

Symptoms of Depression as Indicators of Delirium in Elderly Hospitalized Veterans

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Abstract

Delirium is an acute syndrome characterized by the decline of cognitive functioning. However, due to overlapping symptomology, it may be difficult to distinguish symptoms of delirium from those of other disorders, including depression. Accordingly, delirium is often misdiagnosed as depression, especially among older adults. The purpose of the current investigation was to compare patterns of depressive symptoms in a sample of patients with delirium only, depression only, or no condition. Additionally, we aimed to account for potential antidepressant effects on depressive symptomology. Based on previous research, we hypothesized that dysphoric mood and anhedonia would be commonly occurring depressive features in participants with delirium. Depressive symptomology was assessed with the Symptom Checklist for Major Depressive Disorders (SCMDD; Kashani, McKnew, & Cytryn, 1985), modified to meet *DSM-IV-TR* criteria (APA, 2000) and delirium was evaluated using the Memorial Delirium Assessment Scale (MDAS; Breitbart et al., 1997) in 273 Veteran participants. Chi-square analyses found no significant differences in depressive symptom presence between the participants with delirium and the participants with depression or no condition. Additionally, there was no significant effect of antidepressant use on modified SCMDD performance. These results suggest an overlap between the symptoms of delirium and depression, and emphasize the importance of incorporating specific measures of delirium in the clinical setting, particularly for elderly patients.

Keywords: delirium, depression, Veterans, older adults

Symptoms of Depression as Indicators of Delirium in Elderly Hospitalized Veterans

Delirium is an acute clinical syndrome characterized by confusion, inattention, and the overall decline of cognitive functioning. Its manifestation is always attributed to the presence of an underlying medical condition, which can vary in both nature and severity. Common risk factors for delirium include increasing age, male gender, pre-existing dementia, and severe illness such as malnutrition or stroke (Elie, Cole, Primeau, & Bellavance, 1998; Maldonado, 2008; Pandharipande et al., 2006). Additionally, within the hospital setting, delirium can occur as a result of poorly controlled pain, sleep-deprivation, or as a side effect of exogenous substance use (Maldonado, 2008).

The symptomology of delirium is variable as well. Although its essential features are clearly outlined in the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; *DSM-IV-TR*; American Psychiatric Association [APA], 2000; Appendix A), the actual presentation of delirium differs from person to person. The array of symptoms is extensive and includes both cognitive and non-cognitive features, such as decreased awareness, memory deficits, hallucinations or delusions, sleep-wake disturbances, and alterations in psychomotor activity.

Currently, delirium can be categorized into four subtypes describing the specific psychomotor attributes of the condition, including hyperactive, hypoactive, mixed, and delirium with no significant psychomotor disturbances (Liptzin & Levkoff, 1992; Maldonado, 2008; Yang et al., 2009). Hyperactive delirium is categorized by an increase in motor activity, restlessness, and agitation. Contrastingly, hypoactive type involves slowed motor activity, with periods of decreased alertness and inattention. The most common subtype of delirium is mixed type, which incorporates both hyper- and hypoactive symptoms, typically in a waxing and waning fashion

(O'Keeffe & Lavan, 1999; Sandberg, Gustafson, Brännström, & Bucht, 1999). Least common appears to be delirium with no significant psychomotor disturbances (O'Keeffe & Lavan, 1999).

With regard to prevalence, previous reports have recognized delirium as the most common psychiatric condition identified in the clinical setting (Centeno et al., 2004; Maldonado, 2008). This arouses concern in the medical community, particularly because in addition to signifying the presence of a severe medical problem, delirium in itself is problematic. If left untreated, delirium can lead to outcomes of varying severity, ranging from prolonged and increased cost of hospitalization, to cognitive or functional decline, and increased mortality. Notably, it has been estimated that mortality rates are 7% to 27% higher in patients with delirium when compared to their non-delirious counterparts (Ely et al., 2004a; Francis, Martin, & Kapoor, 1990; McCusker, Cole, Abrahamowicz, Primeau, & Belzile, 2002; Shehabi et al., 2010).

Delirium also has potential long-term impacts on cognitive function (Farrell & Ganzini, 1995; Leslie, Marcantonio, Zhang, Leo-Summers, & Inouye, 2008; Maldonado, Dhimi, & Wise, 2003; Pompei et al., 1994). Levkoff and colleagues (1992) suggested that as many as 57.5% of patients continue to experience some form of cognitive dysfunction six months post hospital discharge, while others (Fong et al., 2009) found that some patients never returned to their baseline level of cognitive function.

Difficulties in Differential Diagnosis

Given the progressive nature and severe implications of delirium, early intervention strategies are recommended (Inouye, Baker, Fugal, & Bradley, 2006). Unfortunately, despite its prevalence, delirium remains highly overlooked in many clinical settings. Previous research (Inouye, 1994) suggests that the diagnosis of delirium is missed in as many as 67% of cases.

Similarly, in a study of elderly medical patients, Collins and colleagues (2010) reported that only 28% of 110 cases of delirium were successfully detected.

Previous attempts (Eissa, Andrew, & Baker, 2003; Ely et al., 2004b) to understand the barriers in clinical recognition of delirium have identified multiple factors that may hinder detection, including insufficient knowledge and training of nurses (Steis & Fick, 2008), as well as clinicians' low prioritization of identifying delirium (Davis & MacLulich, 2009). In addition to these factors, the differential diagnosis is made even more difficult by the overlap of diagnostic criteria between delirium and many other cognitive disorders including dementia and depression (Fick, Agostini, & Inouye, 2002). The overlap of symptoms is particularly noteworthy with regard to depression, because delirium is commonly misdiagnosed as such (Farrell & Ganzini, 1995; Swigart et al., 2008). In a major investigation of patients with delirium referred for psychiatric consultation, Armstrong and colleagues (1997) found that 46% were initially identified as having a different disorder rather than delirium, with depression accounting for 31% of the missed cases. Other studies (Farrell & Ganzini, 1995; Margolis, 1994; Swigart et al., 2008) of psychiatric consultations for depression have similarly found that patients were delirious in at least 37% of cases.

Reliable detection of delirium is also dependent on biases present in clinicians' approaches to diagnosis. Leonard and colleagues (2009) suggested that some clinicians emphasize certain features of delirium more than others. Accordingly, Morency and colleagues (1994) determined that nurses were more likely to overlook the behavioral attributes of delirium, such as hypoactivity, and instead focused on disorientation as a main indicator. Swigart and colleagues (2008) corroborated these claims, suggesting that excessive weight is placed on disorientation in clinical diagnosis. This indicates that if disorientation is absent in a patient who

presents with behavioral or emotional disturbances, it is likely that the symptoms will be misattributed to a mood disorder. Furthermore, Schuurmans and colleagues (2001) suggested that clinicians often justify cognitive symptoms, such as disorientation, as normal aspects of aging. They cited this normalization of cognitive and functional decline in the elderly and chronically ill as a major point of concern. Consequently, even when cognitive symptoms are present and recognized, their significance is often devalued. As a result, hypoactive delirium frequently goes unrecognized in older adults, and behavioral or emotional symptoms can be mistaken for indicators of depression. This may lead to major interferences in treatment, especially for older adults who may suffer most from unrecognized and mismanaged delirium (Witlox et al., 2010).

Additional Links Between Delirium and Depression

Delirium and depression can also be comorbid conditions. Previous research has uncovered numerous potential pathophysiological links between delirium and depression, including dysfunctional neurotransmission and hypersecretion of cortisol (Trzepacz, 1999; Trzepacz & Van der Mast, 2002). Leonard and colleagues (2009) assessed the overlap between clinical diagnosis of depression and delirium in 100 palliative-care inpatients and found that 50% of those with depression also met the criteria for delirium. Still, they noted that it remains unclear whether this overlap stems from the shared symptomatology of the disorders, or if the high rates of comorbidity are accurate.

Depression is also a major risk factor for delirium, further complicating the interaction between the disorders (Leung, Sands, Mullen, Wang, & Vaurio, 2005; Smith, Attix, Weldon, Greene, & Monk, 2009). For instance, increased sleep and decreased self-care are key features of depression (APA, 2000), which may also directly or indirectly induce delirium. More

specifically, a depressed individual may develop delirium because of disturbances in sleep or activity levels, or as a function of inadequate attention to needs such as proper hydration. Consequently, symptoms of pre-existing depression may actually serve to propagate the development of comorbid delirium. For this reason, it is important to evaluate whether overlapping symptoms are indicative of delirium or depression. If both disorders are present, several uncertainties must be addressed to ensure that each condition is treated appropriately, including assessing which symptoms stem from the depression versus delirium, as well as the etiology of the delirium.

The interaction between delirium and depression is further complicated by the anticholinergic potential of some antidepressant medications. As previously mentioned, these drugs have been linked to increased risk of delirium (Campbell et al., 2009; Tune, 2001). Thus, antidepressant use provides additional evidence for depression as a risk factor for delirium (McAvay et al., 2007). Another concern is that if a patient with delirium is treated with antidepressants, he or she may experience worsening symptoms and is at heightened risk for long-term consequences (Maldonado, 2008). These repercussions can be significant; both for patients with delirium that is misdiagnosed as depression, who are prescribed unnecessary antidepressants, as well as for patients with both conditions who require antidepressant medication. However, for the latter group, simply identifying the accurate diagnosis is not enough. Strict treatment plans that involve monitoring of both conditions and various alterations in medication dosages are necessary.

For these reasons, a strong understanding of the nuances of and interactions between delirium and depression is crucial. Clinicians need to be able to accurately differentiate between factors indicative of delirium, depression, or both, and respond accordingly. As the treatment and

ultimate well being of the patient relies on accurate diagnosis, improvement in current methods of identification is essential.

Depressive Symptoms as Indicators of Delirium

Despite the complications presented by overlapping symptoms, indicators of depression may act as useful markers for earlier identification of individuals at-risk for developing delirium. Thus, understanding the subtle differences in patients with delirium, depression, or both conditions, may improve recognition and subsequent management of the disorders. However, relatively few studies have examined the prevalence of specific symptoms of depression in patients with delirium.

