measured with a variable-orifice pneumotachograph that was placed at the junction between the endotracheal tube and the ventilator circuit. Esophageal pressure (indirect measurement of intrapleural pressure) was measured by a special nasogastric tube equipped with an esophageal manometer, which was placed along the patient’s nasogastric tube, and positioned in the low third of the esophagus (Tobin, 1998). The selected nasogastric tube (Smart Cath) is an 8 F, 69-cm-long, medical grade, radiopaque polyurethane device, and the balloon is a .9-cm-
diameter, 10-cm-long, medical grade, low-density polyethylene material with a frequency response of 30 Hz., which was found well tolerated by the subjects (Thomas, Turner, & Tenholder, 1997). The correct positioning of the nasogastric tube in the thorax was confirmed by observation of negative esophageal pressure deflections on the monitor during inspiration (normally between -5 and -10 cmH2O) and by the Baydur, Behrakis, Zin, Jager, & Milic-Emili (1982) method. In addition, it was also validated by the less than 10 percent difference between the Pes and the Paw during the airway occlusion tests (Peslin et al., 1993). The position of the balloon was slightly modified if necessary until satisfactory data were obtained.

The validity of the measurements collected by the Bicore Monitoring System has been supported by lung model testing (Blanch & Banner, 1994). The correlation coefficients ($r$) and coefficients of determination ($r^2$) between the measurements from Bicore Monitoring System and conventional methods were close to .99 ($p < .0001$). The reproducibility of these measurements, by using the Bicore Monitoring System, was proven by Petrini et al’s (1998) study, in which they found that there was no statistically significant difference between five minutes of repeated measurements. Therefore, the satisfactory validity and reliability supported the use of Bicore Monitoring System to measure the respiratory function in this study.

**Measurement of Weaning Outcome**

Weaning outcomes were recorded as the length of mechanical ventilation (LOMV) (in days) starting at the first day of the second ventilator weaning trial, and continuing to the day the patients successfully wean, or for up to three weeks of follow-up, whichever
came first. An evidence-based weaning protocol that had been used in the target medical center, agreed upon by physicians, RTs, and nurses, was implemented to safely wean these subjects seven days a week. Accordingly, the length of mechanical ventilation was recorded accurately.

Successful weaning was defined by the patient’s ability to sustain spontaneous breathing for 24 hours without ventilatory support, which included invasive and noninvasive mechanical ventilation. If the patient presented any intolerant signs or symptoms listed in the weaning trial termination criteria, the weaning trial was terminated immediately, and the patient was returned to partial mechanical ventilation at previously tolerated settings. A three-week follow-up time period was set up as the longest length of ventilatory support for this study. It was used to limit the possibility of missed data in the outcome variable that might be caused by the regulation of the length of ICU and RCC stay, under the policy of the national health insurance in Taiwan. If the subjects were unable to be weaned from the ventilator and died within the three-week follow up, their LOMV was counted as 21 days.

Data Collection Procedure

The whole study was conducted by collaborating with the following respiratory health care providers: physicians, respiratory therapists (RTs) and nurses. The researcher visited ICUs every morning and identified potential subjects with assistance from these health care providers. According to previous studies’ findings (Burns & Dempsey, 2000; Ely et al., 1999; Kollef, Shapiro, & Silver, 1997), the protocol-directed weaning trials, compared with physician-directed weaning trials, can lead to a shorter weaning duration,
and fewer tracheostomies and reintubations. Therefore, the established ventilator weaning criteria and weaning protocol for T-piece trials in the target medical center were unchanged and continuously implemented to safely wean the participants from ventilatory support. The weaning trial termination criteria also apply to early detection of any subjects’ intolerance, in which case the weaning trial would be stopped in a timely manner.

**Weaning Criteria for T-piece Trials**

If patients were receiving partial mechanical ventilation support with pressure support ventilation (PSV), they would be screened daily by the criteria to commence the T-piece weaning process. The weaning criteria were as follows: (1) satisfactory gas exchange: PaO2/FiO2>150 & PEEP ≤ 5 cm H2O, (2) satisfactory resolution of patients’ underlying cause requiring MV, and (3) stable vital signs with only intermittent use of sedatives or low-dose dopamine.

**Weaning Protocol of T-piece Trials**

All subjects recruited in this study were weaned by a protocol-directed weaning strategy, which had been used in the target medical center in Taiwan. All weaning procedures were used for seven days a week, which had been agreed upon by the respiratory health care providers in target medical center. In addition, the weaning trial was implemented only during the day so that the patients could have adequate rest sleep at night.

**T-piece Trials:**

1. Once patients met the criteria of T-piece trial, they were put on T-piece
trial/spontaneous breathing for 2 hrs.

2. If the patient was unable to tolerate the T-piece trial, then he/she was put to a previous tolerated ventilatory support level and rested overnight.

3. If the patient was unable to tolerate this ventilatory support level, then ventilatory support was adjusted to the patient’s comfort level and he/she was placed on this level overnight.

4. The patients’ condition was rechecked to see whether he/she met the criteria of T-piece trial in the next day. If so, the patient was put on T-piece trial again for 2 hrs.

5. Once the patients showed no signs of intolerance on T-piece trial, then patients with an endotracheal tube were considered for extubation. If the patient had a tracheostomy, the T-piece trial remained in place indefinitely.

Criteria for Terminating the Weaning Trial

If patients exhibited the following intolerance conditions, the weaning trial was terminated: (1) oxygen saturation of 90 or less at a FiO2 of .5, (2) diaphoresis, (3) evidence of increasing respiratory distress (increased accessory muscle activity), (4) tachycardia (HR ≥ 140 bpm), (5) arrhythmia, and (6) hypotension (systolic BP ≤ 90 mmHg).

Data Collection

The data were collected prospectively in the proposed study. All data were collected and measured by the researcher. The subjects enrolled in this study were patients who failed to be weaned from the first trial and had returned to complete
ventilatory support for at least 24 hours. RTs or physicians evaluated these patients every day using the weaning criteria established by the target medical center, to decide whether they were ready for the second weaning trial. If patients were ready to commence their second weaning trial, health care providers would inform them about the present study. With patients’ agreement, health care providers notified the researcher to consent patients. Upon patients’ consent to participate, the researcher collected all data and stayed at the patients’ bedside during the whole data collection period. Patients’ weaning procedure did not deviate from the hospital’s standard protocol. No differences were expected in the weaning procedure between patients who did or did not consent to participate in the study. In order to reduce the discomfort from inserting the esophageal balloon catheter that may affect the subjects’ weaning trials, the catheter was inserted after the subject gave consent and 1 hour before the weaning trial. The insertion of the catheter took about 3 minutes.

Conditioned fear, state anxiety, respiratory function, and weaning outcome were four major variables in this study. These four variables were represented by three to five indicators (see Table 1) and were measured in the following timeframe. Prior to the second weaning trial, three physiological indicators of conditioned fear, heart rate, PetCO2, and RSBI, were to be recorded from bedside monitor as the baseline data. These indicators were recorded again within 10 minutes after starting the second weaning trial. The difference between these two sets of data represented the physiological reactions of conditioned fear. After these three physiological indicators were recorded, the researcher used two numerical rating scales (NRSs) to ask the subjects to record their emotional fear and cognitive fear by placing a mark on the numerical scales.
The state anxiety and the physiological indicators of respiratory function were measured after the conditioned fear was measured. The state anxiety was self-reported by the subjects using the NRS-anxiety and NRS-dyspnea and the Chinese version of Chlan et al.’s (2003) 6-item shortened state anxiety scale (SSAS). The researcher used the NRS-anxiety and NRS-dyspnea to ask the subjects to record their present anxiety and dyspnea by placing a mark on a numerical scale. To mitigate the subjects’ response burden, the research investigator read the SSAS to the subjects. The subjects responded to the investigator by pointing to the number or holding a certain number of fingers indicating the desired response. These measurements of conditioned fear and state anxiety directly involved the subject for approximately 15 minutes.

Respiratory function was represented by the measurements/indicators of gas exchange, the ratio of airway occlusion pressure to maximum inspiratory pressure (P0.1/MIP), tension-time index (TTI), and work of breathing (WOB). Gas exchange data (PaO2/FiO2) was calculated from values obtained from the patient’s chart. Routine arterial blood gas monitoring during a weaning trial was a part of the medical center’s standard procedure. The airway occlusion pressure (P0.1), tension-time index (TTI), and work of breathing (WOB) were measured by the esophageal balloon catheter connected with a Bicore Monitoring System at 30 minutes to 60 minutes after starting the T-piece trial, which was found as the most accurate weaning measurements based on findings from previous studies (Gandia & Blanco, 1992; Epstein, 2000). P0.1, TTI, & WOB were measured over 5 minutes to ensure stable measurements. All data were entered to a PC for storage and analysis. The esophageal balloon catheter was removed right after the
measurements were taken.

After all psychological and physiological variables were measured, the researcher also collected information regarding the subjects’ length of ventilatory support until they were successfully weaned from ventilatory support or for up to three weeks follow-up, whichever came first. Subjects’ general information (i.e., age, gender, etiology for mechanical ventilation, and length of mechanical ventilation prior to the current weaning trial) was collected from patients’ medical charts.

Data Analysis

In this study, confirmatory factory analysis (CFA) and structural equation modeling (SEM) techniques with the aid of the software package Analysis of Moment Structural (AMOS) Version 5.0 were the major statistical analysis methods used to test the goodness of fit of the measurement model and structural model of the PVWM, respectively (Table 2). The subjects’ general information was analyzed in terms of measures of central tendency, variability, and the range of data with the aid of the software package SPSS 14.0.

The hypothesized model, PVWM, was tested with a structural equation model (SEM), which is known as a full latent variable model. A full latent variable model comprises both the measurement model and the structural model. The latent variable was the construct that was estimated from the observed variables (indicators) (Shadish, Cook, & Campbell, 2002). Structural equation modeling is used to specify the regression structure between each latent variable and its indicators, which is regarded as the measurement model, and the regression structure among the latent variables, which is
known as the structural model. In the PVWM, conditioned fear, state anxiety, and respiratory function were three latent variables, which were individually represented by three to five indicators to consist of three measurement models. Meanwhile, these three latent variables and the ventilator weaning outcome were connected by one-way arrows, the directionality of which reflected the hypotheses bearing on the causal structure of the variables, which was the structural model in this study.

The measurement model indicated the existence of latent variables and depicted the regression structure between the latent variables and their respective indicators by the pattern of correlations between the indicators. In order to identify the structural model, the measurement model should be first identified. In the measurement model, using multiple indicators to measure a latent variable is more reliable than any individual one. In addition, each indicator will assess a somewhat different facet of the latent variable, which enhances validity. Confirmatory factor analysis (CFA) was used to specify and test a priori measurement models, in which each indicator was specified to load on a single latent variable and to evaluate whether the indicators were measuring the same constructs. To specify the measurement model in the present study, the loading of one indicator per latent variable was fixed to 1.0 (Bentler, 1989; Loehlin, 1992).

Three measurement models with the respective latent variables (factors)—conditioned fear, state anxiety, and respiratory function—were integrated and tested as a whole measurement model, known as a multifactor CFA model. In measurement model testing, the fit of the multifactor model is better than that of the single-factor model to the same data (Kline, 2005). Kline (2005) stated the reason for it is that a multifactor model
allows each indicator to represent only one factor, which provides a precise test of convergent and discriminant validity.

In the hypothesized measurement model, the indicators were regarded as effects of the latent variables. Based on this assumption, high internal consistency among the variables within a latent variable is desirable, indicating that the latent variable is defined accurately. The internal consistency was tested from the Cronbach’s alpha analyzing and the inspection of the matrix of estimated correlation.

The \( \chi^2 \) statistic, Normed Fit Index (NFI), Relative fit index (RFI), Comparative Fit Index (CFI), and Root Mean Square Error of Approximation (RMSEA) (Kline, 2005) were used to test the goodness-of-fit of the measurement models. The goodness-of-fit indices ranging from 0 to 1 are measures of the joint amount of variances and covariances accounted for by the model; the larger, the better. The non-significant \( \chi^2 \) and the values of .9 or greater for NFI, RFI, and CFI were used to determining whether the model would be a good fit to the sample data (Hu & Bentler, 1995). An RMSEA less than .06 was an important index for predicting a good model fit (Hu & Bentler, 1998). In addition, the explained variance of indicators in each measurement model should be inspected. If the explained variance is low (e.g., standardized loading = .10), then the measurement model should be respecified.

As the fit of measurement model was deemed satisfactory, subsequently the structural model was tested. The structural model depicts the relationships among latent variables and describes the amount of unexplained variances, known as the disturbance term, among them, which is based on results derived from measurement models (Kline,
The regression coefficients among latent variables indicated their relationships. Further, the goodness-of-fit indices were used to evaluate how well the proposed model fit the sample data. As with the goodness-of-fit testing in the measurement model, NFI, RFI, CFI, and RMSEA were used to test the overall goodness-of-fit of the PVWM. On the other hand, the PVWM was compared to competing models generated from the post hoc analysis by using the nested model comparison, which evaluated whether the alternative models fit better or were more parsimonious than the hypothesized model. The test of the difference of \( \chi^2 \) between the models and Akaike Information Criterion (AIC) (Browne & Cudek, 1993) was used to determine the best fit model among the competing models.

Table 2.

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>Variables</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEM-Measurement Models</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition Fear</td>
<td>Exogenous variable:</td>
<td>( \chi^2 ) statistic; Normed Fit Index (NFI); Comparative Fit Index (CFI); Relative fit index (RFI); Root Mean Square Error of Approximation (RMSEA)</td>
</tr>
<tr>
<td></td>
<td>Conditioned fear</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Endogenous variables:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Emotional fear</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cognitive fear</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased heart rate</td>
<td></td>
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<tr>
<td></td>
<td>Hyperventilation</td>
<td></td>
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<tr>
<td></td>
<td>Rapid shallow breathing</td>
<td></td>
</tr>
<tr>
<td>State Anxiety</td>
<td>Exogenous variable:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>State anxiety</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Endogenous variables:</td>
<td></td>
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<tr>
<td></td>
<td>STAI-state anxiety</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intensity of Anxiety</td>
<td></td>
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<tr>
<td></td>
<td>Dyspnea</td>
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</tr>
</tbody>
</table>
Respiratory Function  
Exogenous variable: Respiratory function  
Endogenous variables: Gas exchange, Respiratory central drive, Respiratory muscle capacity, Respiratory muscle

<table>
<thead>
<tr>
<th>SEM-Structural Models</th>
<th>Exogenous variable</th>
<th>Endogenous variable</th>
<th>Regression Coefficient (Weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditioned fear to the weaning outcome</td>
<td>Conditioned fear</td>
<td>Weaning outcome</td>
<td></td>
</tr>
<tr>
<td>Conditioned fear to state anxiety</td>
<td>Conditioned fear</td>
<td>State anxiety</td>
<td></td>
</tr>
<tr>
<td>Conditioned fear to respiratory function</td>
<td>Conditioned fear</td>
<td>Respiratory function</td>
<td></td>
</tr>
<tr>
<td>State anxiety to respiratory function</td>
<td>State anxiety</td>
<td>Respiratory function</td>
<td></td>
</tr>
<tr>
<td>State anxiety to the weaning outcome</td>
<td>State anxiety</td>
<td>Weaning outcome</td>
<td></td>
</tr>
<tr>
<td>Respiratory function to the weaning outcome</td>
<td>Respiratory function</td>
<td>Weaning outcome</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SEM-Full Model</th>
<th>Model’s goodness of fit</th>
<th>$\chi^2$ statistic; Normed Fit Index (NFI); Comparative Fit Index (CFI); Relative fit index (RFI); Root Mean Square Error of Approximation (RMSEA)</th>
</tr>
</thead>
</table>

| Nested Model Comparison | PVWM vs. Alternative Models | $\chi^2$ statistic and AIC |
Protection of Human Subjects

Informed Consent Procedures

The researcher visited two ICUs in the target medical center and identified the potential subjects by talking with health care providers, including physicians, RTs, and nurses. If patients met the study criteria, health care providers helped to inform the patients and their families about the study. Upon the patients agreeing to meet with the research investigator, the researcher provided more detailed information about the study in order to recruit the subjects.

The research investigator gave a thorough explanation of the study to potential subjects, which included the purposes, procedures, and risks of the study. Patients were given time to read the entire informed consent document by themselves or with a family member’s help, followed by an opportunity to ask questions. The researcher informed patients about their right to make a decision about participating, which would not affect their health care. As the consent was given, the signed consent form was given a code number and separated from the name of the subject. A copy of the signed consent form was given to the subjects and the original was kept secure by the researcher.

Risk to the Subjects

Although the insertion of esophageal balloon catheters for measuring the respiratory function had not been reported with any risks, the researcher was still aware of the possible discomfort from the insertion of esophageal balloon catheter.

Benefits

There were no direct benefits expected for the subjects in the present study.
Subjects’ Rights as a Participant in This Proposed Study

All subjects were informed about their voluntary participation in this study. No loss of benefits or altered health care would be caused by the subject refusing to participate. Similarly, the participants were informed of their right to terminate or decline participation at any time, which would not result in any loss of benefits.

Minimization of Risks

To minimize the subjects’ discomfort from insertion of the esophageal balloon catheter for measuring respiratory function, well tolerated small catheters were selected (8 F. smart catheter) (Thomas, Turner, & Tenholder, 1997) and were well lubricated by using a sterile, water-soluble lubricant. In addition, the nasogastric tube was removed right after the measurements were completed.

Compliance with HIPAA

All subjects were informed about how their health information was protected and used by the investigator, how they could access their own personal health information, and how they could terminate or decline their authorization. All this information was addressed in the informed consent form, and the subjects were given a copy of the signed consent form.

Summary

A cross-section design study based on the prospective data collection was used to test the Psychophysiological Ventilator Weaning Model (PVWM) in subjects with repeated ventilator weaning failure. Descriptive statistics, confirmatory factor analysis, and structural equation modeling were used to analyze the data and test the goodness of
fit of the PVWM and hypotheses. The protection of subjects enrolled in this study was of utmost importance.
CHAPTER FOUR: RESULTS

The primary goal of this chapter is to share the results of data analysis for this study. The findings are presented in the following five sections: (1) descriptive characteristics of the sample, (2) descriptive data for all latent variables and their respective indicators, (3) model fit analysis, (4) further model fit analysis with a logarithm of outcome variable, and (5) post hoc analysis and model comparisons.

Descriptive Characteristics of the Sample

The means, standard deviations, and frequencies were computed for the demographic variables. The sample (N=102) consisted of mechanically ventilated patients, who had a failure experience on their first T-piece weaning trial, met the hospital’s weaning criteria, and were ready to attempt the second T-piece weaning trial. The subjects were recruited at a 1,200 bed medical center in Taipei, Taiwan, from the Medical (69) and Surgical (22) Intensive Care Units and one Respiratory Care Center (11).

The sample included 46 females and 56 males (Table 3). The major medical diagnoses of these subjects varied (Appendix G), but could be categorized into pulmonary (49) or non-pulmonary (53) disease (Table 3). Chronic obstructive pulmonary diseases (COPD) with acute exacerbation (16) and pneumonia (25) were the two main diagnoses in the sample. In addition, the reasons for these subjects being on mechanical ventilation were classified into acute respiratory failure (81) and post surgery statuses (21). The mean age of the sample was 71.76 (SD = 12.51) years of age with a range of 34 to 91 years (Table 4). The mean length of mechanical ventilation prior to initiating the
second T-piece trial was 9.82 days \((SD = 12.21)\) with a range of one to 80 days (Table 4).

**Descriptive Data for All Latent Variables and Their Respective Indicators**

*Conditioned Fear*

While subjects were undergoing the second T-piece weaning trial, the first latent variable, *conditioned fear*, was measured with the following: the numerical rating scale (NRS) of emotional fear, NRS of cognitive fear, changes in heart rate, end-tidal CO\(_2\) (PetCO\(_2\)), and a rapid shallow breathing index (RSBI) (Table 5). Subjects’ self-reported emotional fear and cognitive fear were assessed by asking subjects to respond to the following questions on 11-point (0-10) Numerical Rating Scales (NRSs): “How frightened/afraid are you now of weaning from ventilator support?” and “What do you think is the chance that you will experience shortness of breath from ventilator weaning?” The mean scores of emotional fear and cognitive fear in this sample were: 3.58 \((SD = 2.8)\) and 4.45 \((SD = 2.77)\), respectively. Of the 20 subjects who did not feel any fear about weaning from the ventilator, only 20 of these subjects rated their fear concerning ventilator weaning 5 or more points on the 11-point (0-10) numerical rating scale. Ten subjects reported a “zero” in response to the item regarding whether they felt there was a chance they would experience shortness of breath from ventilator weaning, but 35 of the subjects responded with more than 5 points in the 11-point (0-10) numerical rating scale to this item.

The physiological indicators of conditioned fear, namely heart rate, PetCO\(_2\), and rapid shallow breathing index (RSBI), were assessed in terms of differences between the values obtained 10 minutes prior to the second weaning trial and 10 minutes within
starting the second weaning trial. Increased heart rate of 10 beats per minute (beats / min) was found in 13 of the subjects. The PetCO₂ dropped within a range of 1 to 6 mmHg in 63 of the subjects. The increase of 30 in the rapid shallow breathing index (RSBI), which was caused by an increase in respiratory rate and/or decrease in tidal volume, was found in 52 of the subjects. In addition, the means of the changes in heart rate, PetCO₂, and RSBI in these subjects were 4.55 beats/min (SD = 5.27), -.93 mm Hg (SD = 2.07), and 35.12 breaths/L/min (SD = 28.65), respectively.

State Anxiety

The second latent variable, state anxiety, was measured via a 6-item Shortened State Anxiety Scale (SSAS) reduced from Spielberger State-Trait Anxiety Inventory (STAI) (Chlan et al., 2003), the NRS-anxiety, and the NRS-dyspnea (Table 5). This 6-item SSAS was pretested in a Taiwanese sample of mechanically ventilated patients, and its reliability (internal consistency) as represented by Cronbach’s alpha was .77, a reasonably good value. Subjects had mean scores of 15.66 (SD = 4.20) with a range of 6 to 24 points on SSAS. When the score of SSAS (6-item) was converted to the full form scores (20-item) of Spielberger’s State-Trait Anxiety Inventory (STAI), in which the total score was between 20 and 80, the mean score of these subjects was 52.2 and regarded as moderate anxiety level (Score of 40-59) (Chlan, 1998; Wong et al., 2001). Subjects were further asked to describe their state anxiety and dyspnea during the second T-piece weaning trial on 11-point (0-10) numerical rating scales (NRSs) for the following items: “How anxious do you feel right now?” and “How short of breath are you right now?” respectively. The mean scores of subjects’ NRS-anxiety and NRS-dyspnea were 4.37 (SD
129

... = 2.59) and 4.54 (SD = 2.61) with a range of 0 to 10 points for each scale.

**Respiratory Function**

The third latent variable, *respiratory function*, was defined by the ratio of arterial oxygen partial pressure to fractional inspired oxygen concentration (PaO$_2$/FiO$_2$), the ratio of occlusion airway pressure to maximum inspiratory pressure (P0.1/MIP), tension-time index (TTI) and work of breathing (WOB) (Table 5). The means of PaO$_2$/FiO$_2$, P0.1/MIP, TTI, and WOB were 256.80 torr (SD = 92.20), .136 (SD = .087), .190 (SD = .103), and 1.19 J / L (SD = .66), respectively.

**Weaning Outcome**

Weaning outcome was recorded as the length (days) of mechanical ventilation (LOMV) starting on the first day of the second ventilator weaning trial and continuing to either the day the patient successfully weaned from ventilation or for up to three weeks, whichever came first (Table 5). Of these 102 subjects, 75 were weaned within 21 days, but 27 subjects were unable to be successfully weaned, including 2 subjects who died during the 3-week period. The mean of the LOMV was 9.74 days (SD = 8.05). Interestingly, 70 of the total subjects were weaned within 2 weeks. Among the subjects who needed more than 2 weeks of MV, 27 out of 32 (84.4%) would continue on MV for 3 weeks or more.

The mean total length of MV for the subjects, which included the length of MV prior to and after the second T-piece weaning, was 18.94 days (SD = 15.94). However, 38 of these subjects who failed the first T-piece trial were on total mechanical ventilation for more than 21 days.
Correlations between Characteristics of the Sample and All Variables

The correlations between sample characteristics and all variables in PVWM were explored with Pearson product-moment correlations (r) and analysis of variance (ANOVA) using SPSS 14.0. Age of subjects was significantly correlated with their respiratory function in P0.1/MIP (r = .24), TTI (r = .22), and WOB (r = .25), but was non-significantly correlated with subjects’ conditioned fear and state anxiety. In addition, age was also significantly correlated with subjects’ weaning outcome—LOMV (r = .31). Male subjects self-reported higher cognitive fear and state anxiety on SSAS than female ones, which was statistically significant (p < .05).

Subjects’ length of MV prior to 2nd weaning did not significantly correlate with their conditioned fear, state anxiety, respiratory function, and the weaning outcome during the 2nd weaning trial. Interesting results were found in outcome variable—LOMV; the researcher ran an analysis to test the difference of psychophysiological performance between the subjects with LOMV ≤ 14 days and > 14 days. The results indicated that subjects who needed the LOMV > 14 days had a significantly worse respiratory function presented in P0.1/MIP, TTI, and WOB, and also had a higher change in RSBI prior to and during the 2nd weaning trial than subjects who needed LOMV ≤ 14 days.

The different performance of psychophysiological variables (conditioned fear, state anxiety, and respiratory function) in the 2nd weaning trial between subjects with two categorized major medical diagnosis (pulmonary and non-pulmonary diseases) and also between subjects with two categorized etiologies of using mechanical ventilation (acute respiratory failure and post surgery statuses) were not statistically significant. In addition,
the subjects recruited from different settings had no significant difference in their psychophysiological performance during the 2nd weaning trial.

Table 3

*General Characteristics of the Sample (N = 102)*

<table>
<thead>
<tr>
<th>Recruitment Settings</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MICU</td>
<td>69</td>
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<tr>
<td>SICU</td>
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<tr>
<td>RCC</td>
<td>11</td>
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</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>46</td>
</tr>
<tr>
<td>Male</td>
<td>56</td>
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</table>

<table>
<thead>
<tr>
<th>Categorized the Major Diagnoses</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Disease</td>
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<tr>
<td>Non-pulmonary Disease</td>
<td>53</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Reasons for Mechanical Ventilation</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Respiratory Failure</td>
<td>81</td>
</tr>
<tr>
<td>Post Surgery Statuses</td>
<td>21</td>
</tr>
</tbody>
</table>

*Note.* MICU = Medical Intensive Care Unit. SICU = Surgical Intensive Care Unit. RCC = Respiratory Care Center.

Table 4

*Descriptive Data of Age and Length of Mechanical Ventilation Prior to the 2nd T-piece Weaning of the Sample (N = 102)*

<table>
<thead>
<tr>
<th></th>
<th>Range</th>
<th>M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34-91</td>
<td>71.76</td>
<td>12.51</td>
</tr>
<tr>
<td>Length of MV prior to the 2nd T-piece weaning (days)</td>
<td>1-80</td>
<td>9.82</td>
<td>12.21</td>
</tr>
</tbody>
</table>
Table 5  
*The Descriptive Data of All Measured Variables in the PVWM (N = 102)*

<table>
<thead>
<tr>
<th>Latent Variables</th>
<th>Measured Variables (Possible Range of Scores)</th>
<th>M</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conditioned Fear</strong></td>
<td>NRS-emotional fear (0 - 10 points)</td>
<td>3.58</td>
<td>2.80</td>
<td>0 - 10</td>
</tr>
<tr>
<td></td>
<td>NRS-cognitive fear (0 - 10 points)</td>
<td>4.45</td>
<td>2.77</td>
<td>0 - 10</td>
</tr>
<tr>
<td></td>
<td>Increased Heart Rate (beats/min)</td>
<td>4.55</td>
<td>5.27</td>
<td>(-5) - 27</td>
</tr>
<tr>
<td></td>
<td>Hyperventilation—PetCO2 (cm H2O)</td>
<td>-.93</td>
<td>2.07</td>
<td>(-6) - 6</td>
</tr>
<tr>
<td></td>
<td>Rapid Shallow Breathing—RSBI (breaths / L / min)</td>
<td>35.12</td>
<td>28.65</td>
<td>(-4) -166</td>
</tr>
<tr>
<td><strong>State Anxiety</strong></td>
<td>SSAS (6 - 24 points)</td>
<td>15.66</td>
<td>4.20</td>
<td>6 - 24</td>
</tr>
<tr>
<td></td>
<td>NRS-anxiety (0 - 10 points)</td>
<td>4.37</td>
<td>2.59</td>
<td>0 -10</td>
</tr>
<tr>
<td></td>
<td>NRS-dyspnea (0 - 10 points)</td>
<td>4.54</td>
<td>2.61</td>
<td>0 -10</td>
</tr>
<tr>
<td><strong>Respiratory Function</strong></td>
<td>Gas Exchange—PaO2/FiO2 (torr)</td>
<td>256.80</td>
<td>92.20</td>
<td>100 - 557</td>
</tr>
<tr>
<td></td>
<td>Respiratory Central Drive—P0.1/MIP</td>
<td>.136</td>
<td>.087</td>
<td>.02 - .52</td>
</tr>
<tr>
<td></td>
<td>Respiratory Muscle Capacity—TTI</td>
<td>.190</td>
<td>.103</td>
<td>.04 - .54</td>
</tr>
<tr>
<td></td>
<td>Respiratory Muscle Workload—WOB (J / L)</td>
<td>1.19</td>
<td>.66</td>
<td>.31 – 3.88</td>
</tr>
<tr>
<td><strong>Outcome Variable</strong></td>
<td>Length of MV—LOMV (1 – 21 days)</td>
<td>9.74</td>
<td>8.05</td>
<td>1 - 21</td>
</tr>
</tbody>
</table>

*Note.* PVWM = Psychophysiological Ventilator Weaning Model. NRS = Numerical Rating Scale. PetCO2 = end-tidal CO2. SSAS = Shortened State Anxiety Scale. PaO2/FiO2 = the ratio of arterial oxygen partial pressure to fractional inspired oxygen concentration. P0.1 /MIP = the ratio of occlusion airway pressure to maximum inspiratory pressure. TTI = tension-time index. WOB = work of breathing. LOMV = Length of Mechanical Ventilation.

Model Fit Analysis

The hypothesized Psychophysiological Ventilator Weaning Model (PVWM) in repeated ventilator weaning failure was tested with structural equation modeling using the Analysis of Moment Structural (AMOS) Version 5. PVWM comprises the measurement model, with three latent variables (conditioned fear, state anxiety, and respiratory function model) and the structural model. Testing PVWM with Structural Equation Modeling (SEM) was completed in a multistage process. First, these indicators were tested with the confirmatory factor analysis (CFA) to analyze the regression.
structures between the latent variables and their respective indicators. Second, when the measurement model was identified, the structural model would be tested. The structural model depicted the relationships among latent variables (conditioned fear, state anxiety, and respiratory function) and, for each variable, the amount of unexplained variance, known as the residual term, which was based on results derived from the measurement model. Goodness-of-fit indices were used to show how well the PVWM fitted the sample data. Third, based on the theoretical and statistical arguments, the alternative models were generated. Finally, the hypothesized models were compared with the alternative models by a nested model comparison, in which PVWM was modified to a better-fitting and more parsimonious model. The following sections will depict the results of the model fit analysis according to these stages.