In 2007, McAvay and colleagues conducted a prospective cohort study to assess the occurrence of depressive symptoms in 416 patients over the age of 69, who developed delirium during their stay at a major university hospital. The Geriatric Depression Scale (GDS; Yesavage et al., 1983) and the Confusion Assessment Method (CAM; Inouye et al., 1990) were used to evaluate the presence of depression and delirium, respectively. It was determined that dysphoric mood and feelings of hopelessness, two core symptoms of depression, were predictive of delirium onset. This was evident even when controlling for aspects of physical and mental health including: age, race, education, diagnosis of dementia, and Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) scores below 24. These results are revealing because they suggest that anhedonia and feelings of hopelessness, which are behavioral symptoms of delirium that clinicians frequently overlook or misattribute, are actually significant indicators of the disorder.

Still, the authors acknowledged several limitations of their investigation. One potential unexamined confound was the effect of medication use prior to hospitalization. As medications

are relevant for both the treatment of depression and delirium, and have been independently implicated in the onset of delirium, the researchers noted that future studies should take this association into account. Additionally, this research may have been limited in reliability due to its utilization of the GDS (Yesavage et al., 1983). The GDS places emphasis on the emotional symptoms of depression, while omitting somatic factors, such as insomnia and fatigue. Questions from the scale largely address patients' evaluations of their own emotions, regarding factors such as life satisfaction, boredom, and hopefulness. The researchers (McAvay et al., 2007) explained that as the somatic symptoms of depression are generally common attributes of aging, by removing these categories, the GDS facilitates the study of depression in older adults. However, arguably, the removal of somatic factors discounts any potential associations between these symptoms and delirium. Moreover, the validity of the GDS as a diagnostic tool has been a topic of debate, and recent research has indicated that the measure is likely to over-diagnose depression (Bieliauskas, Stejskal, Steinberg, & Lamberty, 2011). In contrast, the *DSM-IV-TR* criteria for depression (APA, 2000; Appendix B) are inclusive of somatic, behavioral, and emotional variables. As such, the *DSM-IV-TR* has remained the most widely accepted standard for clinical diagnosis of depression.

In a later study, Leonard and colleagues (2009) examined the prevalence of specific subcategories of depressive symptoms in patients with delirium who were admitted to a palliative care unit ($n = 100$), using *DSM-IV-TR* diagnostic criteria for depression (APA, 2000). Initial presence of delirium was evaluated using the CAM (Inouye et al., 1990) and initial presence of depression was determined with the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). Depressive symptomology as outlined by *DSM-IV-TR* diagnostic criteria (APA, 2000) was compared in participants with clinical or sub-clinical delirium,

depression, and participants without either condition. The researchers reported an apparent overlap in the symptoms endorsed by the depressed group and both delirious groups. Several depressive symptoms were expected to occur during delirium as the consequence of severe illness, such as poor concentration, disturbances of sleep, and abnormal psychomotor activity. These were frequent in patients with clinical and sub-clinical delirium. Moreover, the overlap was still evident when only considering the core symptoms of depression, lowered mood and anhedonia. Notably, *DSM-IV-TR* (APA, 2000) depressive symptoms were found to increase with CAM score. Leonard and colleagues (2009) also assessed how depressed participants performed on the MDAS. The researchers compared the prevalence of MDAS delirious symptoms in patients with clinical and sub-clinical delirium, patients with depression, and a control group. They found no significant differences in depressed patient's performance on the MDAS as compared to the control group. Altogether, these findings emphasize the unique role of behavioral symptoms of depression as major markers of delirium in hospitalized patients.

Nonetheless, current knowledge regarding the relationship between symptoms of depression and presence of delirium remains limited. Moreover, a statistical approach to assessing the relationship between *DSM-IV-TR* (APA, 2000) depressive symptoms and delirium has not been previously employed. This association has also not been previously examined in hospitalized geriatric Veterans. Thus, the purpose of the current study is threefold.

First, we aim to build upon previous work by evaluating the prevalence of specific symptoms of depression, using the Symptom Checklist for Major Depressive Disorders (SCMDD; Kashani, McKnew, & Cytryn, 1985), modified to meet *DSM-IV-TR* criteria (APA, 2000), in elderly hospitalized Veterans diagnosed with delirium in comparison to those with depression alone, and those with neither delirium nor depression. The modified SCMDD is a

measure based on the *DSM-IV-TR* (APA, 2000) diagnostic criteria for depression. By utilizing this measure, we aim to provide a more reliable account of the relationship between symptoms of depression and delirium than in previous investigations. Given the findings reported by McAvay and colleagues (2007), and Leonard and colleagues (2009), we hypothesize that dysphoric mood and anhedonia will be commonly occurring depressive features in patients with delirium.

Secondly, we will examine the effects of antidepressant use. The potential effect of antidepressant use in the overlap between *DSM-IV-TR* depressive symptomology and delirium has not been investigated in earlier studies. As antidepressants may play a propagating role in the development of delirium, we hypothesize that any potential increased depressive symptom endorsement found in patients with delirium will be amplified in those who also take antidepressants.

Lastly, we aim to comparatively assess how depressed patients perform on items of the MDAS as compared to those with no condition. We hypothesize that results will corroborate Leonard and colleagues' (2009) finding that the MDAS was specific to features of delirium, further highlighting the unique nature of delirium symptomology and the importance of using *DSM-IV-TR* (APA, 2000) criteria to assess the symptomology of delirium.

Ultimately, this research aims to build a stronger understanding of the relationship between depression and delirium. It is our intention that by providing a clearer distinction between depressive symptoms that are indicative of delirium and those that are not, and by considering the effects of antidepressant use, we can facilitate a more precise manner of identifying patients at-risk for delirium.

Method

Participants

This study analyzed data from patients admitted to the Community Living Center (CLC), a sub-acute rehabilitation clinic located at the Veteran Affairs Ann Arbor Healthcare System (VAAAHS). The current study was part of a larger study that was approved by the VAAAHS Institutional Review Board. Inclusion criteria for this study required completion of all tests necessary for a full assessment of delirium and depression, as well as availability of previous medical history. In total, 273 Veterans met the conditions of the study and were included in the sample. The participants were predominantly male (95.6%) and ranged in age from 31 to 94 (Mean [M] = 66.32, Standard Deviation [SD] = 11.07). Mean level of education was 12.62 years (SD = 2.43, range: 6-20). Reports of racial identity were distributed among several categories, with 83.5% of participants identifying as Caucasian, 9.2% African American, 2.2% Latino or Hispanic, 0.7% Native American, 0.4% Pacific Islander, and 3.7% Biracial or Multiracial. The remaining 0.4% of participants declined to respond.

Measures

Delirium. Presence of delirium was evaluated using the Memorial Delirium Assessment Scale (MDAS; Breitbart et al., 1997). The MDAS is a 10-item scale designed to quantify the severity of delirious symptoms. Each item is scored on a 0 to 3 rating scale. A score of 0 indicates that no symptom is present, while scores of 1, 2, or 3 signify mild, moderate, and severe symptom levels, respectively. Several items of the MDAS pertain to patient performance on the orientation and memory recall sections of the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975), as well as on the Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV; Wechsler, 2008) Digit Span subtest. These tests provide evaluations of the patient's level of orientation, working memory, and memory functions. Other items on the MDAS involve behavioral observations of attention, awareness, thought organization as

represented by speech patterns, and psychomotor activity, as well as interview-assessed self-reports of sleep patterns, perceptual disturbances, and delusions. In order to comprehensively evaluate severity of symptoms, scores for each item of the MDAS are totaled (range = 0-30), with a cutoff of 7 considered to indicate probable delirium (Lawlor et al., 2000). Although the MDAS has not been validated as an official diagnostic tool, it has been established as a reliable measure of delirium (Breitbart et al., 1997) with high inter-rater reliability ($r = 0.92$) and high internal consistency ($\alpha = 0.91$). Scores on the MDAS are also highly correlated with three major alternative measures of delirium including the Delirium Rating Scale (DRS; Trzepacz, Baker, & Greenhouse, 1988; $r = 0.88, p < 0.0001$), MMSE (Folstein, Folstein, & McHugh, 1975; $r = -0.91, p < 0.0001$), and clinician's global rating of delirium severity ($r = 0.89, p < 0.0001$).

Depressive Symptoms. Depressive symptoms were assessed utilizing the Symptom Checklist for Major Depressive Disorders (SCMDD; Kashani, McKnew, & Cytryn, 1985), which has been modified to correspond to *DSM-IV-TR* (APA, 2000) criteria. The modified SCMDD is an instrument utilized to measure the presence of symptoms of depression as outlined by the *DSM-IV-TR* (APA, 2000) diagnostic criteria for depression. The modified SCMDD appears as a checklist consisting of 21 items. The items are split into nine distinct categories of depressive symptoms ordered as follows: *depressed mood, anhedonia or diminished interest, weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or guilt, diminished concentration or indecisiveness, and suicidal ideation*. Each item is scored using a dichotomous scale, with a value of 0 indicating no symptom presence, or a value of 1 indicating that the symptom is largely present. To screen positive for depression, a patient must endorse one of the first two categories as well as four additional categories. This corresponds to how depression is diagnosed using *DSM-IV-TR* (APA,

2000) criteria, widely acknowledged as the standard criteria for psychiatric diagnosis. The modified SCMDD is also a particularly useful tool for this study because its separation of *DSM-IV-TR* (APA, 2000) depressive symptoms into categories allows for inter-group comparisons to be made.

Procedure

All patients admitted to the CLC of the VAAHS undergo a brief neuropsychological evaluation, administered by trained research assistants. Assessments utilized in the battery include a brief interview, the modified SCMDD (Kashani, McKnew, & Cytryn, 1985), the MMSE (Folstein, Folstein, & McHugh, 1975), the WAIS-IV (Wechsler, 2008) Digit Span subtest, and the MDAS (Breitbart et al., 1997), among others. These tests provide clinicians with valuable insight regarding a patient's cognitive and functional abilities and facilitate recognition of major problems including amnesia, depression, and suicidal ideation. Upon completion, the tests are reviewed, double-scored, and entered into a database. This study retrospectively analyzed the neuropsychological assessment scores of patients admitted to the CLC between the dates of March 28, 2012 and December 4, 2013. Specifically, the data was limited to demographic variables including age, race, level of education, and sex, as well as participants' results on the MDAS and modified SCMDD.