**Measurement Model Fit Analysis**

The confirmatory factor analysis was conducted to test the measurement model of PVWM, with three latent variables fitted to the sample, conditioned fear, state anxiety and respiratory function, using the maximal likelihood approach of structural equation modeling. The overall measurement model fit yielded a variety of fit indices. The chi-square index of the model fit was statistically significant ($\chi^2 (51, N = 102) = 70.19, p < .05$) (Figure 10). The root mean square error of approximation (RMSEA) was .06. The normed fit index (NFI), the comparative fit index (CFI), and the relative fit index (RFI) were .86, .96, and .82, respectively. Except for the CFI, the fit statistics of the measurement model were insufficient and indicated that the measurement model required modification.
Figure 10. Original measurement model: Confirmatory Factor Analysis was used to test the model fit of the measurement models of conditioned fear, state anxiety, and respiratory function ($\chi^2 (51, N = 102) = 70.19, p < .05; \text{CFI} = .96; \text{RMSEA} = .061$)

Note. $\beta$ = regression coefficient. $r^2$ & $R^2$ = explained variance.
Table 6

Regression Weights in the Original Measurement Model (N = 102)

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>NRS-emotional fear ← Conditioned Fear</td>
<td>.94</td>
<td>.14</td>
</tr>
<tr>
<td>NRS-cognitive fear ← Conditioned Fear</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Increased heart rate ← Conditioned Fear</td>
<td>-.12</td>
<td>.25</td>
</tr>
<tr>
<td>PetCO₂ ← Conditioned Fear</td>
<td>.06</td>
<td>.10</td>
</tr>
<tr>
<td>RSBI ← Conditioned Fear</td>
<td>.39</td>
<td>1.36</td>
</tr>
<tr>
<td>SSAS ← State Anxiety</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>NRS-anxiety ← State Anxiety</td>
<td>.69</td>
<td>.09</td>
</tr>
<tr>
<td>NRS-dyspnea ← State Anxiety</td>
<td>.52</td>
<td>.09</td>
</tr>
<tr>
<td>PaO₂/FiO₂ ← Respiratory Function</td>
<td>-30.46</td>
<td>108.57</td>
</tr>
<tr>
<td>P0.1/MIP ← Respiratory Function</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>TTI ← Respiratory Function</td>
<td>1.01</td>
<td>.08</td>
</tr>
<tr>
<td>WOB ← Respiratory Function</td>
<td>6.12</td>
<td>.57</td>
</tr>
</tbody>
</table>

Note. The three latent variables are italicizes. CR = Critical Ratio of Path. Dashes indicate that the standard error and critical ratio of path were not estimated. NRS = Numerical Rating Scale. PetCO₂ = end-tidal CO₂. RSBI = Rapid Shallow Breathing Index. SSAS = Shortened State Anxiety Scale. PaO₂/FiO₂ = the ratio of arterial oxygen partial pressure to fractional inspired oxygen concentration. P0.1/MIP = the ratio of occlusion airway pressure to maximum inspiratory pressure. TTI = tension-time index. WOB = work of breathing. ***p < .001.
Modified Measurement Model Fit Analysis

Inspection of each regression weight (Table 6) and the measurement error calculated for each variable was used to determine which indicators should be dropped to increase the model fit in the second iteration of the measurement model. In the modified measurement model, the changes in heart rate, PetCO₂, and RSBI from conditioned fear were excluded because their regression weights were not statistically significant and had a high error term of 1.0. Likewise, the regression weight of PaO₂/FiO₂ describing respiratory function was very low and had a high error term of 1.0. It was excluded in the final modified measurement model.

The chi-square index of the modified measurement model was not statistically significant (χ² (17, N = 102) = 24.41, and p > .05) (see Figure 11). The overall model fit indices of the modified measurement model were better than those of the original measurement model: NFI = .95; CFI = .98; RFI = .91. The RMSEA was .066, which is quite close to the “acceptable” cutoff criterion (.6) proposed by Hu & Bentler (1998) and may be considered a reasonable error of approximation in the population (MacCallum, Browne, & Sugawara, 1996). The results indicated that the modified measurement model was a good fit to the sample data. All regression weights in the modified measurement model were statistically significant (see Table 7). In addition, the internal consistencies of indicators within the latent variables in the modified measurement model were considerably high (see Table 8).
Table 7  

*Regression Weights in the Modified Measurement Model (N = 102)*

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>NRS-emotional fear ← <em>Conditioned Fear</em></td>
<td>.94</td>
<td>.14</td>
</tr>
<tr>
<td>NRS-cognitive fear ← <em>Conditioned Fear</em></td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>SSAS ← <em>State Anxiety</em></td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>NRS-anxiety ← <em>State Anxiety</em></td>
<td>.69</td>
<td>.09</td>
</tr>
<tr>
<td>NRS-dyspnea ← <em>State Anxiety</em></td>
<td>.52</td>
<td>.09</td>
</tr>
<tr>
<td>P0.1/MIP ← <em>Respiratory Function</em></td>
<td>1.00</td>
<td>-</td>
</tr>
<tr>
<td>TTI ← <em>Respiratory Function</em></td>
<td>1.01</td>
<td>.08</td>
</tr>
<tr>
<td>WOB ← <em>Respiratory Function</em></td>
<td>6.11</td>
<td>.57</td>
</tr>
</tbody>
</table>

*Note.* The three latent variables are italicizes. CR = Critical Ratio of Path. Dashes indicated the standard error and critical ratio of path were not estimated. NRS = Numerical Rating Scale. SSAS = Shortened State Anxiety Scale. P0.1 /MIP = the ratio of occlusion airway pressure to maximum inspiratory pressure. TTI = tension-time index. WOB = work of breathing.  

***p < .001
Table 8

*Internal Consistencies of Indicators within the Latent Variables*

<table>
<thead>
<tr>
<th></th>
<th>Conditioned Fear</th>
<th>State Anxiety</th>
<th>Respiratory Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS-emotional fear</td>
<td></td>
<td>NRS-anxiety</td>
<td></td>
</tr>
<tr>
<td>NRS-cognitive fear</td>
<td></td>
<td>NRS-dyspnea</td>
<td></td>
</tr>
<tr>
<td>SSAS</td>
<td></td>
<td>P0.1/MIP</td>
<td></td>
</tr>
<tr>
<td>TTI</td>
<td></td>
<td>WOB</td>
<td></td>
</tr>
</tbody>
</table>

Internal Consistency

(Cronbach’s $\alpha$) .79 .79 .90

*Note.* NRS = Numerical Rating Scale. SSAS = Shortened State Anxiety Scale. P0.1 / MIP = the ratio of occlusion airway pressure to maximum inspiratory pressure. TTI = tension-time index. WOB = work of breathing.
Figure 11. Modified Measurement Model: the model fit testing when the changes in heart rate, PetCO₂, and RSBI, and also PaO₂/FiO₂ were excluded from the original measurement model ($\chi^2 (17, N = 102) = 24.41, p > .05; \text{CFI} = .98; \text{RMSEA} = .066$).

Note. $\beta = \text{regression coefficient.} \quad r^2$ & $R^2 = \text{explained variance.}$
The measurement model fit analysis and further modification of the original measurement model resulted in a modified measurement model with two indicators, NRS-emotional fear and NRS-cognitive fear, for conditioned fear; three indicators, SSAS, NRS-state anxiety, and NRS-dyspnea, for state anxiety; and three indicators, P0.1/MIP, TTI, and WOB, for respiratory function (Figure 12). The resulting modified measurement model was established for further structural model analysis.

*Structural Model Fit Analysis and Hypothesis Testing*

Having established the measurement model to quantify the PVWM, a series of hypothesis tests were run for empirically validating the model. The interplay of three latent variables, conditioned fear, state anxiety and respiratory function, was hypothesized to affect the weaning outcome. The weaning outcome was determined by the length (in days) of mechanical ventilation (MV) that subjects required after initiating the second T-piece weaning trial. The results of the structural model fit analysis and hypothesis testing are presented in the following order: (1) the results of the hypothesized structural model fit analysis; (2) results of testing Hypothesis 1, which posits that conditioned fear has direct and indirect effects on state anxiety, respiratory function, and weaning outcome; (3) results of testing Hypothesis 2, which posits that state anxiety has direct and indirect effects on respiratory function and weaning outcome; and (4) results of testing Hypothesis 3, which posits that only respiratory function has direct effects on weaning outcome.
Results of the Hypothesized Structural Model Fit Analysis

The fit of the hypothesized structural model was tested with AMOS 5.0 using the sample covariance matrix as input and a maximum likelihood solution. The chi-square index of the hypothesized structural model, taking into account the modified measurement model (see Figure 12), was not statistically significant ($\chi^2 (22, N = 102) = 31.22, p > .05$), and model fit indices were: NFI = .93; CFI = .98; RFI = .89. The RMSEA was .064. Overall, the model fit indices indicated the PVWM was a good fit to the sample data. The variables in the hypothesized model were able to account for 19% of variance in the LOMV. Regression weights of only two paths were statistically significant: from conditioned fear to state anxiety and from the respiratory function to LOMV (see Table 9). The total effects (including the direct and indirect effects) of conditioned fear, state anxiety, and respiratory function on the weaning outcome are described in Table 10.
Figure 12. PVWM with Modified Measurement Model: Effects of conditioned fear, state anxiety, and respiratory function on the length of mechanical ventilation ($\chi^2 (22, N = 102) = 31.22, p > .05; \text{CFI} = .98; \text{RMSEA} = .064$).

Note. $\beta = \text{regression coefficient. } r^2 & R^2 = \text{explained variance. LOMV = Length of Mechanical Ventilation.}$
Table 9

Regression Weights among Variables in Psychophysiological Ventilator Weaning Model (PVWM) \( (N = 102) \)

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>State Anxiety ← Conditioned Fear</td>
<td>1.08</td>
<td>.18</td>
</tr>
<tr>
<td>Respiratory Function ← Conditioned Fear</td>
<td>-.00</td>
<td>.01</td>
</tr>
<tr>
<td>LOMV ← Conditioned Fear</td>
<td>-0.03</td>
<td>.04</td>
</tr>
<tr>
<td>Respiratory Function ← State Anxiety</td>
<td>.01</td>
<td>.01</td>
</tr>
<tr>
<td>LOMV ← State Anxiety</td>
<td>.04</td>
<td>.03</td>
</tr>
<tr>
<td>LOMV ← Respiratory Function</td>
<td>2.43</td>
<td>.54</td>
</tr>
</tbody>
</table>

Note. CR = Critical Ratio of Path. LOMV = Length of Mechanical Ventilation.

*** \( p < .001 \)
Table 10
*Direct Effects, Indirect Effects, and Total Effects among Variables in Psychophysiological Ventilator Weaning Model (PVWM)*
*(N = 102)*

<table>
<thead>
<tr>
<th></th>
<th>Standardized Direct Effects</th>
<th>Standardized Indirect Effects</th>
<th>Standardized Total Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>State Anxiety</td>
<td>Respiratory Function</td>
<td>State Anxiety</td>
</tr>
<tr>
<td>Conditioned Fear</td>
<td>.77</td>
<td>-.01</td>
<td>-.10</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>.00</td>
<td>.23</td>
<td>.20</td>
</tr>
<tr>
<td>Respiratory Function</td>
<td>.00</td>
<td>.000</td>
<td>.39</td>
</tr>
</tbody>
</table>

*Note.* LOMV = Length of Mechanical Ventilation.
Further Model Fit Analysis with Logarithm of Outcome Variable

That the relationships between three latent variables and the outcome variable might be nonlinear was suspected, based on the researcher’s empirical observation. In addition, the nonnormality of residual distribution presented in statistical graphics (see Appendix H), when using these three latent variables to predict the LOMV, suggested nonlinear functions. Therefore, the logarithmic transformation of the LOMV was carried out to alleviate possible problems stemming from nonlinearity and nonnormality in PVWM (Cohen et al., 2003).

The model fit in the reiteration of the hypothesized model with the logarithm of LOMV, was evaluated by AMOS 5.0 with a maximum likelihood resolution. The results indicated that, again, the chi-square index was not statistically significant ($\chi^2 (22, N = 102) = 29.02, p > .05$). All the model fit indices were: NFI = .94; CFI = .98; RFI = .90. The RMSEA was lower (.056) when compared to the hypothesized model with the non-transformed data (RMSEA = .064) (see Table 11). The overall fit indices indicated that the hypothesized model was a good fit to the log-transformed data.

The variables in the hypothesized model were able to account for 25% of variance in the logarithm of the LOMV (see Figure 13). Compared with the effects generated from the non-transformed data, the total effects (including the direct effects and the indirect effects) of conditioned fear, state anxiety, and respiratory function on the weaning outcome all increased (see Table 12). The results of the three hypotheses to be tested were the same as those for the model with the non-transformed data. The better model fit indices and greater explained variance for the transformed weaning outcome variable
supported the idea that relationships were not linear. Therefore, the three hypotheses were also tested for the transformed outcome variable.
Figure 13. PVWM with Log-LOMV: The Model fit of Psycholophysiological Ventilator Weaning Model (PVWM) was tested with log-transformed LOMV data set ($\chi^2 (22, N = 102) = 29.02, p > .05;\ CFI = .98;\ RMSEA = .056$)

Note. $\beta$ = regression coefficient. $r^2$ & $R^2$ = explained variance. LOMV = Length of Mechanical Ventilation.
Table 11
*Model Fit Indices Presented in Model Fit Analysis of PVWM with the Non-transformed and Transformed Data Sets*

<table>
<thead>
<tr>
<th></th>
<th>$\chi^2$</th>
<th>NFI</th>
<th>CFI</th>
<th>RFI</th>
<th>RMSEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-transformed Data Set</td>
<td>31.218; $p &gt; .05$</td>
<td>.93</td>
<td>.98</td>
<td>.89</td>
<td>.064</td>
</tr>
<tr>
<td>Transformed Data Set</td>
<td>29.019; $p &gt; .05$</td>
<td>94</td>
<td>.98</td>
<td>.90</td>
<td>.056</td>
</tr>
</tbody>
</table>

*Note.* PVWM = Psychophysiological Ventilator Weaning Model.

Table 12
*Regression Weights in PVWM with the Non-transformed and Transformed Data Sets*

<table>
<thead>
<tr>
<th></th>
<th>Standardized Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-transformed</td>
</tr>
<tr>
<td><strong>State Anxiety ← Conditioned Fear</strong></td>
<td>.77***</td>
</tr>
<tr>
<td><strong>Respiratory Function ← Conditioned Fear</strong></td>
<td>-.01</td>
</tr>
<tr>
<td><strong>LOMV ← Conditioned Fear</strong></td>
<td>-.10</td>
</tr>
<tr>
<td><strong>Respiratory Function ← State Anxiety</strong></td>
<td>.23</td>
</tr>
<tr>
<td><strong>LOMV ← State Anxiety</strong></td>
<td>.20</td>
</tr>
<tr>
<td><strong>LOMV ← Respiratory Function</strong></td>
<td>.39***</td>
</tr>
</tbody>
</table>

*Note.* LOMV = Length of Mechanical Ventilation.

*** $p < .001$
Results of Testing Research Hypothesis 1

The first hypothesis was: Conditioned fear acquired from the first T-piece weaning failure has both direct and indirect effects on the outcome of the weaning trial following the first T-piece weaning failure. The indirect effect of conditioned fear on the weaning outcome is mediated by state anxiety and respiratory function. The purpose of this hypothesis was to determine how strong conditioned fear would affect the weaning outcome through direct and indirect paths. The results indicated that conditioned fear had a significant regression weight (.77) on state anxiety, but non-significant regression weight on respiratory function (-.02) and the LOMV (-.13) (see Table 13). Conditioned fear did, however, have small indirect effects on the respiratory function and LOMV, .18 and .288, respectively (see Table 14). In summary, the first hypothesis was partially supported by the sample data: (1) conditioned fear had a positive direct effect on state anxiety; (2) conditioned fear had no significant direct effects on the respiratory function or weaning outcome; and (3) conditioned fear had indirect effects on the respiratory function and weaning outcome mediated by state anxiety.

Table 13

Regression Weights between Condition Fear and Other Latent Variables in PVWM

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized Estimate</th>
<th>SE</th>
<th>CR</th>
<th>Standardized Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>State Anxiety← Conditioned Fear</td>
<td>1.08</td>
<td>.18</td>
<td>5.92</td>
<td>.77***</td>
</tr>
<tr>
<td>Respiratory Function← Conditioned Fear</td>
<td>-.00</td>
<td>.01</td>
<td>-.07</td>
<td>-.02</td>
</tr>
<tr>
<td>LOMV ← Conditioned Fear</td>
<td>-.03</td>
<td>.04</td>
<td>-.67</td>
<td>-.13</td>
</tr>
</tbody>
</table>

*Note. PVWM = Psychophysiological Ventilator Weaning Model. CR = Critical Ratio of Path. *** p < .001*
Table 14

*Direct and Indirect Effects between Conditioned Fear and Other Variables in PVWM*

<table>
<thead>
<tr>
<th></th>
<th>Standardized Direct Effect</th>
<th>Standardized Indirect Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>State Anxiety</td>
<td>Respiratory Function</td>
</tr>
<tr>
<td>Conditioned Fear</td>
<td>.77</td>
<td>-.02</td>
</tr>
</tbody>
</table>

*Note.* PVWM = Psychophysiological Ventilator Weaning Model. LOMV = Length of Mechanical Ventilation.

Results of Testing Research Hypothesis 2

The second hypothesis was: State anxiety derived from unresolved fear has both direct and indirect effects on the weaning outcome. The indirect effect of state anxiety on the weaning outcome is mediated by the respiratory function. The purpose of this hypothesis was to test how well state anxiety would affect weaning outcome through direct and indirect paths. Regression weights of paths from state anxiety to both respiratory function and the LOMV were positive but not statistically significant: .24 and .28, respectively (see Table 15). The indirect effect of state anxiety on the LOMV was small, .10 (see Table 16). Accordingly, the results indicated that state anxiety had at most only small effects on respiratory function and weaning outcome.
Table 15
Regression Weights among State Anxiety and Other Variables in PVWM (N = 102)

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized Estimate</th>
<th>SE</th>
<th>CR</th>
<th>Standardized Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Function ← State Anxiety</td>
<td>.01</td>
<td>.01</td>
<td>1.03</td>
<td>.24</td>
</tr>
<tr>
<td>LOMV ← State Anxiety</td>
<td>.04</td>
<td>.03</td>
<td>1.41</td>
<td>.28</td>
</tr>
</tbody>
</table>

Note. PVWM = Psychophysiological Ventilator Weaning Model. CR = Critical Ratio of Path. LOMV = Length of Mechanical Ventilation.

Table 16
Direct and Indirect Effects of State Anxiety on other variables in PVWM (N = 102)

<table>
<thead>
<tr>
<th>Standardized Direct Effect</th>
<th>Standardized Indirect Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Function</td>
<td>LOMV</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>.24</td>
</tr>
</tbody>
</table>

Note. PVWM = Psychophysiological Ventilator Weaning Model. LOMV = Length of Mechanical Ventilation.

Results of Testing Research Hypothesis 3

The third hypothesis was: The respiratory function itself, or as affected by conditioned fear and anxiety, has a direct effect on patients’ ventilator weaning outcomes.

This hypothesis was to test the relationship between respiratory function and the length of MV. The results indicated that respiratory function had a positive direct effect on the length of MV, .42, which was statistically significant (see Table 17). This third hypothesis was supported.
In conclusion, the hypothesized PVWM, after some modifications, was a good fit to the sample data. Standardized total effects of conditioned fear on state anxiety, respiratory function, and weaning outcome were .77, .17, and .16, respectively. The total effects of state anxiety on the respiratory function and weaning outcome were .24 and .38, respectively. In addition, respiratory function had a total effect of .42 on the weaning outcome. Conditioned fear had a significant direct effect on state anxiety, but it did not have a statistically significant direct effect on either respiratory function or weaning outcome. State anxiety had only small direct and indirect effects on respiratory function and weaning outcome. However, respiratory function significantly affects weaning outcome and has a direct path to it.

Post Hoc Analysis and Model Comparisons

As acknowledged, this study is novel by relating conditioned fear to ventilator weaning outcome. Given the somewhat exploratory nature of this preliminary study, but consistent with contemporary research findings and theoretical hypotheses, it was reasonable to carry out a post hoc analysis. This analysis was based on inspection of the results from the hypothesized model fit analysis and justification from original
hypotheses. Respecification of the model to generate competing alternative models was then tried. Two competing alternative models were established and tested in this study. The alternative models were nested within the hypothesized model; therefore, nested model comparisons were used to test the differences of the chi-square value according to their associated degree of freedom between the alternative models and the hypothesized model. These nested model comparisons provided the statistical basis on which to generate a model that was best fitting and most parsimonious. Akaike Information Criterion (AIC) (Browne & Cudek, 1993) is another fit index, which was also used to determine which of the three competing models was best fitting to the sample data. Smaller AIC values indicate better-fitting models.

*Alternative Model Fit Analysis and Hypothesis Testing*

*The First Alternative Model Fit Analysis and Hypothesis Testing*

The first alternative model eliminated two direct paths (the dash lines in Figure 14), those from conditioned fear to “respiratory function” and to “weaning outcome”—the LOMV, which had unexpected negative, although non-significant path coefficients. The hypotheses of the first alternative model were: (1) conditioned fear has a direct effect on state anxiety that will further indirectly affect the respiratory function and LOMV; (2) state anxiety has a direct effect on the respiratory function and both direct and indirect effects on the LOMV; (3) respiratory function has a direct effect on the LOMV.

Fit of this alternative model with the transformed data of the LOMV was evaluated. The chi-square index of the first alternative model was not statistically significant ($\chi^2 (24, N = 102) = 29.49, p > .05$) (see Figure 15). The model fit indices were:
NFI = .94; CFI = .99; RFI = .91. The RMSEA was lower at .048 when compared to the originally hypothesized model (RMSEA = .056) (see Table 18). All these indices indicate that the first alternative model was a good fit to the sample data. The variables in the first alternative model were able to account for 24% of the variance in the log LOMV.

The results of hypothesis tests for the first alternative model indicated that: (1) conditioned fear had a statically significant direct effect (.77) on the state anxiety; (2) state anxiety had a significant direct effect (.22) on respiratory function, but a non-significant direct effect (.17) on LOMV; and (3) respiratory function did significantly and directly affect (.42) LOMV (see Table 19). The total effects of the conditioned fear, state anxiety, and respiratory function on the LOMV were .20, .26, and .42, respectively (See Table 20).

Table 18

<table>
<thead>
<tr>
<th>Model Fit Indices of the Original Hypothesized Model—PVWM and the First Alternative Model (N = 102)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>χ²</strong></td>
</tr>
<tr>
<td>Original Hypothesized Model</td>
</tr>
<tr>
<td>First Alternative Model</td>
</tr>
</tbody>
</table>

*Note. PVWM = Psychophysiological Ventilator Weaning Model.*
Figure 14. The First Alternative Model: Two direct paths (dash lines) from conditioned fear to respiratory function and LOMV were eliminated from PVWM ($\chi^2 (24, N = 102) = 29.49, p > .05; CFI = .99; RMSEA = .048$).

Note. $\beta$ = regression coefficient. $r^2$ & $R^2$ = explained variance. LOMV = Length of Mechanical Ventilation.
Table 19  
*Regression Weights among Variables in the First Alternative Model (N = 102)*

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>State Anxiety ← Conditioned Fear</td>
<td>1.07</td>
<td>.18</td>
</tr>
<tr>
<td>Respiratory Function ← State Anxiety</td>
<td>.01</td>
<td>.00</td>
</tr>
<tr>
<td>LOMV ← State Anxiety</td>
<td>.03</td>
<td>.02</td>
</tr>
<tr>
<td>LOMV ← Respiratory Function</td>
<td>2.44</td>
<td>.54</td>
</tr>
</tbody>
</table>

*Note.* The first alternative model was established by eliminating two direct paths from conditioned fear to respiratory function and LOMV from the original hypothesized model. CR = Critical Ratio of Path. LOMV = Length of Mechanical Ventilation.  
*** p <.0001; *p <.05
Table 20

Direct Effects, Indirect Effects, and Total Effects among Variables in the First Alternative Model ($N = 102$)

<table>
<thead>
<tr>
<th></th>
<th>Standardized Direct Effects</th>
<th>Standardized Indirect Effects</th>
<th>Standardized Total Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>State Anxiety</td>
<td>Respiratory Function</td>
<td>LOMV</td>
</tr>
<tr>
<td>Conditioned Fear</td>
<td>.77</td>
<td>.00</td>
<td>.00</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>.00</td>
<td>.22</td>
<td>.13</td>
</tr>
<tr>
<td>Respiratory Function</td>
<td>.00</td>
<td>.00</td>
<td>.39</td>
</tr>
</tbody>
</table>

Note. The first alternative model was established by eliminating two direct paths from conditioned fear to respiratory function and LOMV from the original hypothesized model. LOMV = Length of Mechanical Ventilation.
The Second Alternative Model Fit Analysis and Hypothesis Testing

The path (the dash line) from state anxiety to the LOMV was not statistically significant in the first alternative model, and it was eliminated in the second alternative model (Figure 15). The chi-square index of the second alternative model was not statistically significant ($\chi^2 (25, N = 102) = 33.28, p > .05$). The RMSEA of the second alternative model (.054) was slightly larger than in the first alternative model (.048), but the overall model fit indices were good: NFI = .93; CFI = .98; RFI = .90. All these indices indicated that the second alternative model was a good fit to the sample data; however, these indices were not better than those of the first alternative model.

All the hypotheses in the second alternative model were supported by the sample data (see Table 21) which were: (1) conditioned fear had a direct effect on the state anxiety; (2) state anxiety had a significantly direct effect on respiratory function; and (3) respiratory function significantly affected LOMV. These direct, indirect, and total effects among variables in the second alternative model are given in Table 22.
Figure 15. The Second Alternative Model: One direct path (dash line) from state anxiety to LOMV was eliminated from the first alternative Model ($\chi^2 (25, N = 102) = 32.28, p > .05; \text{CFI} = .98; \text{RMSEA} = .054$).

Note. $\beta =$ regression coefficient. $r^2$ & $R^2 =$ explained variance. LOMV = Length of Mechanical Ventilation.
Table 21

Regression Weights among Variables in the Second Alternative Model (N = 102)

<table>
<thead>
<tr>
<th>Paths</th>
<th>Unstandardized</th>
<th>Standardized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>State Anxiety ← Conditioned Fear</td>
<td>1.06</td>
<td>.18</td>
</tr>
<tr>
<td>Respiratory Function ← State Anxiety</td>
<td>.01</td>
<td>.00</td>
</tr>
<tr>
<td>LOMV ← Respiratory Function</td>
<td>2.66</td>
<td>.53</td>
</tr>
</tbody>
</table>

Note. The second alternative model was established by eliminating a direct path from state anxiety to LOMV from the first alternative model. CR = Critical Ratio of Path. LOMV = Length of Mechanical Ventilation. ***p < .0001; *p < .05
Table 22

*Direct Effects, Indirect Effects, and Total Effects among Variables in the Second Alternative Model (N = 102)*

<table>
<thead>
<tr>
<th></th>
<th>Standardized Direct Effects</th>
<th></th>
<th>Standardized Indirect Effects</th>
<th></th>
<th>Standardized Total Effects</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>State Anxiety</td>
<td>Respiratory Function</td>
<td>LOMV</td>
<td>State Anxiety</td>
<td>Respiratory Function</td>
<td>LOMV</td>
</tr>
<tr>
<td>Conditioned Fear</td>
<td>.78</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.17</td>
<td>.08</td>
</tr>
<tr>
<td>State Anxiety</td>
<td>.00</td>
<td>.22</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.10</td>
</tr>
<tr>
<td>Respiratory Function</td>
<td>.00</td>
<td>.00</td>
<td>.46</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
</tr>
</tbody>
</table>

*Note.* The second alternative model was established by eliminating a direct path from state anxiety to LOMV from the first alternative model. LOMV = Length of Mechanical Ventilation.
Model Comparisons between Competing Models

Nested model comparison with the chi-square difference was used to test whether the first alternative model was better-fitting and more parsimonious than the originally hypothesized model. The chi-square difference was calculated by subtracting the $\chi^2$ value of the hypothesized model (29.02) from the $\chi^2$ value of the first alternative model (29.49), which was .37. The associated degree of freedom, which was two, was determined by subtracting the value for the hypothesis model ($df = 22$) from the value of the first alternative model ($df = 24$). The critical value for a $\chi^2$ with 2 degrees of freedom at $p < .05$ was 5.99. This $\chi^2$ value of .37 was much lower than the critical value and was not a significant difference ($p > .05$). In addition, Akaike Information Criterion (AIC) of the hypothesized model was 93.02. In comparison, AIC of the first alternative model was 89.49, smaller than the AIC value in the hypothesized model. Accordingly, the $\chi^2$ difference test and AIC values comparison suggested that the first alternative model was better-fitting to the sample data and more parsimonious than the hypothesized model.

The chi-square difference between the second ($\chi^2 = 32.28; df = 25$) and the first ($\chi^2 = 29.48; df = 24$) alternative model was 2.80, and the associated degree of freedom was 1. The critical value for a $\chi^2$ with 1 degree of freedom at $p < .05$ was 3.84. This $\chi^2$ value of 2.80 was lower than the critical value, indicating that the second alternative model was also a good fit to the sample data but more parsimonious in having one less variable. However, the AIC of the second alternative model (90.28) was higher than the AIC of the first alternative model (89.49), which indicated the second alternative model was not a better fit to the sample data than the first hypothesized model. On the other hand, the total
effects of conditioned fear and state anxiety on the LOMV were both near zero, which is contrary to both theoretical and empirical arguments. Therefore, the second alternative model was not considered an alternative model to replace the hypothesized model.
CHAPTER FIVE: DISCUSSION

This section will discuss the results and the implications of this study in the field in the following manner. The characteristics of the sample will be addressed first. This will be followed by the discussion of findings from the model fit analysis. Next, the implications of the findings from this study will be addressed. Finally, the limitations of the study and direction for future research in the area of repeated ventilator weaning failure will be highlighted.