Previous diagnosis of depression and antidepressant use was subsequently determined through review of the patients' relevant medical records.

Design

All statistical analysis was conducted utilizing SPSS version 22 (IBM corp., 2013).

Part One. The presence of delirium was determined based on MDAS (Breitbart et al., 1997) score. Scores below the clinical cutoff of 7 were coded as "0", indicating no presence of

delirium. Scores of 7 or greater were coded as “1”, indicating delirium. Additionally, data regarding previous diagnosis of depression was coded dichotomously as present (1) or absent (0). A group variable was computed based on the combination of delirium presence and previous diagnosis of depression: delirious only ($n = 24$), depressed only ($n = 77$), and no condition ($n = 167$), coded nominally from 1 to 3, respectively. Additionally, a variable for diagnosis of depression was calculated based on the criteria from the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) for comparative purposes. Data from individual symptom endorsements was compiled and presence of depression was marked as positive for participants meeting the diagnostic criteria. This data was coded dichotomously as positive (1) or negative (0). For the first part of the study, the five participants with both conditions were disregarded, as these results would not inform the hypothesis.

Point biserial correlations were computed to examine the relationship between MDAS score and performance on each item of the modified SCMDD. Participants previously diagnosed with depression ($n = 77$) were excluded as potential confounds. Scatterplots were then created to examine the direction of the relationship between MDAS score and each depression item. Initial chi-square tests of independence were performed to assess if any of the three groups, delirious only, depressed only, and those with no condition, differentially endorsed each of the significant modified SCMDD items. For items with significant chi-square results, post-hoc chi-square tests were conducted between the delirious only and depressed only groups, and delirious only and no condition groups, to determine which groups differed specifically. Additionally, a chi-square test of independence was performed to determine if the three groups (delirious only, depressed only, and those with no condition) differed in whether they met *DSM-IV-TR* criteria for depression based on the modified SCMDD. Post-hoc chi-square tests were conducted between coupled

combinations of the three groups to determine which groups were significantly different in SCMDD screening of depression.

Part Two. To determine the effect of antidepressant use, data regarding current antidepressant use was coded dichotomously as positive (1) or negative (0). Participants were divided into four groups: delirious only ($n = 20$), taking antidepressants only ($n = 107$), no condition ($n = 137$), and delirious with antidepressant use ($n = 9$). The same statistical methods were utilized as in the first part of this study.

Part Three. To determine the effect of depression on MDAS score, a one-way ANOVA was computed between MDAS (Breitbart et al., 1997) score for three groups: delirious only ($n = 24$), depressed only ($n = 77$), and those with no condition ($n = 167$). In accordance with the first part of the study, the five participants with both conditions were disregarded.

Results

Delirium and the Modified SCMDD

Table 1 depicts symptom prevalence for each modified SCMDD (Kashani, McKnew, & Cytryn, 1985) item across the three condition groups. Point biserial correlations determined a significant correlation between MDAS (Breitbart et al., 1997) score and modified SCMDD item performance on the *depressed mood* ($r(194) = 0.24, n = 196, p = 0.001$), *anhedonia* ($r(194) = 0.14, n = 196, p = 0.003$), *increased appetite* ($r(194) = 0.15, n = 196, p = 0.03$), *feelings of guilt* ($r(194) = 0.20, n = 196, p = 0.005$), *diminished concentration* ($r(194) = 0.21, n = 196, p = 0.003$), and *indecisiveness* ($r(194) = 0.19, n = 196, p = 0.007$) items of the modified SCMDD. For nearly all of the significant items, increases in MDAS score were correlated with the presence of the modified SCMDD symptom. The exception was the item pertaining to *increased appetite*, for which modified SCMDD symptom presence was associated with lower MDAS

score. The relationship between MDAS score and the *psychomotor agitation* ($r(194) = 0.13, n = 196, p = 0.07$) and *feelings of worthlessness* ($r(194) = 0.13, n = 196, p = 0.08$) items approached statistical significance. A weak trend suggests an association between increased MDAS score and the presence of psychomotor agitation or feelings of worthlessness.

Chi-square analyses showed that the relationship between group (delirious only, depressed only, and no condition) and modified SCMDD item endorsement was significant only for the item *indecisiveness*, $\chi^2(1, 116) = 9.93, p = .01$. Trends that did not quite approach significance were apparent for the items *depressed mood*, $\chi^2(2, 268) = 5.97, p = .05$, *loss of interest in activities*, $\chi^2(2, 268) = 4.78, p = .09$, *weight loss*, $\chi^2(2, 268) = 5.17, p = .08$, *psychomotor retardation*, $\chi^2(2, 268) = 5.61, p = .06$, *excessive self-blame*, $\chi^2(2, 268) = 4.84, p = .09$, *feelings of guilt*, $\chi^2(2, 268) = 5.18, p = .08$, and *feelings of worthlessness*, $\chi^2(2, 268) = 5.85, p = .05$ (Table 4). No significant relationships were found for the remaining items. These results indicate that the distribution of patient condition across modified SCMDD item endorsement did not differ at a statistically significant level for any items besides *indecisiveness*. A post-hoc chi-square analysis evaluating which of the three condition groups differed specifically in association with presence of *indecisiveness* similarly found no significant differences between the delirious and depressed groups, $\chi^2(1, 101) = .002, p = .97$, and the delirious and no condition groups, $\chi^2(1, 191) = 3.11, p = .08$. A significant effect on *indecisiveness* was only found between the depressed and no condition groups, $\chi^2(1, 244) = 7.44, p = .006$. Notably, however, the delirious and no condition groups did approach significant trend levels, with the delirious group having higher proportions of *indecisiveness* item endorsement. Bar charts illustrate these results (Figures 1-9).

Chi-square analyses comparing modified SCMDD diagnoses of depression found significant differences, $\chi^2(2, 268) = 9.22, p = .01$, among the participants in the delirious only, depressed only, and no condition groups. Post-hoc analyses revealed that the difference was only significant between the depressed only and no condition groups, $\chi^2(1, 244) = 8.36, p = .004$. No significant relationships were found between the delirious only and depressed only groups, $\chi^2(1, 101) = 2.61, p = .12$, and the delirious only and no condition groups, $\chi^2(1, 191) = .04, p = .85$. Figure 10 depicts these results.

Effects of Antidepressant Use

A preliminary chi-square test of independence found a significant relationship between all groups (delirious only, taking antidepressants only, no condition, and delirious with antidepressant use) and symptom presence for the items *difficulty sleeping*, $\chi^2(3, 273) = 8.62, p = .04$, and *feelings of guilt*, $\chi^2(3, 273) = 8.05, p < .05$. A near significant trend was found for the *feelings of worthlessness* item, $\chi^2(3, 273) = 7.09, p = .07$. A follow-up chi-square analysis was conducted to determine which of the four condition groups specifically differed in presence of *difficulty sleeping* and *feelings of guilt*. No significant differences were found between delirious only and delirious with antidepressant use for *difficulty sleeping*, $\chi^2(1, 29) = .22, p = .64$. Similar insignificant results were found for the *feelings of guilt* item, $\chi^2(1, 29) = 1.08, p = .3$.

A chi-square analysis comparing diagnoses of depression based on the modified SCMDD among all groups (delirious only, taking antidepressants only, no condition, and delirious with antidepressant use) determined no significant differences, $\chi^2(3, 273) = 5.23, p = .16$.

Depression and the MDAS

A one-way ANOVA found a significant effect of condition on scores on the MDAS ($F(3, 269) = 121.2, p < .001$). A Tukey post-hoc analysis revealed that the delirious group ($M = 9.46$,

$SD = 2.92$) had higher MDAS scores than the depressed ($M = 2.33$, $SD = 1.62$) and no condition groups ($M = 2.73$, $SD = 2.68$). No significant differences were found in MDAS scores between the depressed and no condition groups.

Discussion

The present study compared patterns of performance on the Symptom Checklist for Major Depressive Disorders (SCMDD; Kashani, McKnew, & Cytryn, 1985) modified to meet *DSM-IV-TR* (APA, 2000) criteria in participants with delirium, depression, and neither condition. Our main hypothesis was that findings would reflect those of previous studies (Leonard et al., 2009; McAvay et al., 2007), suggesting that participants with delirium would endorse the depressive symptoms *dysphoric mood* and *anhedonia* at a significantly higher proportion than their non-delirious counterparts. Results indicated that for the modified SCMDD items measuring *depressed mood*, *anhedonia*, *feelings of guilt*, *diminished concentration*, and *indecisiveness*, there was a positive trend of increased delirium, suggesting that individuals who endorsed the trait were likely to be higher in delirium severity. *Diminished concentration* and *indecisiveness* are expected during delirium as these features reflect the decreases in cognitive functioning that are symptomatic of delirium. However, the presence of *depressed mood* and *anhedonia* during delirium provides potential support for the current hypothesis and is in accordance with previous studies (Leonard et al., 2009; McAvay et al., 2007). The positive association between the *feelings of guilt item* and delirium severity was unexpected. This association should be addressed in future work to determine if this finding was unique to the current study. In addition, a weak positive trend was apparent for the items *psychomotor agitation* and *feelings of worthlessness*. The reverse relationship was found for only the *increased appetite* item, in which symptom presence related to lower MDAS scores. This latter

finding makes intuitive sense, as patients with hypoactive delirium would be unlikely to have an increased appetite given their symptoms of delirium.

However, contrary to our hypothesis, chi-square analyses found that condition type (delirium only, depression only, or no condition) played no significant role in symptom endorsement for nearly every modified SCMDD item. This is reflective of a major overlap in symptomology among participants with delirium, participants with depression, and the general, hospitalized population. Table 1 emphasizes this variability in high symptom endorsement levels for each condition type group. Therefore, while participants with only depression showed higher proportions of endorsement for most items, several were more highly present in the no condition, or delirium only groups. For instance, the no condition group showed the highest proportions of endorsement for the *nocturnal awakening*, *psychomotor agitation*, and *suicidal ideation* items. However, these *nocturnal awakenings* may be specific to the sample population as it consisted of older, hospitalized patients who may have been more likely to be awakened in the night by nurses. Additionally, *suicidal ideation* may have been indicative of a sign of depression in previously undiagnosed members of the no condition group. The single significant association between condition type and symptom presence was found for the modified SCMDD item *indecisiveness*. Yet, a follow-up analysis comparing the delirium group and the depression group found no significant differences. This was true when the delirium group was compared to the no condition group as well. However, the delirium and no condition group approached significance, with the delirious group showing higher proportions of *indecisiveness*. This suggests a potential for *indecisiveness* to be a depressive symptom specific to delirium, which has not been accounted for by previous studies. Still, results largely suggested an overlap between all groups

and depressive symptomology, a factor that may contribute to high levels of delirium misdiagnosed as depression.

Additionally, we assessed whether or not differences existed between the groups in proportions of diagnosed depression as evaluated by the modified SCMDD. As expected, we found that the depressed group showed higher proportions of diagnosis of depression than the no condition group, suggesting proper specificity of the diagnostic criteria. However, this is challenged by the insignificant differences evident in diagnosed depression between the delirious and depressed groups. This result reinforces the findings indicative of an overlap between depressive and delirious symptomology. However, despite the insignificant chi-square results, the raw proportions of diagnosed depression in the delirious and depressed groups did differ (Table 2). Furthermore, the delirious group did not show a significantly increased presence of diagnosed depression when compared to the no condition group. Thus, in contrast to the overlapping results found for individual symptoms of the modified SCMDD, the findings regarding overlap in the actual diagnosis of depression are inconclusive. Accordingly, further research in larger samples may be necessary.

Another goal of this study was to account for potential antidepressant effects on modified SCMDD performance in patients with delirium. However, results indicated that the use of antidepressants made no significant impact on modified SCMDD performance in patients with delirium. Additionally, no significant effect of antidepressant use was apparent for overall modified SCMDD diagnosis of depression. However, this may have been a factor specific to this sample, considering the high amounts of medications often prescribed to the general hospitalized Veteran population.

Lastly, we aimed to compare performance on the MDAS among groups. We hypothesized that our findings would support those found by Leonard and colleagues (2009), indicating that participants with depression did not perform differently from the general sample on the measure. Results corroborated Leonard and colleagues' (2009) findings. Patients with delirium attained significantly higher mean scores on the MDAS than either the patients with depression or the general sample without delirium or depression. As the MDAS is intended to be a measure of delirium severity, these results are as expected. Furthermore, the depressed and no condition groups did not differ significantly and were also below the clinical cutoff for presence of delirium.

Limitations, Further Research, and Implications

A limitation to the present study was the inclusion of unequal group sizes in the sample. This was specifically relevant in our attempt to determine the role played by antidepressant use in the relationship between delirium and modified SCMDD (Kashani, McKnew, & Cytryn, 1985) performance. No significant relationship was found, which may be because the sample size for patients with delirium and prescribed antidepressant medication was much lower ($n = 9$) than for any other group. Therefore, the results are not necessarily generalizable and potential relationships may be unapparent. For this reason, one major future direction for this research is to account for antidepressant use in a much larger sample. Similarly, the sample size for participants with delirium was much lower ($n = 24$) than that of the depressed ($n = 77$) and no condition ($n = 167$) groups. Therefore, the findings of this investigation should be examined in larger samples, with regard to the overlap found in diagnosed depression based on the modified SCMDD between the depressed and delirious groups, as these results may have serious implications regarding the specificity of *DSM-IV-TR* criteria for depression. Additionally, future

research may examine MDAS performance in individuals who are prescribed antidepressants and those who are not.

Another sample-related drawback may also be interpreted as a main strength. This is in reference to the participants largely consisting of elderly, male Veterans. Although such a limited sample hinders the potential for results to be generalized to the general population, it also provides for specialized results in a population for which the data is particularly relevant. Accordingly, future efforts should extend the investigation to various groups including younger patients, non-Veterans, and females.

Additionally, this study was complicated by the use of patient medical records to determine previous diagnoses of depression. Medical records do not provide necessary information regarding the measures or criteria involved in certain diagnoses. In addition, methods of diagnosis are often highly variable and may range from subjective clinician reports to *DSM-IV-TR* (APA, 2000) criteria. Furthermore, this study lacked information regarding the time periods and relative severity of depression in the participants. Thus, it is apparent that future investigations should utilize standardized measures to ascertain presence of depression in participant groups.

It is also important to note the difficulties of working with patients with delirium. Namely, delirium often leads to unreliable reports of symptoms from patients. As the patient's cognitive functioning diminishes, so too does the reliability of his or her neuropsychological assessment results. Still, potential inaccuracies in symptom presence do not detract from the main focus of this study, which was to assess patterns of endorsement. The finding that large overlaps exist in depressive and delirious symptom endorsement, which may lead to high rates of misdiagnosis, is important regardless of the accuracy of self-reported symptoms. Patients are

often diagnosed with depression based on self-reported symptoms, and to this aim, our results further emphasize the importance of creating more specific measurements of depression.

Despite the present limitations, this investigation is the first to take a statistical approach in differentiating performance on a *DSM-IV-TR* (APA, 2000) criteria-based assessment of depression in participants with delirium, depression, and no condition. Accordingly, this work contributes valuable information to current understandings regarding the overlap between depressive and delirious symptom features. As this apparent overlap between symptoms of delirium and depression may serve to be problematic, it is imperative for future research to investigate the nuances of delirium and depression, and to ensure that measurement tools of each condition have adequate specificity. Furthermore, *DSM-IV-TR* (APA, 2000) based symptoms of depression were not found to be strongly specific to depression, and were often representative of delirium. This finding emphasizes the need to employ effective measures of delirium in clinical settings, rather than relying on patient self-report or subjective judgments of clinical staff. This is especially important as *DSM-IV-TR* (APA, 2000) based measures of depression are routinely administered in clinics prior to any testing for delirium. Accordingly, assessments of delirium should be employed early upon hospitalization, so as to avoid the misdiagnosis of depression that is made so common by the overlapping symptoms. By addressing these shortcomings in current diagnostic standards for depression and delirium, future research may facilitate lowered rates of misdiagnosis of delirium and eventually contribute to better patient outcomes, especially in the elderly.

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Table 1

Proportion of participants endorsing modified SCMDD (Kashani, McKnew, & Cytryn, 1985) items within each condition group

Modified SCMDD Item	Condition Group		
	Delirious Only	Depressed Only	No Condition
Depressed mood	2 (8.33%)	12 (15.58%)	10 (5.99%)
Anhedonia	1 (4.17%)	5 (6.49%)	8 (4.79%)
Loss of interest in work	2 (8.33%)	12 (15.58%)	15 (8.98%)
Loss of interest in activities	4 (16.67%)	21 (27.27%)	26 (15.57%)
Appetite loss	5 (20.83%)	25 (32.47%)	50 (29.94%)
Increased appetite	4 (16.67%)	8 (10.39%)	22 (13.17%)
Weight loss	12 (50.00%)	57 (74.03%)	118 (70.66%)
Weight gain	6 (25.00%)	15 (19.48%)	37 (22.16%)
Difficulty sleeping	5 (20.83%)	32 (41.56%)	64 (38.32%)
Nocturnal awakening	9 (37.5%)	36 (46.75%)	79 (47.30%)
Early morning awakening	9 (37.5%)	35 (45.45%)	75 (44.91%)
Hypersomnia	8 (33.33%)	33 (42.86%)	49 (29.34%)
Psychomotor agitation	8 (33.33%)	27 (35.06%)	60 (35.93%)
Psychomotor retardation	14 (58.33%)	63 (81.82%)	122 (73.05%)

Fatigue	8 (33.33%)	36 (46.75%)	61 (36.53%)
Excessive self-blame	6 (25.00%)	24 (31.17%)	31 (18.56%)
Feelings of guilt	8 (33.33%)	21 (27.27%)	29 (17.37%)
Feelings of worthlessness	2 (8.33%)	15 (19.48%)	15 (8.98%)
Diminished concentration	5 (20.83%)	18 (23.38%)	24 (14.37%)
Indecisiveness	8 (33.33%)	26 (33.77%)	30 (17.96%)
Suicidal ideation	0 (0.00%)	0 (0.00%)	4 (2.40%)

Table 2

Proportion of participants screening positive for depression on the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each condition group

Screen Results	Condition Group		
	Delirious Only	Depressed Only	No Condition
Negative	22 (91.70%)	59 (76.60%)	151 (90.40%)
Positive	2 (8.30%)	18 (23.40%)	16 (9.60%)