Characteristics of the Sample

Several sample characteristics are important to highlight. These include gender, age, the recruiting settings, the length of MV prior to the 2nd weaning trial, and the total length of MV. All mechanically ventilated subjects recruited for the study had failed in their first T-piece weaning trial. Since psychophysiological impacts from the first weaning failure were considered to be affecting weaning outcome of subsequent weaning trials in MV patients, a heterogeneous population was targeted for this study. Both male and female subjects with a variety of diagnoses were enrolled in the present study (see Appendix G). Interestingly, the results indicated that male subjects had a significantly higher level of self-reported cognitive fear and state anxiety than female subjects. This finding was consistent with prior animal and human studies (Gupta, Sen, Diepenhorst, Rudick, & Maren, 2001; Sorg, Swindell, & Tschirgi, 2004; Zorawski, Blanding, & Kuhn, 2006), in which males showed a higher level of conditioned fear and anxiety than females did. However, this observed gender difference in fear and anxiety had no significant relationship with performances in respiratory function.
Most of the subjects enrolled in the present study were 70 years of age or older. However, there was not a great difference between the mean age of the sample and the mean age of the mechanically ventilated ICU patients in the target medical center. Interestingly, age was found to have a significant correlation with the performance of respiratory function and length of mechanical ventilation (LOMV). Seneff et al. (1996) found that if case-mix and severity of disease were controlled, age alone was not a strong predictor for the duration of mechanical ventilation. Due to the small sample size and lack of severity measures in this study, the control of case-mix and severity of disease were unable to be performed to further test the prediction of age alone on LOMV.

Due to the higher rate of successful initial weaning in the SICU than in the MICU, most of the subjects were recruited from the MICU, so only a small proportion of them were from the SICU. This representation is consistent with current literature; for example, in Seneff et al. (1996) and Yende & Wunderink (2002), there were 20% of MICU patients and 5% of SICU patients who failed in their initial weaning trial. However, subjects recruited from different settings had no significantly different performance in their conditioned fear, state anxiety, respiratory function, and LOMV. In addition, medical diagnoses (pulmonary or non-pulmonary diseases) and etiologies for mechanical ventilation (ARF or post surgery statuses) were not significant predictors of conditioned fear, state anxiety, respiratory function, or LOMV in this study.

Subjects’ length of MV prior to 2nd weaning trial and the total length of MV were found to have no significant correlation with their conditioned fear, state anxiety, respiratory function, and weaning outcomes in the 2nd weaning trial. However, the mean
total length of MV (18.9 days) for the sample was longer than reported from prior studies—most MV patients (80%) are successfully weaned from ventilation within 7 days (Gilmartin et al., 1999; Seneff et al., 1996).

Findings and Interpretations

The results of statistical analysis combined with underpinning theoretical arguments help to modify and further establish a better resulting model. This section will detail findings and interpretations of the original PVWM and resulting PVWM.

Findings and Interpretations of the Measurement Model Fit Analysis

A significant chi-square value and two model fit indices less than .9 from the model fit analysis of the multifactor measurement model indicated that the originally specified measurement model was a misfit with the sample data. Accordingly, modification of the measurement model was conducted, which was based on theoretical and statistical considerations. For instance, in the hypothesized measurement model, three latent variables affected their respective indicators, which means that indicators were effects of these latent variables. Therefore, the internal consistency among the indicators and corresponding latent variable and the statistical significance of each effect of latent variables on their respective indicator were indices used to direct the modifications of the original model in the study.

Measurement Model of Conditioned Fear

Emotional fear and cognitive fear, which were self-reported by the subjects when they underwent their second T-piece weaning trial, demonstrated a good correlation with each other. The results indicated that subjects felt more strongly that there was a chance
of experiencing shortness of breath from ventilator weaning than how they rated their emotional fear of ventilator weaning. In addition, the overall self-reported fear was only moderate in these subjects, which was less than expected. A likely explanation for the overall self-reported moderate fear of T-piece weaning is that perhaps most of these subjects were worried that they would be delayed in the initiation of their subsequent weaning trial if they reported that they were fearful. Interestingly, they reported this sentiment in spite of being assured that their response on the NRSs would not affect their treatment and medical intervention. On the other hand, the continual presence of the researcher during the data collection time might be consider a safety-signal for subjects as they undergo the second weaning trial and might have reduced their self-reported fear (Sartory, Master, & Rachman, 1989).

Three indicators representing physiological reactions of conditioned fear, the changes in heart rate, PetCO₂ and rapid shallow breathing index, were found to have a low correlation with self-reported conditioned fear. In addition, the correlations between each of the physiological reactions and other indicators of conditioned fear were all non-significant (see Appendix J). The changes in heart rate during the second T-piece weaning trial were minute, and the changes in PetCO₂ were all lower than the reduction level required for categorizing it as a positive hyperventilation of 10 mmHg (Kroeze & Van den Hout, 1998). The changes noted in RSBI varied among subjects, but these were not correlated with other indicators of conditioned fear.

The effects of conditioned fear on emotional fear and cognitive fear were statistically significant. The internal consistency between emotional fear and cognitive
fear was also high. In addition, the correlation between these two indicators was higher than the correlations between these two indicators and indicators from other measurement models (models for state anxiety and respiratory function). The effects of conditioned fear on those three physiological reactions were not statistically significant (see Table 7). The poor internal consistency of the measurement model, including these three indicators, could overrule the assumption of the latent variable of conditioned fear represented by its indicators. In addition, subjects’ self-reported fears were considered as their true inner most feelings about ventilator weaning and were the primary focus of the present study. Accordingly, indicators of the changes in heart rate, PetCO₂, and RSBI were removed from the measurement model of conditioned fear.

In summary, results from testing the measurement model of conditioned fear in this study indicated that during the second T-piece weaning trial, subjects self-reported moderate fear but had a high internal consistency. Unfortunately, the three physiological indicators of conditioned fear taken from the subjects during the second T-piece weaning trial were neither consistent with each other nor with the subjects’ self-reported fear. These results were inconsistent with Lang’s (1968) theoretical framework and findings from Campbell et al. (1964), in which a series of physiological responses under conditioned fear were expected: increased respiration rate and heart rate and self-reports of fear. One likely explanation for these results is that the high disease severity of these ICU patients could cause compromised autonomic functions (Schmidt, Werdan, & Müller-Werdan, 2001), in which the normal physiological reactions to conditioned fear might decrease accordingly. On the other hand, the results were consistent with prior
studies; the covariance of subjective feelings and specific physiological activity was not found, especially not in clinically significant emotions (Hugdahl, 1981; Lang et al., 1972; Rachman, 1978). In addition, these results were also consistent with Obrist’s (1968) finding: there was no consistent relationship between respiration and the cardiac changes in human subjects during classical aversive conditioning.

**Measurement Model of State Anxiety**

Using the SSAS, subjects in this present study reported their state anxiety mostly at a moderate level when it was converted into the full form of Spielberger’s State-Trait Anxiety Inventory (STAI). This is consistent with the recent studies of Chlan (1998) and Wong et al. (2001); the mean anxiety score of mechanically ventilated subjects in their studies also was reported as moderate. In addition, the mean scores of subjects’ NRS-anxiety and NRS-dyspnea were approximately the same as those of Knebel’s (1990) study, in which the subjects self-reported their anxiety and dyspnea on 100mm visual analogue scales during 0% ventilator support weaning.

The subjects’ report of moderate anxiety level in the present study was not consistent with the findings from Logen & Jenny’s (1997) qualitative study, in which patients, who were weaned from mechanical ventilation, recalled their weaning process as a miserable experience. The likely explanation for this controversial finding is that the continual presence of the researcher at the subjects’ bedsides before and during the second weaning trial served to reduce subjects’ anxiety; this was suggested by findings from previous studies (Jenny and Logan, 1994; 1996; Logan & Jenny, 1997; Wunderlich et al., 1999).
The effects of state anxiety on indicators of SSAS, NRS-state anxiety, and NRS-dyspnea were all statistically significant (see Table 7). These three indicators presented a high internal consistency, and of the three indicators the correlation between any two was also high (see Appendix J). In addition, in the state anxiety measurement model the correlation between two of the three indicators was higher than the correlations between these three indicators and indicators from other measurement models (conditioned fear and respiratory function). In summary, as hypothesized, the latent variable of state anxiety was correctly defined with these three indicators: SSAS, NRS-state anxiety, and NRS-dyspnea.

Measurement Model of Respiratory Function

According to Whiteley, Gavaghan, & Hahn (2002), the P/F ratio of 150 or less suggests impaired gas exchange. In the present study, only few subjects had a P/F ratio less than 150 during the second T-piece weaning. In fact, most of these subjects had a good gas exchange status. This is likely due to one of the weaning criteria at the target medical center that required a P/F ratio greater than 150. Therefore, this measurement also demonstrated stable gas exchange and was not affected by the weaning process in this study.

With the exception of gas exchange, all the indicators of respiratory function indicated that most of the subjects in the present study had a compromised respiratory function. Based on prior literature these patients had respiratory function values that would not predict successful weaning from mechanical ventilation in the current T-piece trial. Since few studies have examined repeated ventilator weaning failure, these findings
are new. The extent of respiratory function in this group of patients had not been previously described and was unexpected. The mean of P0.1/MIP ratio (.14) in the sample was far worse than the cut-off level of .09 or less to successfully wean (Capdevila et al., 1995), and in actuality, most of the subjects had a P0.1/MIP ratio of .09 or more. The mean of TTI (.19) of these subjects was worse than the threshold of .15 for predicting failed ventilator weaning (Vassilakopoulos et al., 1998). Similar to the P0.1/MIP ratio and TTI, the mean of WOB (1.19) was also less than ideal for increasing the likelihood of successful weaning; the ideal value is .80 J/L or less. Accordingly, the high proportion of subjects with compromised respiratory function during the second T-piece weaning is worth noting, especially by health care providers, when initiating weaning trials for patients with repeated ventilator weaning failure.

The effects of respiratory function on the indicators were statistically significant, but its effect on gas exchange was not significant (see Table 7). Internal consistency among the three standardized indicators was considerably high; however, the P/F ratio did not correlate well with each of the three indicators in the measurement model of respiratory function (see Appendix J). As previously mentioned, a possible reason for this poor statistical result was that the P/F ratio was treated as a criterion for patient eligibility to undergo the T-piece weaning trial. In this study, all subjects had an acceptable P/F ratio prior to T-piece weaning. Consistent with findings from Torres et al. (1989), there was no significant reduction of PaO2 due to simultaneous increase in cardiac output at the time of discontinuing ventilator support. Consequently, gas exchange was removed from the measurement model of respiratory function.
The modified measurement model was established by eliminating four indicators from their respective latent variable (see Figure 12). As a result, all subsequent model fit indices of the modified measurement model indicated a good fit to the sample data. In summary, the three hypothesized latent variables were proven to be well identified by their respective indicators in the modified measurement model (see Figure 12).

**Findings and Interpretations of the Structure Model Fit Analysis and Hypothesis Testing**

Having integrated the modified measurement model, the overall model fit indices indicated that the PVWM was a good fit to the sample data. An interesting empirical finding implied that the weaning outcome might have a nonlinear relationship with the psychophysiological variables in PVWM. The results of prior studies have indicated that the longer the duration of ventilatory support, the greater the risk for potential complications related to mechanical ventilation (Gilmartin et al., 1999; Tobin, 1994). These complications included both pulmonary and nonpulmonary problems, which were not all included in PVWM. However, these complications might affect or be affected by the three latent variables in PVWM, which could be the cause of the inconsistent relationships in PVWM. This phenomenon was suspected because it was consistent with the researcher’s empirical observation during data collection.

Based on this empirical implication for the sample, a difference was found in psychophysiological performance between subjects with weaning outcome—LOMV ≤ 14 days and > 14 days in the second weaning trial. Subjects with LOMV > 14 days demonstrated poorer respiratory function as measured by TTI, WOB, and P0.1/MIP than subjects with LOMV < 14 days, but there was no significant difference in subjects’
conditioned fear and state anxiety between these groups. This result indicated that the relationships between the three latent variables and weaning outcome—LOMV—were inconsistent for subjects with different needs on LOMV. This finding, combined with empirical observation and the results from prior studies, suggested that nonlinear relationships exist between LOMV and other variables. In addition, when the three latent variables were used to predict weaning outcome, a nonnormality of residual distribution was found in the statistical graphs (see Appendix H). This again would indicate that transformation of variables would be needed to avoid the problems of nonlinearity and nonnormality in PVWM.

To avoid the problems of nonlinearity in PVWM and nonnormality of residuals affecting the accuracy of the statistical tests, logarithmic transformation of the outcome variable was suggested (Cohen et al., 2003; Frank, 1966). In addition, due to the considerable variability of the duration of mechanical ventilation between the patients, a logarithmic transformation was used in Esteban et al.’s (1994) study. Accordingly, common log (base 10 logarithms) transformation of the LOMV was used to generate an approximate linear relationship between the three latent variables and the LOMV. The importance of log transformation of the LOMV was that the rate of change in the LOMV was more emphasized than its absolute amount of change in the PVWM (Frank, 1966). In other words, by using the logarithmic transformation of the LOMV, the research redefined the relationship in proportional terms between three latent variables and the outcome variables in PVWM.

The results of further model fit analysis of PVWM with the logarithmic
transformation of the LOMV indicated that: (1) the overall model fit indices were better than those in the model analysis with the original data set of the outcome variables (see Table 11), (2) the explained variance of weaning outcome was increased by all latent variables in PVWM, and (3) the estimated strengths of all hypothesized paths were greater than those found with the original outcome data; however, the significance of these hypothesized paths did not change (see Table 12). The normality of residual distribution, resulting from the use of the three latent variables to predict the outcome variable, was improved in the logarithmic data set and could be visualized in statistical graphs. These results indicated that the logarithmic transformation was needed to help remedy the problems of nonlinearity and nonnormality existing in non-transformed data (see Appendix I).

*Paths from Conditioned Fear to Weaning Outcome*

Consistent with the findings from contemporary studies, conditioned fear was strongly correlated with state anxiety and suggested as a precursor for the development of anxiety (Barlow, 2002; Rosen & Schulkin, 1998). Under fear stimuli, the amygdala and its connections, which play a core role in both fear and anxiety, will increase both the hyperexcitability and the release of neuroendocrine hormones; thereby, further heightened anxiety (Rosen & Schulkin, 1998).

Ley (1999) indicated that several potential ventilatory changes, such as hyperventilation, decreased PetCO₂, and increased total respiratory resistance, were found during the adaptive process of conditioning emotions. These ventilatory changes were considered to further affect respiratory function. However, these ventilatory changes
were not found to covary with the subjects’ emotional fear and cognitive fear during the second weaning trial in the present study.

Conditioned fear, represented by self-reported emotional and cognitive fear in the present study, did not have a significant direct effect on respiratory function, which was represented by the central drive, the capability of respiratory muscles, and the workload of respiratory muscles. The correlation between conditioned fear and respiratory function appears contradictory in prior studies. Asmundson and Stein (1994) tested the correlation between the level of dyspnea /suffocation fear and respiratory function, based on dyspnea/suffocation-fear theory (Ley, 1989), in which they used the rate of forced expiratory air flow in L/min at the moment when vital capacity was half (50%) the volume at the onset of expiration, known as FEF 50%. They found that subjects with low FEF 50%, indicating worse respiratory function, had higher scores on self-reported measures of dyspnea fear or panic fear than subjects with high FEF 50%. In contrast to these findings, Spinhoven et al. (1995) found that the performance of FEF 50% did not correlate with the scores on self-reported dyspnea fear. The results of the present study were similar to Spinhoven’s (1995) findings.

The present study gathered preliminary data by testing how strongly conditioned fear, acquired from the first T-piece weaning failure, would affect weaning outcome. The results failed to support the hypothesis and indicated that conditioned fear did not have a significantly direct effect on weaning outcome. Although conditioned fear was not named in a previous study, McCartney & Boland (1994) suggested that the experience of failed ventilator weaning in physically and mentally unprepared patients can lead to prolonging
the weaning process. The theoretical suggestion posed by McCartney & Boland (1994), however, did not indicate the mechanism by which the failed experience and the prolonged weaning process interacted, if any. Unfortunately, the results of this study were unable to prove McCartney & Boland’s (1994) theoretical hypothesis.