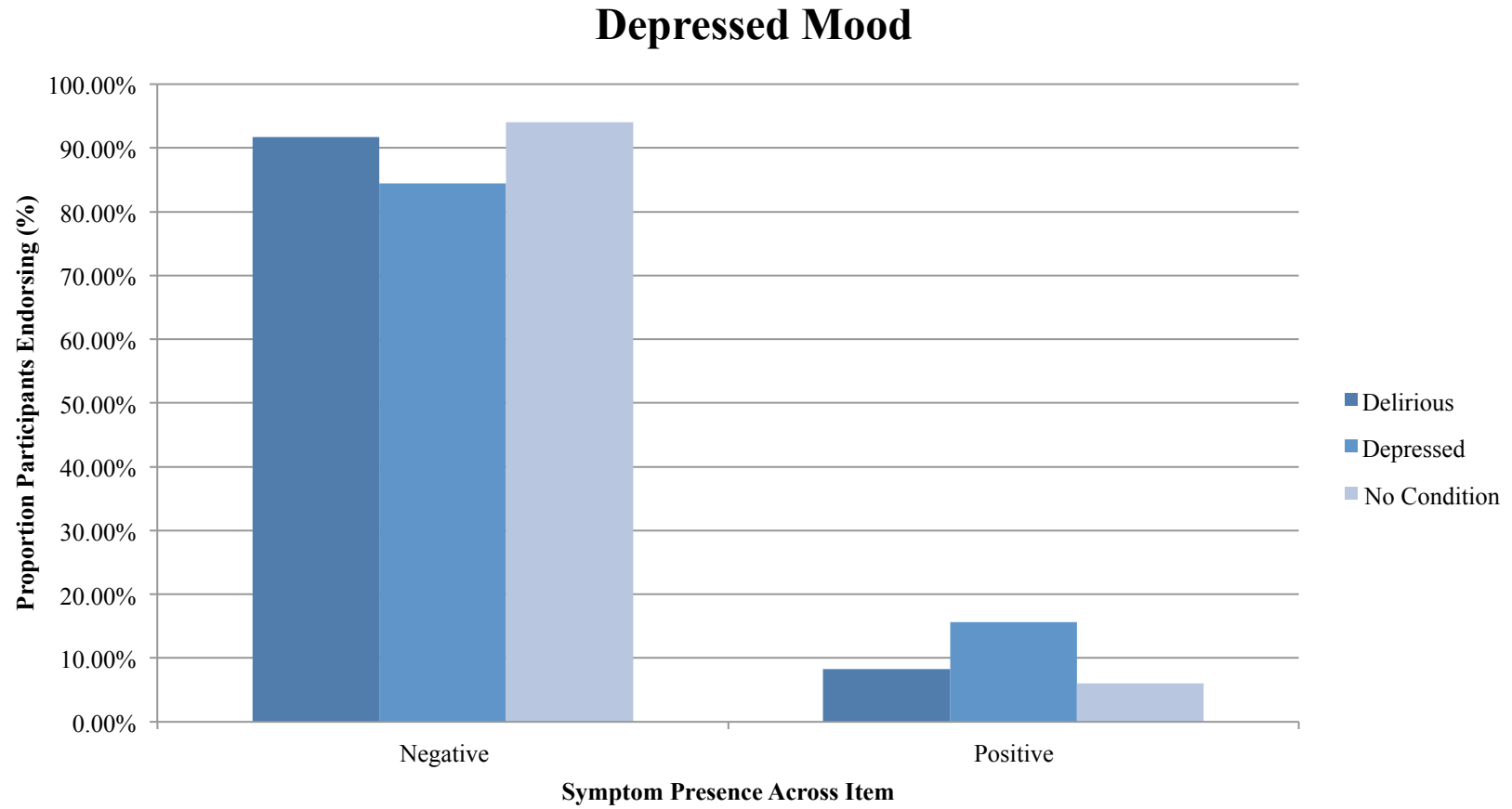


Figure 1. Percentage of participants endorsing the *depressed mood* item of the *depressed mood* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

Anhedonia or Diminished Interest

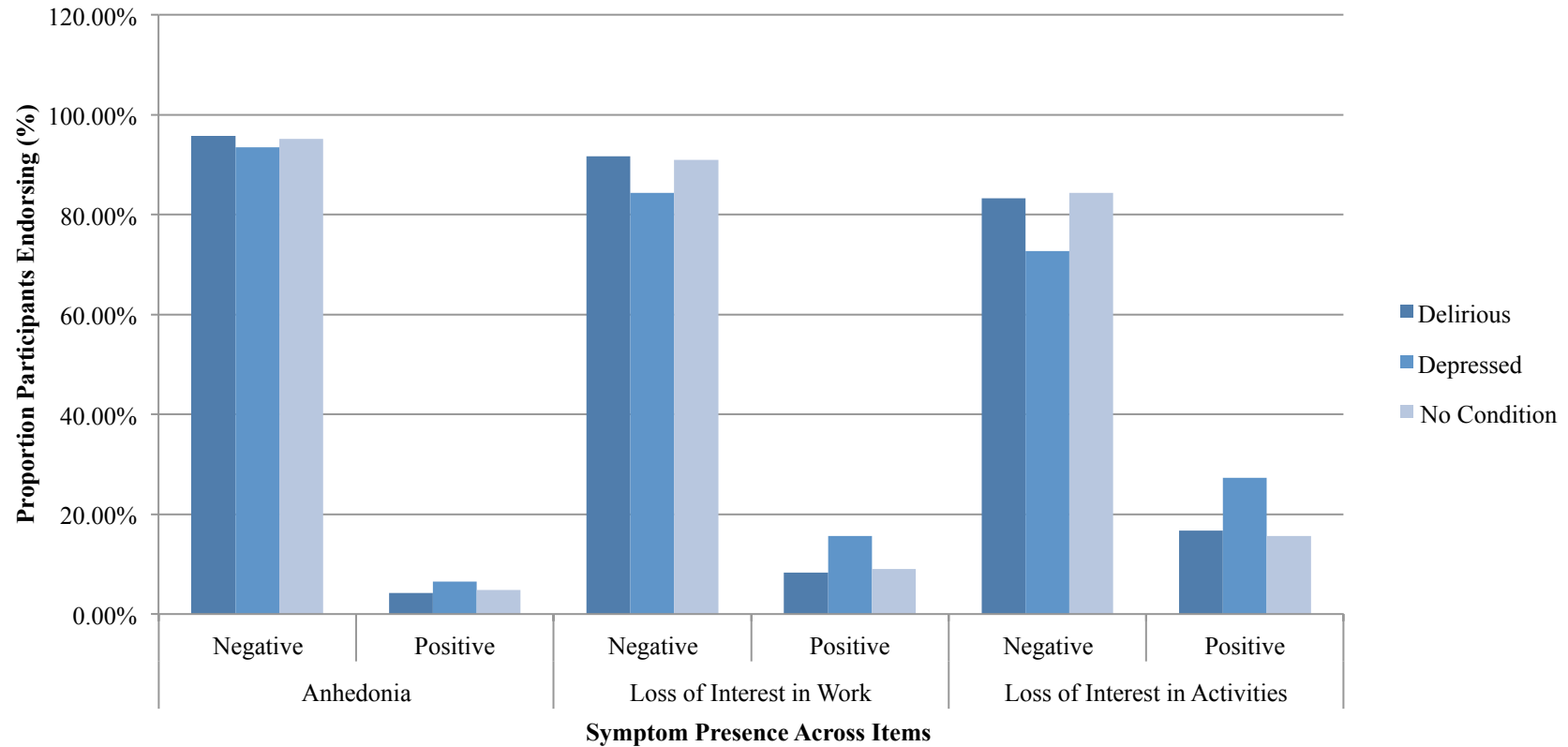


Figure 2. Percentage of participants endorsing the *anhedonia*, *loss of interest in work*, and *loss of interest in activities* items of the *anhedonia or diminished interest* category of the modified SCMD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious*, *depressed*, and *no condition*).

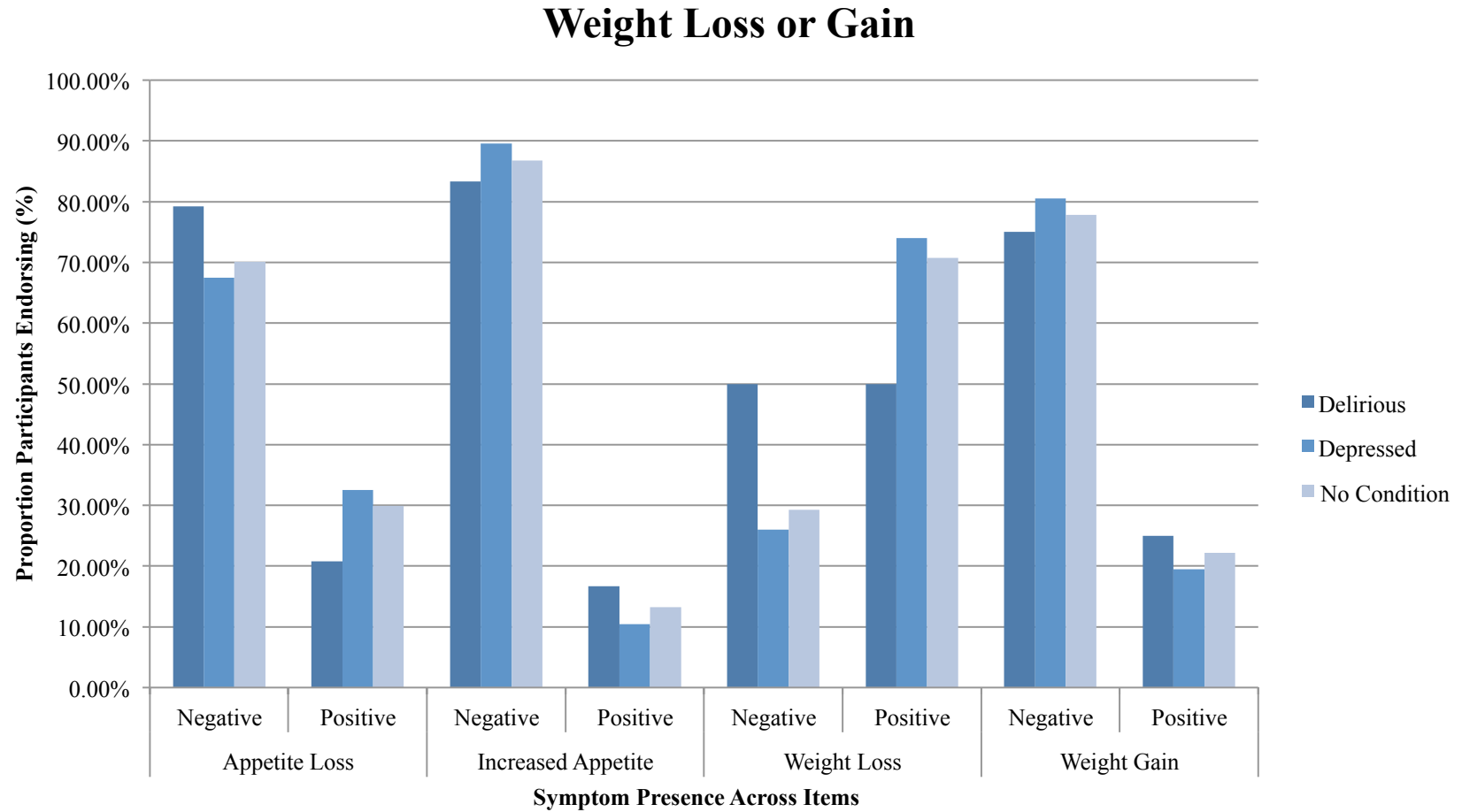


Figure 3. Percentage of participants endorsing the *appetite loss, increased appetite, weight loss, and weight gain* items of the *weight loss or gain* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

Insomnia or Hypersomnia

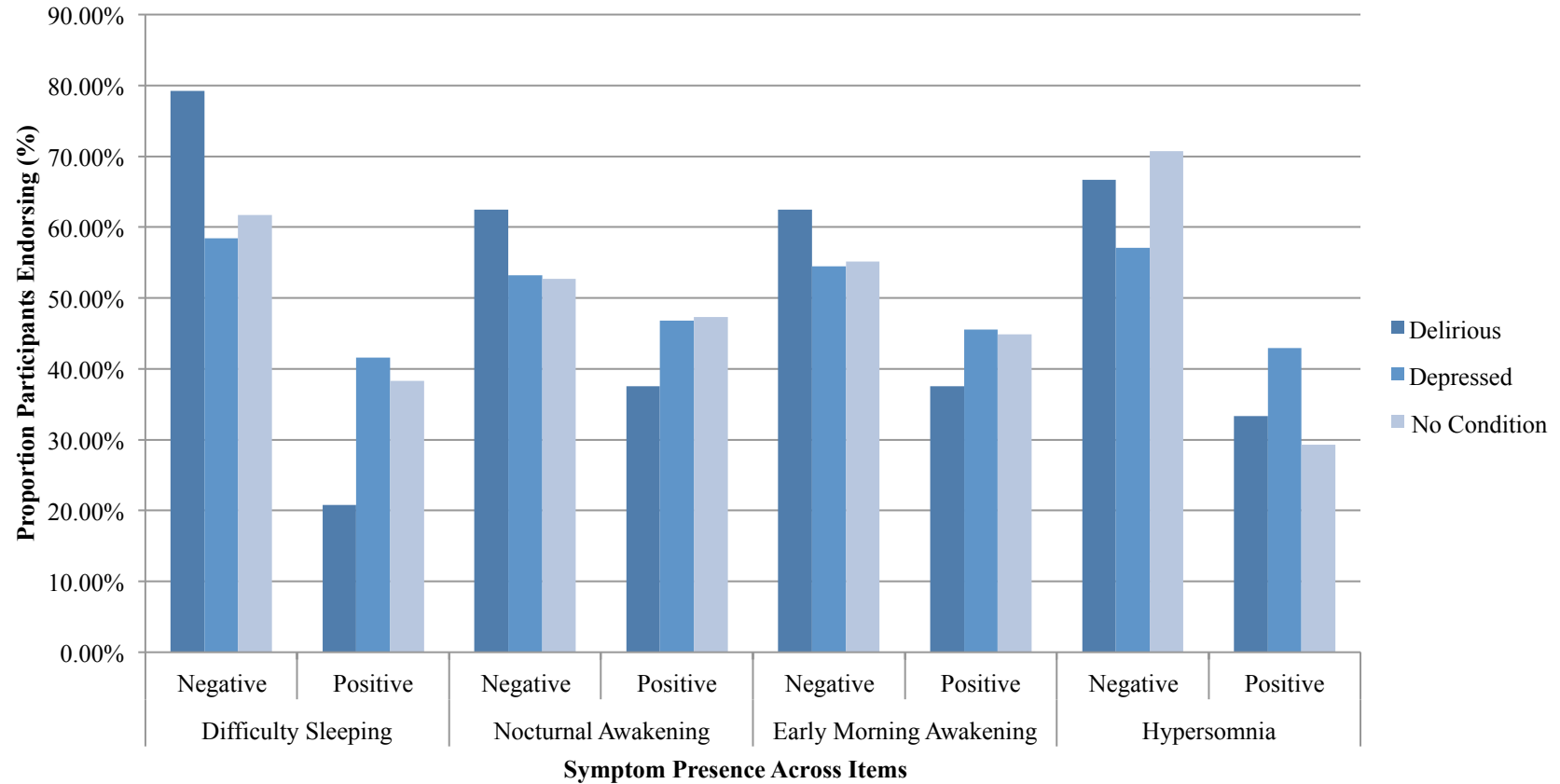


Figure 4. Percentage of participants endorsing the *difficulty sleeping, nocturnal awakening, early morning awakening, and hypersomnia* items of the *insomnia or hypersomnia* category of the modified SCMD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

Psychomotor Agitation or Retardation

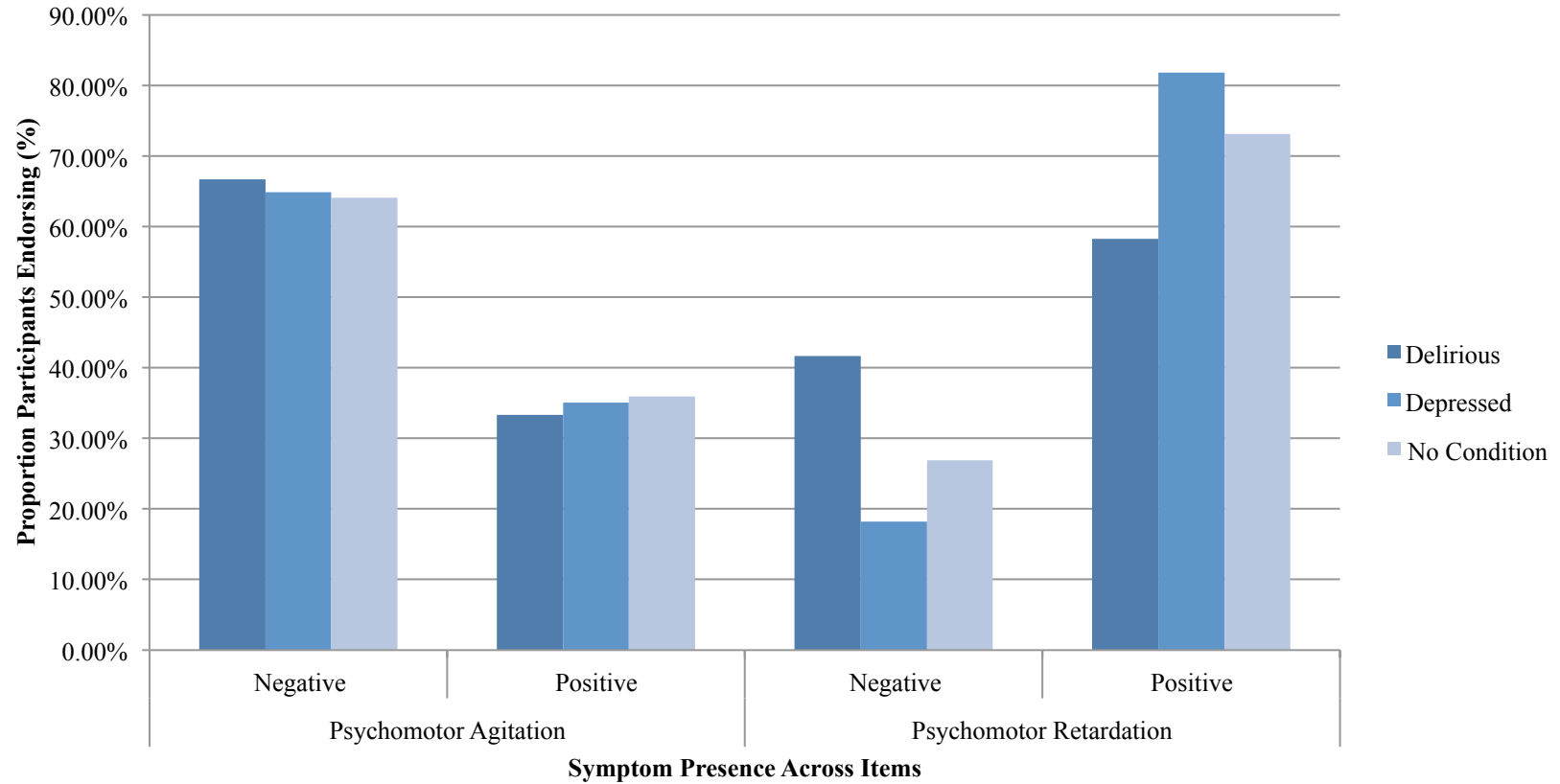


Figure 5. Percentage of participants endorsing the *psychomotor agitation and psychomotor retardation* items of the *psychomotor agitation or retardation* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