*Paths from State Anxiety to Weaning Outcome*

Similar to the findings from prior studies, the results from the original model testing, where state anxiety was measured during subjects’ second T-piece weaning trial, did not present a statistically significant direct effect on either respiratory function or weaning outcome. From theoretical and empirical views, anxiety is regarded to be an important factor impacting respiratory function and, further, ventilator weaning outcome (Connelly et al., 2000; Grossbach-bandis, 1980; Knebel, 1990); however, the correlation between state anxiety to both respiratory function and weaning outcome was not statistically supported from the prior studies. The small sample size might have led to a possible type II error and perhaps can account for posing a statistical problem that explains why the testing failed to detect the direct effects of the state anxiety on respiratory function and weaning outcome.

However, after removal of the two direct paths from conditioned fear to respiratory function and to weaning outcome, state anxiety was found to have a significant direct effect on respiratory function in the first alternative model testing (see Figure 15). Even though the direct effect of state anxiety on weaning outcome still remained non-significant in the first alternative model analysis, measuring this relationship continued in the modified version of PVWM. The reasons for retaining it
will be detailed in the section *The Rationale of Model Modification.*

**Paths from Respiratory Function to Weaning Outcome**

The direct effect of respiratory function on the LOMV in the second T-piece weaning was hypothesized in the present study. The results supported the hypothesis and indicated that respiratory function had a significant impact on the weaning outcome. Three indicators of respiratory function, the central drive (P0.1 / MIP), the capability of respiratory muscles (TTI), and the workload of respiratory muscles (WOB), are well-established and commonly and successfully used in predicting the outcome (successful or failed) of a weaning trial (Capdevila et al., 1995; Vassilakopoulos et al., 1998; Gluck et al., 1995). However, these potent weaning predictors were rarely used to predict the length of mechanical ventilation.

In Seneff et al.’s (1996) study, they combined the subjects’ clinical and demographic characteristics with ICU information charted on Day 1 about disease and severity of illness to predict the duration of mechanical ventilation. They found that these patient characteristics accounted for 60% of the variance of subsequent length of mechanical ventilation. However, they did not incorporate respiratory function measurements in their study and suggested that the respiratory measurements might provide unique and important incremental information to their predictions. Even though the prediction of LOMV in the present study was not the same as Seneff et al.’s study, the predictive value of respiratory function on the LOMV shown in the present study will provide a different view to evaluate the patient’s prognosis for health care providers.
The Rationale of Model Modification

The overall model fit indices indicated PVWM had a good fit to the sample data, but four hypothetical direct effects among the variables were not statistically significant. Due to the pilot nature of this study, model modification coupled with post hoc analysis was conducted to improve model fit. All model fit indices of the first alternative model were better than the original hypothesized PVWM (see Table 18). Based on the nested model comparison between the original model and the first alternative model, the first alternative model was a better fit to the sample data and more parsimonious than the original. In addition, the theoretical direct path from state anxiety to respiratory function was supported with statistical significance. Using Cohen’s effect sized calculation (1988), 24% of explained variance of the LOMV, accounted for by the three latent variables in the alternative PVWM, would represent a moderately high effect size, .32.

Although the direct path from state anxiety to the LOMV remained non-significant in the first alternative model, it was determined that the model should be maintained for the following reasons. First, in order to avoid capitalization on chance and a data-driven result, the second alternative model was excluded (Kline, 2005). Second, the small sample size in the present study might have led to statistically describing the effect of state anxiety on the LOMV as non-significant. Third, eliminating the hypothetical direct path from state anxiety to the LOMV would decrease the explained variance of the LOMV. Lastly, and most importantly, the direct effect of state anxiety on the LOMV was theoretically acceptable (Green et al., 1998); that was also accidentally found in subgroup of the sample (LOMV ≤ 14 days). Based on the findings from the
present study, the effect of state anxiety on weaning outcome is greater on MV patients with shorter LOMV (≤ 14 days) than on patients with longer LOMV (> 14 days). If MV patients require LOMV > 14 day, their respiratory function and other unidentified physiological factors will obscure the effect of state anxiety on weaning outcome. Therefore, the direct effect of state anxiety on weaning outcome is considered important and was thus retained the resulting model.

*The First Alternative Model as the Resulting Model*

Based on statistical analysis of nested model comparisons and underpinning theoretical arguments, the first alternative model is recognized as the resulting Model in the present study. The resulting model (see figure 14) indicates that patients with high acquired conditioned fear from the first ventilator weaning failure will have high state anxiety during the second weaning trial. High state anxiety will cause compromised respiratory function during the weaning process and further cause prolonged mechanical ventilation in the subsequent weaning. The outcomes in the subsequent weaning trial will also be directly determined by MV patients’ state anxiety and respiratory function. The resulting model will need further study for cross-validation in another sample, which would facilitate the generalization of the model in MV patients with repeated ventilator weaning failure.

**Implications**

In the present study, some hypotheses on the relationships among conditioned fear, state anxiety, respiratory function, and weaning outcome were supported; however, some hypotheses failed to be validated. These findings have multiple implications for
Implications for Measurement

Based on the theoretical framework (Lang, 1968) and previous research findings (Campbell et al, 1964), conditioned fear was originally regarded as a latent variable and hypothesized to have effects on five indicators, known as effect indicators. Statistically speaking, indicators are affected or caused by the latent variable. The poor internal consistency among the subjective and objective indicators of conditioned fear suggested that these indicators might be the cause of conditioned fear but might not be the effect of it. In other words, conditioned fear presented in this study might be an emergent variable rather than a latent variable.

The indicators of an emergent variable are thought to cause rather than be caused by the emergent variable. Each indicator may have its different contribution to the emergent variable, but these indicators do not necessarily correlate with each other (Kline, 2006). Bollen & Lennox (1991) also argued that the indicators in a latent variable should be positively correlated with one another; however, whether the correlation among indicators in an emergent variable should be positive, negative, or non-existent is unknown. This finding was consistent with several prior studies, in which self-reported fear had no significant relationship with physiological responses to the fear acquired from conditioning (Hugdahl, 1981; Ost, 1991; Withers & Deane, 1995). Accordingly, this finding provided another way of thinking about conditioned fear as an emergent variable in patients who repeatedly experience ventilator weaning failure and may be applied to future studies.
Remarkably, the results indicated that gas exchange did not have a strong correlation with the three other indicators of respiratory function in the present study, even though the PaO$_2$/FiO$_2$ (P/F) ratio is considered a good indicator of gas exchange in contemporary knowledge. In the present study, subjects had to meet the weaning trial criterion of a P/F ratio of 150 or more, and not surprisingly, most maintained a good status of gas exchange during the weaning trial. This P/F ratio did not correspond with other indicators of respiratory function. Based on this finding, it suggested that it is not considered to be a good indicator of respiratory function to predict the LOMV during the second T-piece weaning trial.

**Implications for Theory**

The proposed PVWM was newly designed and tested with structural equation modeling (SEM). Among all hypothesized variables, the results indicated that respiratory function had the most potent effect on the LOMV following the second weaning trial. Compared to the effect of respiratory function, the psychological factors, conditioned fear and state anxiety, had only a small effect on the weaning outcome. An interesting question one can pose from these results is whether the psychological factors were relevant and could significantly affect the weaning outcome by their small effects. The nested model comparison was used to compare the PVWM with the model that had no paths from both conditioned fear and state anxiety to the respiratory function and the LOMV. The significant chi-square difference from the comparison of the two models suggested that including the psychological variables in the model was more favorable. This result supported the theoretical hypothesis and the empirical sense of the importance
of psychological factors in ventilator weaning, especially the second T-piece weaning.

Based on the assumption of SEM, the relationship between the independent variables and the dependent variable should be linear. However, the dependent variable, the length of MV, was suspected to have a nonlinear relationship with the independent variables, the three latent variables in PVWM. Empirical observation from the data collection period found that several unidentified variables (e.g., nosocomial infection and other further psychophysiological complications) that may occur after the second weaning trial might affect or be affected by the hypothetical variables in PVWM. This might have led to the nonlinearity between the independent variables (the conditioned fear, state anxiety, and respiratory function) and the dependent variable (the weaning outcome) in this study.

Applying the logarithm of the outcome variable, length of MV, and factoring it into the model analysis would improve the accuracy of the results; therefore, this was used to remedy the nonlinearity between the hypothesized psychophysiological factors and the weaning outcome. The better model fit indices and a higher explained variance of the outcome variable accounted by the three independent variables were found in the model analysis using log 10 transformation of the LOMV. The results supported the nonlinear relationship between psychophysiological factors (conditioned fear, state anxiety, and respiratory function) and the LOMV. The inclusion of the logarithm of the length of MV is recommended when replicating the study with the PVWM.

Implications for Research

This study was a preliminary attempt to test whether the psychophysiological
factors are impacted from failing the first weaning trial, and if so, to determine how these affected psychophysiological factors may influence the outcome of a subsequent weaning trial. Due to the partial exploratory nature of this preliminary study, the resulting model needs cross-validation in further research studies. The debatable amount of the explained variance of the LOMV accounted by the three latent variables in PVWM suggests that other potential variables should be included to better predict weaning outcome. Nevertheless, this study provides new knowledge about this complex problem of prolonged mechanical ventilation and offers new insights on possible future directions.

Compromised respiratory function during the weaning process was found to have the strongest effect on weaning outcome in PVWM. A large proportion of subjects whose condition met the weaning criteria, thus enabling them to commence their second weaning trial, still performed with compromised respiratory function during the weaning process in this study. Accordingly, detecting the proper weaning criteria for patients to undergo the second T-piece weaning trial, which might be different from the weaning criteria used for the first weaning trial, needs to be further studied.

Even though RSBI of 105 breath/min/L or more prior to weaning trials was found to accurately predict a failed weaning trial with high sensitivity (.97) and moderate specificity (.3 -.64) in prior studies (Capdevila et al., 1995; Yang & Tobin, 1991), researchers had in common the difficulty of finding what was responsible for RSBI. RSBI was suggested as a response of the respiratory center to the anxiety that occurred during the weaning trial (Holliday & Hyers, 1990; Vassilakopoulos et al., 1998). Based on suggestions from previous studies and Ley’s dyspnea/suffocation-fear theory (1989;
1999), the change in the Rapid Shallow Breathing Index (RSBI) during the second T-piece weaning was treated as an indicator of conditioned fear in this study. However, inspection of the correlation matrix for all variables found that the change in RSBI did not significantly correlate with any of the indicators of conditioned fear or state anxiety. It did have a significant correlation with indicators of respiratory function in the P0.1/MIP ratio, TTI, and WOB. Therefore, the change in RSBI might not be the indicator response to anxiety in the second weaning trial; the identity of RSBI in ventilator weaning needs further study. Another interesting finding from the present study was that the value of RSBI prior to the second T-piece weaning trial would neither predict the performance of respiratory function during weaning nor predict weaning outcome. Accordingly, the prediction power of RSBI in the first weaning trials might need to be considered differently in the second weaning trial.

Implications for Practice

In contrast to the unmodifiable variables (patient characteristics) accounting for 60% of the variance in patient’s duration of mechanical ventilation in the Seneff et al. (1996) study, the 24% of variance in the LOMV after the second T-piece weaning was accounted for by three modifiable variables in this study. Although the established model might need further studies to validate it, the results of this study allow health care providers to weigh the possible adverse impact of failed weaning trials on mechanically ventilated patients. According to the findings from prior studies, facilitating ventilator weaning to shorten patients’ mechanical ventilation will prevent these patients from utilizing a disproportionate number of technological and financial resources in the
clinical setting (Needham, 2005; Wagner, 1989). Therefore, the establishment of an intervention based on the findings in the present study will have important cost-benefits for taking care of patients who have repeated ventilator weaning failure.

As acknowledged, there is no prior evidence of a failed weaning trial adversely affecting the subsequent weaning outcome. This study is first to demonstrate that conditioned fear, acquired from the first T-piece weaning failure, and state anxiety were found to contribute to prolonged mechanical ventilation. Therefore, an intervention based on operant and counter-conditioning principles, such as biofeedback, progressive muscle relaxation, and systematic desensitization strategies (Hannich et al., 2004; Jacavone et al., 1998; Holliday & Lippman, 2003), is suggested to reduce fear and anxiety associated with a failed weaning experience. In addition, the continual presence of a health care provider at patients’ bedsides during their weaning process can be treated as a “safety-signal” for patients to reduce their fear and anxiety (Jenny and Logan, 1994; 1996; Sartory et al., 1989).

The principle of biofeedback is to externalize the physiological functions and transform them into acoustic or visual signals that can be perceived by patients. Through these signals, patients can develop cognitive effects such as passive concentration to counteract fearful thoughts and images and further influence the physiological parameters (Hannich et al., 2004). The combination of biofeedback and progressive muscle relaxation can reduce anxiety and the neural respiratory drive (NRD) and further improve the respiratory muscle electromyograph (EMG) efficiency during the weaning process (Holliday & Hyers, 1990; Jacavone et al., 1998; LaRiccia, et al., 1985). Accordingly, the
effectiveness of these interventions will facilitate successful weaning and reduce the total
time on mechanical ventilation.

The purpose of systematic desensitization, such as reciprocal inhibition, is to
desensitize patients’ respiratory responses in situations that formerly elicited the aversive
respiratory responses (Moore, 1965). Reciprocal inhibition is a specific procedure by
which conditioned responses are diminished or eliminated through the use of guided
imagery; this desensitization technique was used to successfully treat asthma patients
(Moore, 1965). Reciprocal inhibition helps the patient learn to relax, lowers arousal and
vigilance level, reduces the perception of incoming stimuli, increases tolerance towards
the symptoms, alters the parasympathetic tone, and creates a favorable psychological
milieu incompatible with broncho-constriction (see e.g., Moore, 1965). If patients
experience conditioned fear that evokes strong physiological reactions, an intervention
based on the principle of systematic desensitization for the T-piece weaning may reduce
the psychophysiological impacts incurred from a failed weaning experience, especially
for those patients with repeated ventilator weaning failure (Wolpe, 1958).

The safety-signal has been used as a conditioned inhibitor or positive reinforcer to
reduce conditioned fear (Falls & Davis, 1995; Sartory et al., 1989). Consistent with
findings from qualitative nursing studies, the continual presence of a health care provider
(e.g., nurse) to inform, reassure, emotionally support, and comfort patients during
ventilator weaning is suggested to reduce patients’ fear and anxiety (Jenny and Logan,
1994; 1996). Therefore, the continual presence of a health care provider can behave as a
safety-signal for patients with repeated ventilator weaning failure to overcome their fear
and anxiety in subsequent ventilator weaning trials.

Limitations

Limitations of this study included the small sample size, the restrictions for the subjects, the impact of researcher’s presence, and issues of study design. Structural equation modeling is a large-sample technique. The sample of 102 subjects in the present study was relative small, although the sample size was initially estimated by using Bentler & Chou’s (1987) suggestion that the minimum sample size to the number of estimated parameters can be as low as 5:1 to test a structural equation model. Based on MacCallum et al.’s (1996) framework for power analysis and minimum sample size estimation in SEM, a minimum sample of 375 was considered sufficient to attain the power of .80 for an alternative model (df = 24; α = .05). Therefore, the stability of the good model fit results was also relatively limited. In addition, the direct effect of state anxiety on the weaning outcome might accordingly fail to be supported.