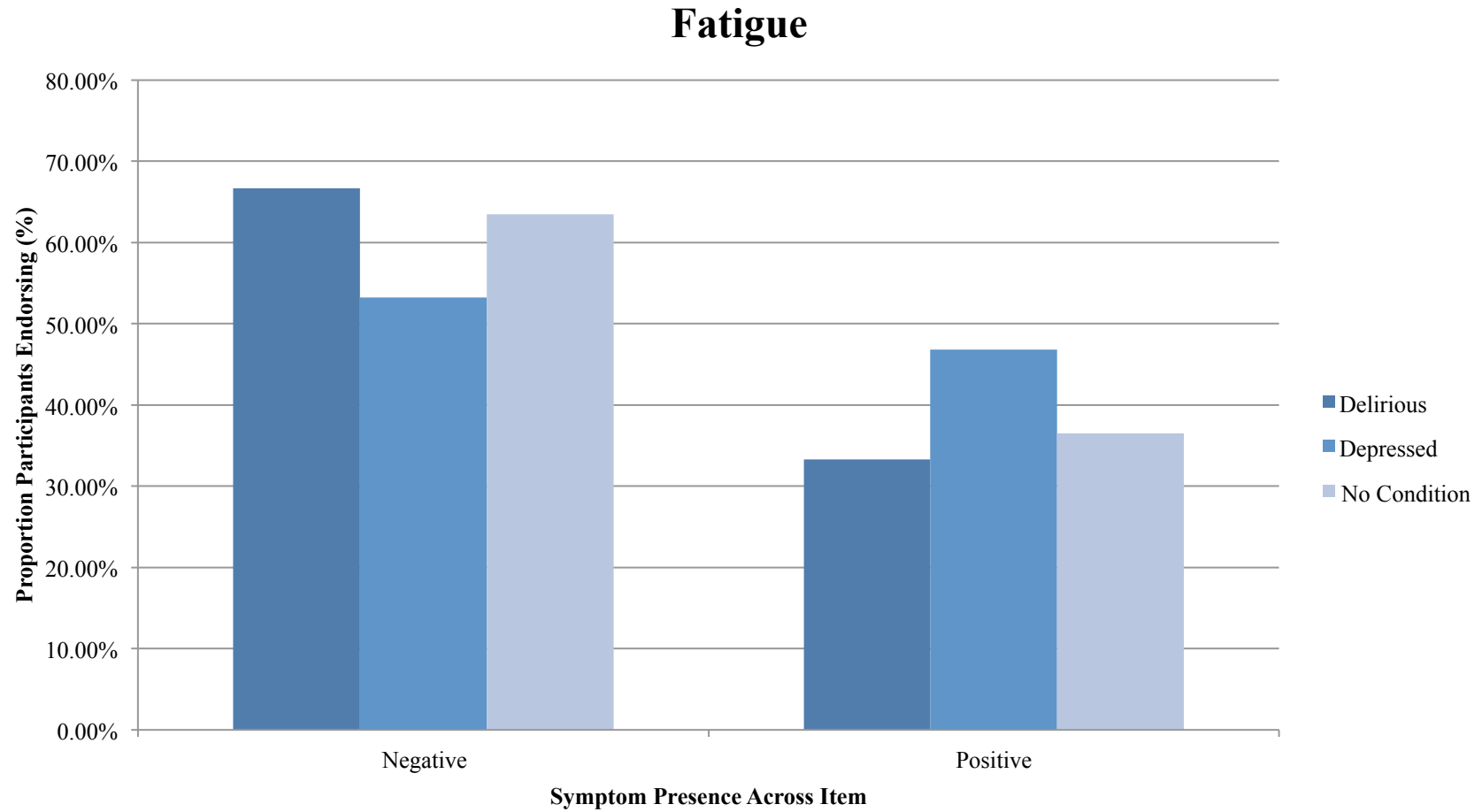


Figure 6. Percentage of participants endorsing the *fatigue* item of the *fatigue* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

Feelings of Worthlessness or Guilt

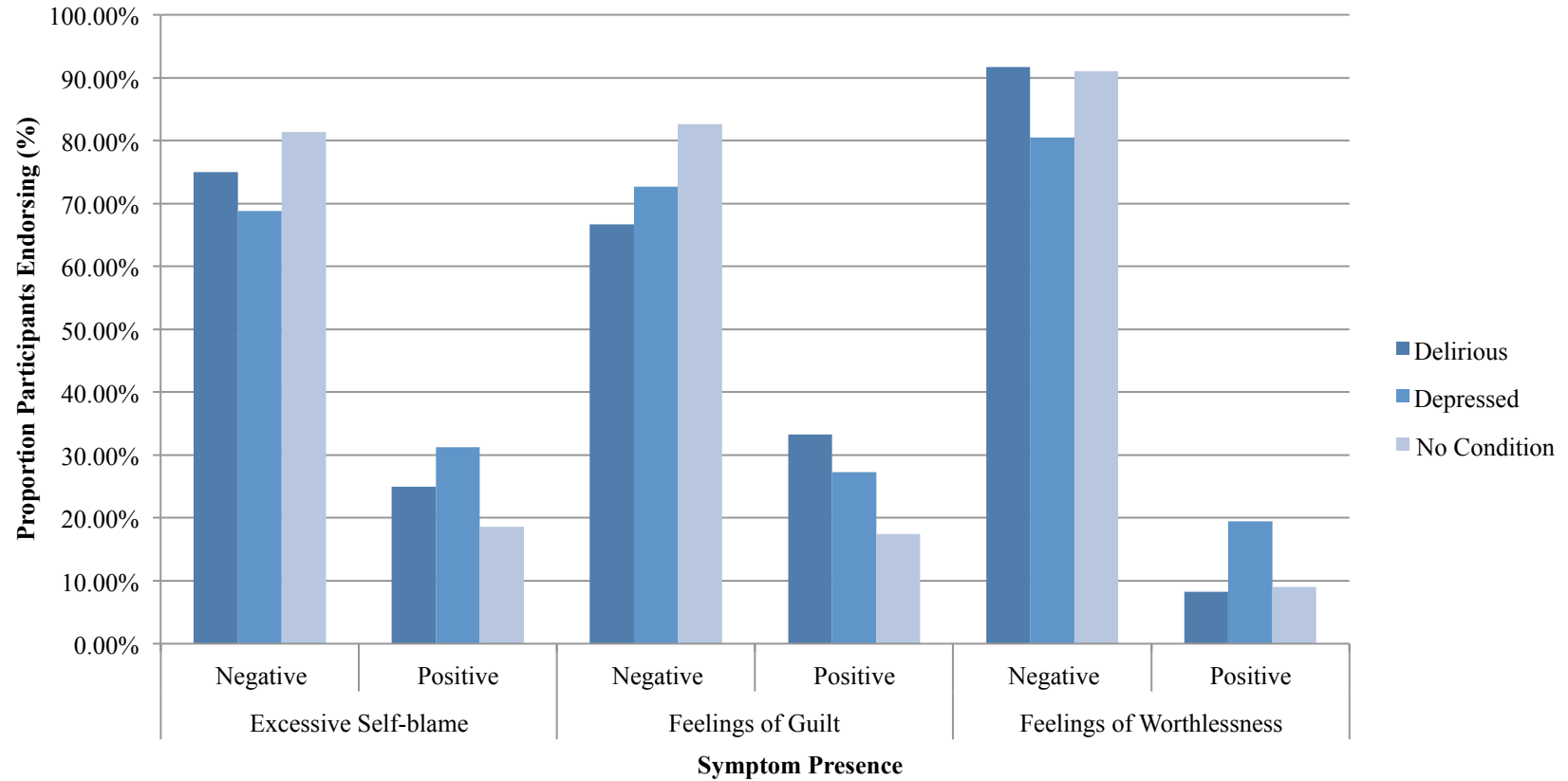


Figure 7. Percentage of participants endorsing the *excessive self-blame*, *feelings of guilt*, and *feelings of worthlessness* items of the *feelings of worthlessness or guilt* category of the modified SCMD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious*, *depressed*, and *no condition*).

Diminished Concentration or Indecisiveness

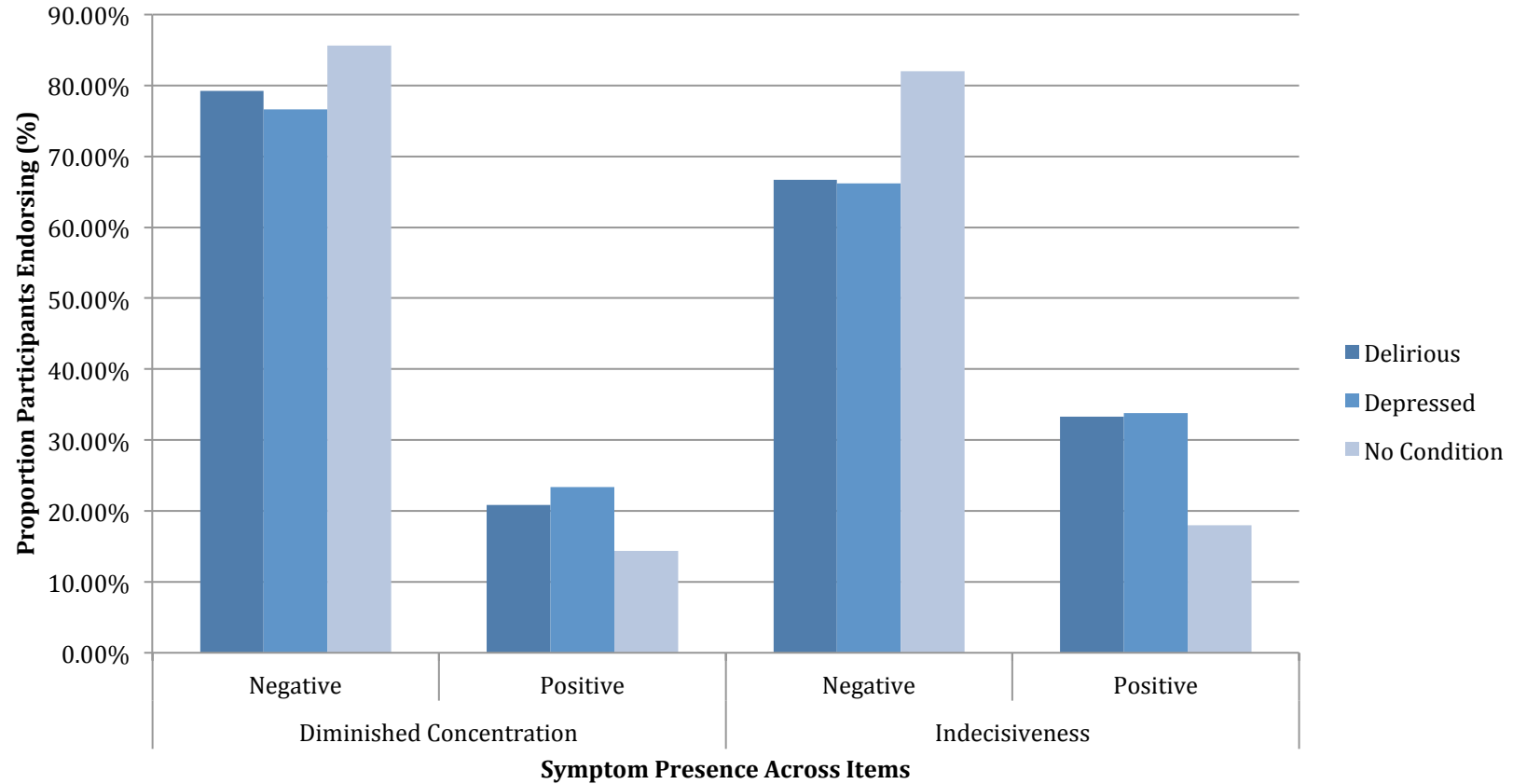


Figure 8. Percentage of participants endorsing the *diminished concentration*, and *feelings of worthlessness* items of the *feelings of worthlessness or guilt* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

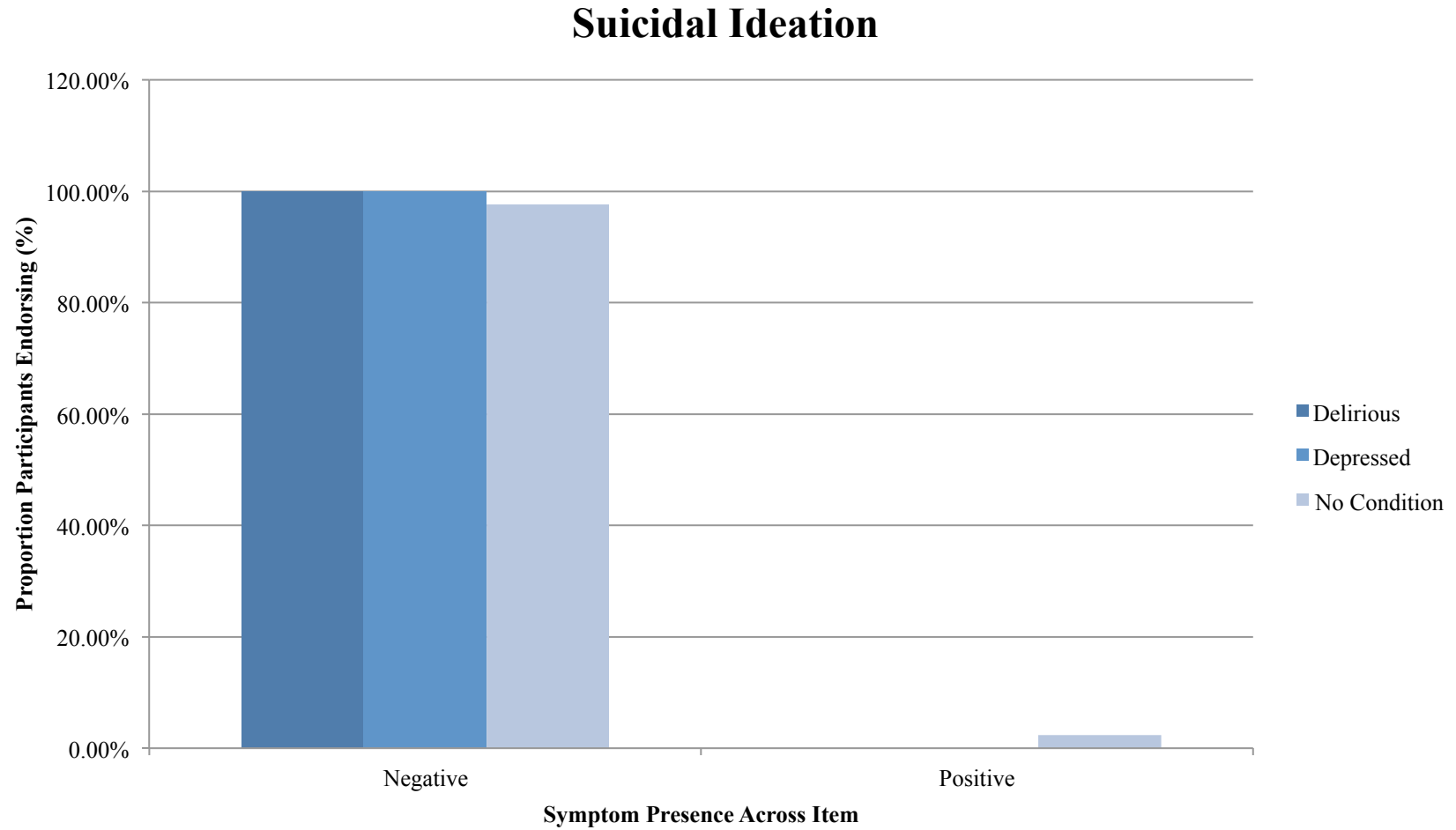


Figure 9. Percentage of participants endorsing the *suicidal ideation* item of the *suicidal ideation* category of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (*delirious, depressed, and no condition*).

Depression as Diagnosed by the Modified SCMDD (Kashani, McKnew, & Cytryn, 1985)

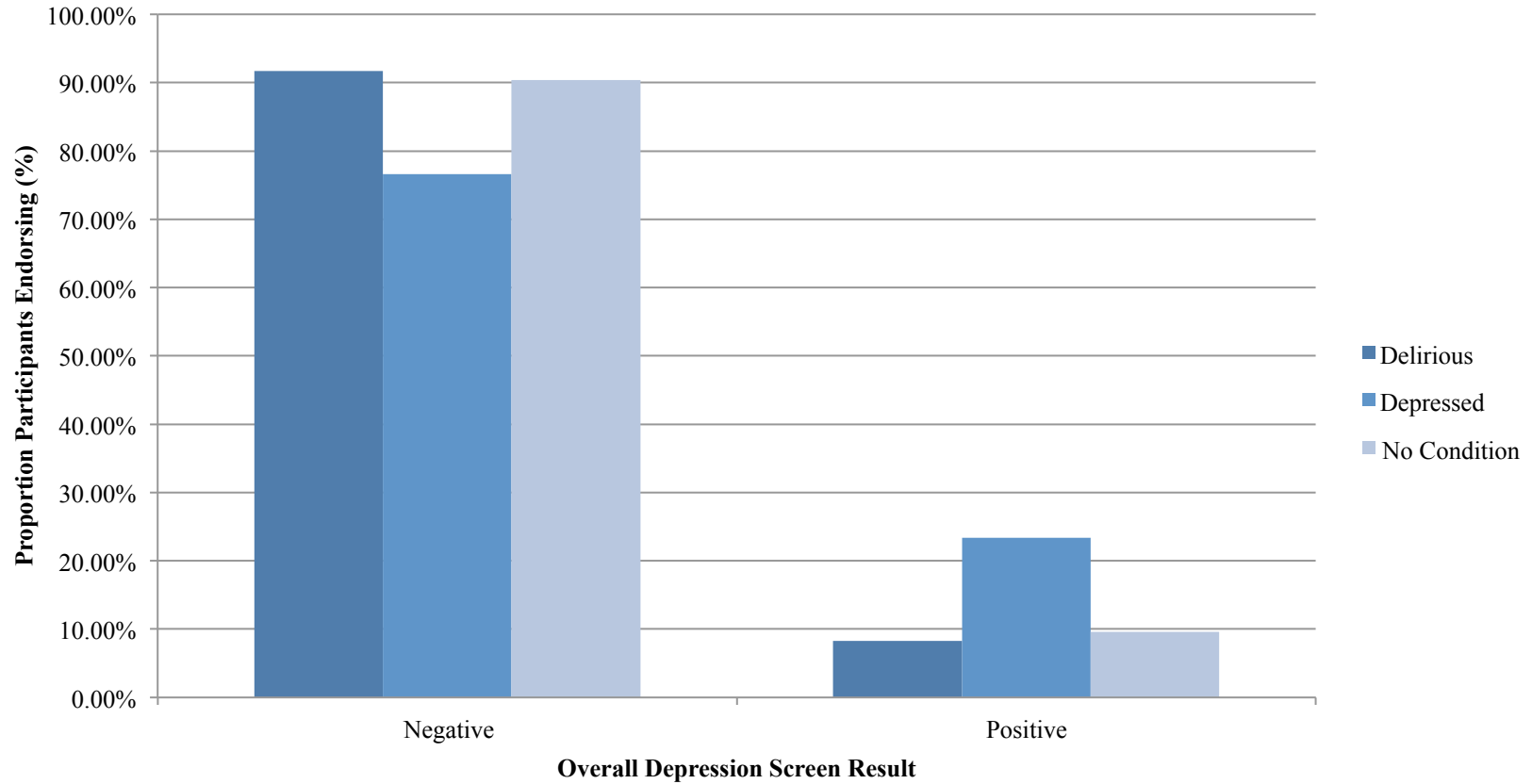


Figure 10. Percentage of participants endorsing a negative or positive screening result of the modified SCMDD (Kashani, McKnew, & Cytryn, 1985) within each of the three condition groups (delirious, depressed, and no condition).

Appendix A

DSM-IV-TR Diagnostic Criteria for Delirium (APA, 2000)

- A. Disturbance of consciousness (i.e., reduced clarity of awareness about the environment) with reduced ability to focus, sustain, or shift attention.
- B. A change in cognition (e.g., memory deficit, disorientation, language disturbance) or development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia.
- C. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of a day.
- D. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by direct physiologic consequences of a general medical condition.

Appendix B

DSM-IV-TR Diagnostic Criteria for Major Depressive Disorder (APA, 2000)

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning. At least one of the symptoms is (1) depressed mood or (2) loss of interest or pleasure.

Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

- 1) Depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others.
- 2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.
- 3) Significant weight loss when not dieting or significant gain, or decrease or increase in appetite nearly every day.
- 4) Insomnia or hypersomnia nearly every day.
- 5) Psychomotor agitation or retardation nearly every day.
- 6) Fatigue or loss of energy nearly every day.
- 7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
- 8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
- 9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or specific plan for

committing suicide.

- B. The symptoms do not meet the criteria for a mixed episode
- C. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
- D. The symptoms are not due to the direct physiological effects of a substance (for example, a drug of abuse, a medication), or a general medical condition (for example, hyperthyroidism).
- E. The symptoms are not due to the direct physiological effects of a substance (for example, a drug of abuse, a medication), or a general medical condition (for example, hyperthyroidism).