Compared with the average sample size of 30 in prior studies conducted in the same field, recruiting 102 subjects for the present study was a challenging task for the researcher. There was only a small proportion (20% to 25%) of mechanically ventilated patients that might have failed their first T-piece weaning trial (Gilmartin et al., 1999; Tobin & Alex, 1994), and only half of these patients were alert. In addition to the challenges of recruiting a large sample size of this patient population, finding subjects who were qualified and who would agree to enroll in this type of study was an unusual task for the researcher, consuming both time and finances. In the future, the feasibility of conducting a similar study with a large sample size can be facilitated by generous grant
support.

The second limitation of this study was the restriction on the subjects. Obviously the subjects were mechanically ventilated and easily became tired when even responding to 10 short questions, in which the accuracy of self-reported fear and anxiety was also a concern. Involving the reports of the primary nurse and caregiver about the subjects’ fear and anxiety would be considered as additional sources of data to increase the accuracy of a future study. However, the acceptable values of internal consistency within and between measurements of conditioned fear and state anxiety supported the reliability of measurements in this study.

The third limitation was caused by the researcher’s presence during data collection. The researcher was continuously at the patients’ bedside during data collection, which included the pre-weaning and weaning period. It is important to note that the attention paid to the subjects was very different from what ICU nurses could afford to give in reality. Most of these subjects appreciated the researcher’s presence during their ventilator weaning period. This phenomenon was suspected to have a positive impact (safety-signal effect) on subjects’ emotions, which was also discussed in Knebel’s study (1990). This limitation might be considered to have caused the subjects to minimize their feelings of fear and anxiety. Therefore, creating a clinical setting that is as realistic as possible is recommended for a future study.

The final limitations were related to the study design. Due to the nature of cross-section design, all independent variables were measured at one point in time; however, these variables were used to predict the length of mechanical ventilation subsequently
required by the condition of the subjects. Several unidentified variables may have been involved in affecting the need for prolonged mechanical ventilation, which would be considered the major limitation to stabilize the hypothesized model. Therefore, incorporating the potential variables into the PVWM is strongly suggested for a future study. The three-week criterion was considered another limitation of the study design. Of the total subjects, 21 needed mechanical ventilation for more than 21 days after the second weaning trial, in which the LOMV was truncated into 21 days of MV. The restrictive range for the outcome variable might be misrepresenting the strength of how the independent variables affected the outcome variables. However, the logarithmic transformation of the LOMV was considered to remedy this limitation.

Directions for the Future Research

Three directions for future research were suggested by the results of the present study. The first direction for future research is to detect the potent indicators that might predict respiratory function during the second weaning trial. Among the three psychophysiological factors, respiratory function had the strongest effect on the length of MV. In addition, most subjects in this study at minimum had a compromised indicator of respiratory function during the second T-piece weaning, even though they all met the weaning criteria before their second weaning trial. This finding indicates that the weaning criteria used to predict the weaning outcome in the first weaning trial were not good enough to predict the weaning outcome in the second weaning trial. Therefore, future research should focus on determining the proper weaning criteria to assess readiness for the second T-piece weaning trial for patients with repeated ventilator weaning failure.
The second direction for future study is to develop an intervention study that focuses on reducing conditioned fear and state anxiety in the second T-piece weaning trial. The combination of biofeedback and progressive muscle relaxant might be applied as an intervention for taking care of mechanically ventilated patients who failed the first weaning trial. The effect of this intervention on the length of MV can be tested in future research.

The third direction for future study is based on a limitation of the present study. As mentioned in the discussion of the study’s limitations, several unidentified variables in PVWM might be considerably affected by the three identified psychophysiological variables, and further extend the length of MV. One could argue, based on the researcher’s observations during data collection, that the compromised immune system might be considered as one of these unidentified variables. To explore this further, psychological events and mood states have been suggested to have potential effects on dysregulation of the immune system (Fleshner et al., 1993; Maier et al., 1994). Moreover, compromised immune function might lead to an increased incidence of nosocomial infection, which in turn could result in prolonged mechanical ventilation. Accordingly, conducting a study to involve immune function into the PVWM is strongly suggested.

Conclusion

Contemporary studies related to ventilator weaning have focused on predicting weaning outcome, aimed at avoiding prolonged mechanical ventilation. As acknowledged, prolonged mechanical ventilation has considerable risks. However, the adverse impact of a failed weaning trial has not been fully explored, and the psychological effects on
weaning outcome have not been well tested. The present study is the first to examine the psychophysiological impact of a failed weaning trial on the subsequent weaning trial in terms of the length of mechanical ventilation necessitated by the first failed weaning trial. The resulting model was proven to be a good fit to the sample data. Conditioned fear acquired from the first failed weaning trial had a direct effect on state anxiety during the subsequent weaning trial, and by mediating state anxiety, conditioned fear had indirect effects on respiratory function and weaning outcome. Further, state anxiety during the second T-piece weaning trial had direct and indirect effects on respiratory function and weaning outcome. In itself, respiratory function strongly affected the length of MV. Findings from the present study provide a different perspective, new insight, and a direction for health care providers to consider when managing the care of patients with repeated ventilator weaning failure. In addition, the results of this study suggest several implications for measurement, theory, and future research related to the care of patients with repeated ventilator weaning failure.
APPENDIX A: DATA COLLECTION FORM

(1) Subject Code: _____  (2) Enrolled Date: _____ / _____ / _____  (3) MICU: __ SICU: ___

### Subjects General Information

<table>
<thead>
<tr>
<th>(4) Age:</th>
<th>(5) Sex: F _____  M _____</th>
<th>(6) Major Diagnosis: ____________________________</th>
</tr>
</thead>
<tbody>
<tr>
<td>(7) Etiology for MV: ______________________________________________________________________</td>
<td>(8) Length of MV prior to 2\textsuperscript{nd} weaning trial: ___________________</td>
<td></td>
</tr>
</tbody>
</table>

### Measurement Data

<table>
<thead>
<tr>
<th>Conditioned Fear</th>
<th>State Anxiety</th>
<th>Respiratory Function</th>
<th>Weaning Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(9) NRS-emotional fear: __________ mm</td>
<td>(14) Shorten CSAI: ______.</td>
<td>(17) Gas exchange</td>
<td>(21) Date of 2\textsuperscript{nd} weaning trial</td>
</tr>
<tr>
<td>(10) NRS-cognitive fear: __________ mm</td>
<td>(15) NRS-anxiety: ______ mm</td>
<td>PaO2/FiO2: __________.</td>
<td>/ _____ / _____</td>
</tr>
<tr>
<td>(11) Increased heart rate: ________ bpm</td>
<td>(16) NRS-dyspnea: ______ mm</td>
<td>(18) Respiratory Central drive</td>
<td>(22) Date of successfully weaned</td>
</tr>
<tr>
<td>Prior weaning: _________________ bpm</td>
<td></td>
<td>P0.1/MIP: __________.</td>
<td>/ _____ / _____</td>
</tr>
<tr>
<td>During weaning: _________________ bpm</td>
<td></td>
<td>(19) Respiratory muscle capacity</td>
<td></td>
</tr>
<tr>
<td>(12) Hyperventilation (ΔPetCO2): ______ mmHg</td>
<td></td>
<td>TTI: ________________ .</td>
<td></td>
</tr>
<tr>
<td>Prior weaning: _________________ mmHg</td>
<td></td>
<td>(20) Respiratory muscle workload</td>
<td></td>
</tr>
<tr>
<td>During weaning: _________________ mmHg</td>
<td></td>
<td>WOB: _________________</td>
<td></td>
</tr>
<tr>
<td>(13) Rapid shallow breathing (RSBI): ______.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX B1: NUMERICAL RATING SCALE (NRS)-EMOTIONAL FEAR

NRS-Emotional Fear

Subject Code: _____  Enrolled Date: ______ / ______ /______

Directions: You will be asked to place a tick mark on the following line to indicate how you are feeling right now.

“How frightened/afraid are you now of weaning from ventilatory support?”

0  Not afraid at all
1
2
3
4
5
6
7
8
9
10  Most afraid you can be
APPENDIX B2: CHINESE VERSION OF NRS-EMOTIONAL FEAR

數字化量表—情緒性的恐懼

個案代碼: ________ 收案日期: ________年______月______日

請您在下面的數字表上指出代表您對以下問題的感受程度:
“您現在對呼吸機脫離的害怕程度如何?”

0  感覺一點都不害怕
1
2
3
4
5
6
7
8
9
10  感覺最大的害怕
NRS-Cognitive Fear

Subject Code: _____  Enrolled Date: _____ / _____ / ______

Directions: You will be asked to place a tick mark on the following line to indicate how you are feeling right now.

“What do you think is the chance that you will experience shortness of breath from ventilator weaning?”

0  None
1
2
3
4
5
6
7
8
9
10  Extremely high chance
APPENDIX C2: CHINESE VERSION OF NRS-COGNITIVE FEAR

數字化量表—意識性的恐懼
個案代碼:______  收案日期:______年______月______日

請您在下面的數字表上指出代表您對以下問題的感受程度:
“您認為您有多大的機會在呼吸機脫離過程中會感受到呼吸困難呢?”

0 毫無機會
1
2
3
4
5
6
7
8
9
10 極度高的機會
APPENDIX D1: NUMERICAL RATING SCALE (NRS)-STATE ANXIETY

NRS-State Anxiety

Subject Code: _____  Enrolled Date: _________/_________/_______

Directions: You will be asked to place a tick mark on the following line to indicate how you are feeling right now.

“How anxious are you feeling right now?”

0  Not anxiety at all
1
2
3
4
5
6
7
8
9
10  Most anxious you can be
APPENDIX D2: CHINESE VERSION OF NRS –STATE ANXIETY

數字化量表—焦慮
個案代碼: ________ 收案日期: ________年 ________月 ________日

請您在下面的數字表上指出代表您對以下問題的感受程度:
“您感覺您現在有多焦慮呢?”

<table>
<thead>
<tr>
<th>0</th>
<th>感覺一點也不焦慮</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
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<td></td>
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<td>7</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>感覺最大的焦慮</td>
</tr>
</tbody>
</table>
APPENDIX E1: NUMERICAL RATING SCALE (NRS)-DYSPNEA

NRS-Dyspnea
Subject Code: _____  Enrolled Date: ________ / ________ / ________

Directions: You will be asked to place a tick mark on the following line to indicate how you are feeling right now.

“How shortness of breath are you right now?”

0  No shortness of breath

1

2

3

4

5

6

7

8

9

10  The worst possible shortness of breath
APPENDIX E2: CHINESE VERSION OF NRS DYSPNEA

數字化量表—呼吸困難感受
個案代碼: _______ 收案日期: ______ 年 ______ 月 ______ 日

請您在下面的數字表上指出代表您對以下問題的感受程度:
“你感覺你現在呼吸困難的程度如何呢?”

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
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<tr>
<td>一點也沒有呼吸困難的感覺</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>感覺極度呼吸困難</td>
</tr>
</tbody>
</table>

---
APPENDIX F1: THE SHORTENED VERSION OF THE SPIELBERGER STATE
ANXIETY INVENTORY

SELF-EVALUATION QUESTIONNAIRE

Subject Number_____________________________________________ Date_______________ S______
Age_________ Sex M__ F__ T______

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then blacken in the appropriate circle to the right of the statement to indicate how you feel right now, that is, at this moment. There are not right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

1. I feel at ease……………………………………………………………………………….. (1) (2) (3) (4)
2. I feel frightened……………………………………………………………… (1) (2) (3) (4)
3. I feel comfortable…………………………………………………………… (1) (2) (3) (4)
4. I feel nervous……………………………………………………………… (1) (2) (3) (4)
5. I am worried………………………………………………………………… (1) (2) (3) (4)
6. I feel pleasant………………………………………………………………… (1) (2) (3) (4)
APPENDIX F2: CHINESE VERSION OF THE SHORTEN VERSION OF THE SPIELBERGER SAI

自我評量問卷

個案代碼: 日期:  年 月 日
年齡: 性別:  男  女

作答說明: 下面有一些人們用來描述自己的問句，作答時，先看各提的語句，然後根據您現在的感受—也就是這個時刻的感受，在右方式的答案處，將圓圈圈黑。答案並沒有對錯之別，只要選出最能說明您目前感受的答案即可，不必在每一題上花太多時間。

<table>
<thead>
<tr>
<th>項目</th>
<th></th>
<th></th>
<th>頗為</th>
<th>非常</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>我覺得輕鬆自在</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>2</td>
<td>我覺得焦慮</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>3</td>
<td>我覺得舒適</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>4</td>
<td>我覺得焦急</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>5</td>
<td>我擔憂</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
<tr>
<td>6</td>
<td>我覺得愉快</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
</tr>
</tbody>
</table>
APPENDIX G: THE MAJOR MEDICAL DIAGNOSIS OF THE SUBJECTS IN THE SAMPLE ($N = 102$)

<table>
<thead>
<tr>
<th>Major Diagnosis</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Brain Stem Infarction</td>
<td>1</td>
</tr>
<tr>
<td>Acute Hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>Acute Myocardiac Infarction</td>
<td>5</td>
</tr>
<tr>
<td>Acute Pancreatitis</td>
<td>2</td>
</tr>
<tr>
<td>Acute Pulmonary Edema</td>
<td>2</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>1</td>
</tr>
<tr>
<td>Aspiration Pneumonia</td>
<td>1</td>
</tr>
<tr>
<td>Breast Ca</td>
<td>1</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>1</td>
</tr>
<tr>
<td>CAD &amp; CABG</td>
<td>7</td>
</tr>
<tr>
<td>CBD stone</td>
<td>1</td>
</tr>
<tr>
<td>CHF &amp; Valve Replacement (AVR)</td>
<td>2</td>
</tr>
<tr>
<td>CHF &amp; Valve Replacement (AVR,MVR,TVR)</td>
<td>1</td>
</tr>
<tr>
<td>CHF &amp; Valve Replacement (MVR)</td>
<td>2</td>
</tr>
<tr>
<td>Chronic Osteomyelitis of Right Hip</td>
<td>1</td>
</tr>
<tr>
<td>Cirrhosis of Liver</td>
<td>2</td>
</tr>
<tr>
<td>CO Intoxication</td>
<td>1</td>
</tr>
<tr>
<td>CO2 Narcosis</td>
<td>1</td>
</tr>
<tr>
<td>Major Diagnosis</td>
<td>Numbers</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Colon Ca</td>
<td>1</td>
</tr>
<tr>
<td>Colon Ca &amp; S/p Splenectomy</td>
<td>1</td>
</tr>
<tr>
<td>COPD with Acute Exacerbation</td>
<td>16</td>
</tr>
<tr>
<td>DM</td>
<td>2</td>
</tr>
<tr>
<td>Fournier Gangrene</td>
<td>1</td>
</tr>
<tr>
<td>Functional Diarrhea</td>
<td>1</td>
</tr>
<tr>
<td>Gastric Ca</td>
<td>1</td>
</tr>
<tr>
<td>Gaut L't, Cellulitis</td>
<td>1</td>
</tr>
<tr>
<td>HCVD &amp; CHF</td>
<td>1</td>
</tr>
<tr>
<td>Ileus &amp; Hernia</td>
<td>1</td>
</tr>
<tr>
<td>Interstitial Lung Disease</td>
<td>1</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Massive Pericardial Effusion</td>
<td>1</td>
</tr>
<tr>
<td>NIDDM &amp; DM Foot S/P OP</td>
<td>1</td>
</tr>
<tr>
<td>Pancreatic Head Tumor S/P OP</td>
<td>1</td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>23</td>
</tr>
<tr>
<td>PPU</td>
<td>1</td>
</tr>
<tr>
<td>R/O UGI Bleeding</td>
<td>2</td>
</tr>
<tr>
<td>Rhadomyolysis</td>
<td>1</td>
</tr>
<tr>
<td>Major Diagnosis</td>
<td>Numbers</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>S/P AK, Rt</td>
<td>1</td>
</tr>
<tr>
<td>SLE</td>
<td>1</td>
</tr>
<tr>
<td>Spondylolisthesis of L2-L3</td>
<td>1</td>
</tr>
<tr>
<td>Stridor</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic Aortic Aneurysm Excision</td>
<td>1</td>
</tr>
<tr>
<td>UTI</td>
<td>2</td>
</tr>
<tr>
<td>VHD with Moderate MR &amp; AR</td>
<td>1</td>
</tr>
</tbody>
</table>
APPENDIX H: STATISTICAL GRAPHIC OF RESIDUALS IN PVWM WITH NON-TRANSFORMED DATA

Histogram

Dependent Variable: LOMV

Normal P-P Plot of Regression Standardized Residual

Dependent Variable: LOMV

Scatterplot

Dependent Variable: LOMV
APPENDIX I: STATISTICAL GRAPHIC OF RESIDUALS IN PVWM WITH TRANSFORMED DATA (N = 102)

Histogram

Dependent Variable: log-LOMV

Normal P-P Plot of Regression Standardized Residual

Dependent Variable: log-LOMV

Scatterplot

Dependent Variable: log-LOMV
APPENDIX J: COVARIANCES AND CORRELATIONS BETWEEN ALL VARIABLES (N = 102)

a. Implied Covariances in logarithm of LOMV data set

<table>
<thead>
<tr>
<th></th>
<th>LOMV</th>
<th>WOB</th>
<th>P0.1/MIP</th>
<th>TTI</th>
<th>NRS-dyspnea</th>
<th>NRS-anxiety</th>
<th>SSAS</th>
<th>NRS-emotional fear</th>
<th>NRS-cognitive fear</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOMV</td>
<td>.242</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>WOB</td>
<td>.118</td>
<td>.436</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P0.1/MIP</td>
<td>.019</td>
<td>.045</td>
<td>.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTI</td>
<td>.019</td>
<td>.045</td>
<td>.007</td>
<td>.010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-dyspnea</td>
<td>.224</td>
<td>.195</td>
<td>.032</td>
<td>.032</td>
<td>6.719</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-anxiety</td>
<td>.291</td>
<td>.253</td>
<td>.041</td>
<td>.042</td>
<td>3.613</td>
<td>6.665</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSAS</td>
<td>.433</td>
<td>.377</td>
<td>.062</td>
<td>.062</td>
<td>5.374</td>
<td>6.987</td>
<td>17.461</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-emotional fear</td>
<td>.166</td>
<td>.190</td>
<td>.031</td>
<td>.031</td>
<td>2.809</td>
<td>3.651</td>
<td>5.432</td>
<td>7.773</td>
<td></td>
</tr>
</tbody>
</table>

b. Implied Correlations in logarithm of LOMV data set

<table>
<thead>
<tr>
<th></th>
<th>LOMV</th>
<th>WOB</th>
<th>P0.1/MIP</th>
<th>TTI</th>
<th>NRS-dyspnea</th>
<th>NRS-anxiety</th>
<th>SSAS</th>
<th>NRS-emotional fear</th>
<th>NRS-cognitive fear</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOMV</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOB</td>
<td>.364</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P0.1/MIP</td>
<td>.453</td>
<td>.781</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTI</td>
<td>.387</td>
<td>.667</td>
<td>.829</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-dyspnea</td>
<td>.175</td>
<td>.114</td>
<td>.142</td>
<td>.121</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-anxiety</td>
<td>.229</td>
<td>.149</td>
<td>.185</td>
<td>.158</td>
<td>.540</td>
<td>1.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSAS</td>
<td>.210</td>
<td>.137</td>
<td>.170</td>
<td>.145</td>
<td>.496</td>
<td>.648</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRS-emotional fear</td>
<td>.121</td>
<td>.103</td>
<td>.128</td>
<td>.109</td>
<td>.389</td>
<td>.507</td>
<td>.466</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>NRS-cognitive fear</td>
<td>.131</td>
<td>.111</td>
<td>.138</td>
<td>.118</td>
<td>.419</td>
<td>.547</td>
<td>.503</td>
<td>657</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Note. NRS = Numerical Rating Scale. SSAS = Shortened State Anxiety Scale. P0.1 /MIP = the ratio of occlusion airway pressure to maximum inspiratory pressure. TTI = tension-time index. WOB = work of breathing.
23 March 2006

Yu-Ju Chen, Ph.D. Candidate
College of Nursing
PO Box 210203

RE: HSC #06-050 PSYCHOPHYSIOLOGICAL DETERMINANTS OF REPEATED VENTILATOR WEANING FAILURE

Dear Ms. Chen:

We reviewed your 10 March 2006 letter and accompanying revised Project Approval Form/Verification of Training Form, revised Consent Form, and revised PHI Authorization Form for the above referenced project. All of the conditions as set out in Committee’s 2 March 2006 letter (relevant to the 28 February 2006 Full Board review) were addressed in the investigator’s 10 March 2006 letter and the accompanying submitted revised Project Approval Form, revised Consent and PHI Authorization Forms. Therefore, approval of for this subjects-at-risk project was granted an expiration date of 28 February 2007.

The Institutional Review Board (IRB) of the University of Arizona has a current Federalwide Assurance of compliance, FWA00004218, which is on file with the Department of Health and Human Services and covers this activity.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or to the consent form(s) used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee (IRB) and your College or Departmental Review Committee. Any research related physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely,

[Signature]

David G. Johnson, M.D.
Chairman, Biomedical Committee
UA Institutional Review Board

DGI:ajl
cc: Departmental/College Review Committee
11 April 2006

Yu-Ju Chen, Ph.D. Candidate
College of Nursing
PO BOX 210203

RE: HSC #06-030 PSYCHOPHYSIOLOGICAL DETERMINANTS OF REPEATED VENTILATOR WEANING FAILURE

Dear Ms. Chen:

We received your Request for Amendment Form [undated; received 4/4/06] and accompanying revised Consent Form and 4 Numerical Rating Scales and Anxiety Inventory [English and Chinese language versions for each] for the above cited project. The protocol has been modified to replace visual analogue scales with numerical rating scale [subjects will hold up 0-10 fingers or point to the appropriate number on a chart to indicate response] for measurement of patients’ emotional fear, cognitive fear, anxiety, and dyspnea. Additionally, an abbreviated Spielberger State Anxiety Inventory consisting of 6 vs. 20 items will be utilized to lessen burden on patients. A Consent Form and English/Chinese versions of the modified scales have been provided for review. Approval for these changes is granted effective 11 April 2006.

The Institutional Review Board (IRB) of the University of Arizona has a current Federalwide Assurance of compliance, FWA00004218, which is on file with the Department of Health and Human Services and covers this activity.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or to the consent form(s) used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee (IRB) and your College or Departmental Review Committee. Any research related physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,

[Signature]

David G. Johnson, M.D.
Chairman
Biomedical Committee
UA Institutional Review Board (IRB)

DGJ:jpm
cc: Departmental/College Review Committee
研究個案同意書

研究題目: HSC# 06-030 重複呼吸機脫離失敗的心生理決定因子之探討

若您同意參與此研究，請您細讀以下的文件，以確保您已被清楚的告知此研究相關的性質及方法。在此表格簽名表示您已經清楚的被告知且同意參與此研究。根據政府的法律規定，在參與此研究前，您必須簽署此份同意書，以利您明白您所參與的研究的性質及可能的危險性，據此您可自由決定您的參與與否。

研究目的
您已被邀請自主的參與上面所提及的研究，此研究的主要目的是想清楚的了解您在呼吸機脫離時所經歷的情緒反應及肺功能的狀況。

收案標準
為符合收案標準，您必須正在使用呼吸機且有一次未成功的呼吸機脫離經驗。而且您必須符合醫院所制定之呼吸機脫離的標準且準備做第二次呼吸機脫離。為了您呼吸機脫離過程的安全考量，您此次使用呼吸機的病因應已被解決，且您的生命跡象及營養狀況應為醫師認定是穩定的。同時，您必須是至少年滿 18 歲、意識清楚、有定向感、能合作、且能了解或說或讀懂中文。本研究預計總共招收 100 名個案

研究執行流程
以下的訊息將描述您在此研究中的參與事項:

- 若您同意參與此研究，在您進行第二次呼吸機脫離前 1 小時，一根小的食道球管(直徑約為 0.27 公分，材質為聚氨脂酯)，將放入您的食道下三分之
一處中，其放入的長度約為 35 公分左右。管子放置前將會使用水溶性的
潤滑液已潤滑以減輕可能造成的不適。放置食道球管的過程中，您將被鼓
勵喝些水，以利管子的置放。為確認管子已置於正確位置，您將被要求作
用力吸氣的動作。整個放置過程約為 3 分鐘

- 在您進行第二次呼吸機脫離的 30-60 分鐘內，研究員將利用床旁監視器記
  録您呼出的二氧化碳值、心跳、及呼吸型態。之後，研究員將問您 4 個問
  題並請您指出或以嘴型說出在數字表上的適當數字，以代表您真實的反
  應。另外，研究員將陪出一份 6 題的問卷給您，您將被請求用手指指出或
  比劃出最符合您感受的答案，全部問答含食道球管放置的時間約為 15 分
  鐘

- 緊接著在您休息時，研究員將用食道球管連接 Bicore 監測系統來測量您的
  肺功能，而整個肺功能測量過程將不影響您的呼吸或呼吸機的輔助設定。
  這個測量過程將不超過十分鐘。當您肺功能測試完畢，食道球管將被立即
  拔除。管子拔除前，您將被指導用力吸氣後緩慢吐氣，於吐氣時您的管子
  將被拔出。

- 同時，您的一般資料如年齡、性別、目前病因、參與研究前使用呼吸機的
  時間，以及呼吸機脫離試驗的總次數，研究員都將其由病例紀錄填錄下
  來。您使用呼吸機的時間及次數亦將被紀錄，直到您呼吸機脫離成功或持
  續到 3 星期的追蹤。另外，您的動脈血氧分壓也將由病例紀錄得來

危險性

食道球管的放置可能造成您些許的鼻子不適。所以，此研究將選用較小(直徑約
0.27 公分)且易忍受的食道球管，配合醫院鼻胃管放置標準潤滑來減低您因放置食
道球管所可能引起的不適。另外，您的鼻胃管有可能因著拔除食道球管而被移位，
然而從相關的研究中並未發現有如此的報導。雖然，您的參與本研究不會造成你任
何身體上的危害，但因著參與研究而增加的注意力，將有可能使您的焦慮加深。

益處

本研究對您將無直接的益處。但您的參與本研究，將有助於醫護人員對未來有呼吸
機脫離困難病患提供進一步的了解及照護。因此，本研究將會有利於未來社會。
隱私性
為求維持您個人資料的隱私性，將於您同意參與研究時，分派一個個案代碼置於您所有的資料上，同時您所有相關資料將被妥善的鎖放在研究櫃內，而且所有的資料將只有研究主持人及她的研究指導老師可獲取。您所有的相關資料將只被運用於此研究，未來研究結果的發表亦將不會透露可確認您個人的相關訊息。

參與研究的花費及補償
除了需您的時間來參與，此研究毋須您額外的花費。整個研究測量過程(含食道球管的放置及測量、問卷調查、床旁監視器指數的測量)，總計需花您約25分鐘來直接參與此研究。但因您的食道球管將於您第二次呼吸機脫離的前一小時放置，所以您的參與本研究總計約為2小時。對您的參與，本研究並無實質的補償。

聯絡人
您若對本研究若需有進一步諮詢，可與研究主持人陳玉如(博士班學生)聯絡，聯絡電話是0939-332-653。若您對當一個研究個案相關權益有疑問時，您可與亞利桑那大學研究個案保護中心聯絡，聯絡電話為0021-866-287-1455。

責任與負擔
即便使用最高的照護標準，副作用或傷害都有可能發生在任何一個研究，即便在您或研究主持人都沒有犯錯之情況下，它還是有可能發生。已知的副作用已經在這同意書內提起，但是未見的傷害仍有可能發生且需進一步的照護。您的任何合法權益都將不會因為簽署這份同意書而喪失。若您認為您的醫療費用的支付或增加，可能與研究有關，請立即與研究計畫主持人陳玉如(博士班學生)聯絡，聯絡電話是0939-332-653。

授權聲明
在我簽署此份同意書前，研究相關的方法、不便性、危險性及益處已充分的向我說明，而我的疑問也獲得滿意的答覆。我知道我可以在任何時間提出對研究疑問，而且我隨時有退出研究的自由，即使研究沒有引起任何的不好感受或影響我的醫療照護。然而，研究計畫主持人或計畫案支持者若要中斷我的研究參與需提
供我一個合理的解釋。在研究中新發展出來的新資訊可能會影響我參加研究的意願，所以，當有新的資訊發展出來時，研究者應立即告知我。此份同意書應被歸檔在研究個案委員會管理的區域，而且資料的取用應僅限於此研究計畫主持人陳玉如(博士班學生)或護理學院的權利代表。我絕不因簽署此份同意書而放棄我任何的法定權益。一份已簽署同意書的複印本應提供給我個人保存。

姓名

日期

父母或法定監護人姓名(如果需要)

日期

見證人姓名(如果需要)

日期

研究計畫主持人之具結書

我已詳細向個案對以上研究的性質做了清楚的說明。我亦可證實個案簽署同意書前已對研究的性質、需求、參與研究的益處、及危險性已有充分的了解。

具呈人姓名

日期

研究主持人姓名

日期

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個案簡稱
個案之受保護健康資料授權研究使用聲明書

研究題目：HSC# 06-030 重複呼吸機脫離失敗的生理性決定因子探討

根據美國政府所新制定的隱私法規定，參與研究個案的隱私權應受保護。隱私法
的設立是為保護個案健康資訊的保密性。此份文件是用以明確您個人權益在您授
權個人的健康資訊予此研究使用，以及這些資訊將如何被使用於此研究。

研究目的

您已被邀請自主的參與上面所提的研究，此研究的主要目的是想清楚的了解您在
呼吸機脫離時所經歷的情緒反應及肺功能的狀況。

受保護健康資料之使用及公開

您的一般資訊(如年齡、性別、近來之病史，在參與本研究前的使用呼吸機的時
間及嘗試呼吸機脫離的次數)，氣體交換的情形，以及續用呼吸機的時間等相關
資訊，即將由您的病例中獲取。這些資料將提供有關整個研究對象的描述性資
料。上述資料由病例中獲取後將由研究員收集並直接記錄於有您代表號的資料收
集表單上，為確保您個人資料的保密性，這表單上將不會有可辨認您身分的訊
息。為強調您健康資訊受保護的權益，若研究對您個人的醫療及療效造成影

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連絡人

您若想進一步了解相關訊息，請打電話 0939-332-653 與研究主持人博士班學生
陳玉如做聯繫，若您有關研究受試者相關權益問題，您可洽詢人權保護辦公室，
電話為 0021-520-626-6721。

授權聲明

我以此據授權研究使用或公開我個人的健康資訊，我可能隨時以書面通知研究計
畫主持人停止此授權。研究計畫主持的住址為台北市民權東路六段 280 巷 36 號
3 樓。如果我終止授權，則在此之前資料仍可繼續被使用。根據此授權，我的
健康資料將被研究者或機構使用，而此資訊的使用將不受政府的隱私法所規範。

然而，我亦可以拒絕簽署此份聲明書，我不簽署此份授權書表示我不參與此研
究。拒絕簽署此授權書，將不影響我目前或未來的醫療照護，而且我將不會喪失
我應有的權益。此份授權書將失效於研究結束日。我將擁有一份簽署授權書的複
印本。
REFERENCES


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