PROFILING PSYCHOPATHOLOGY IN A UNIQUE POPULATION OF CHRONICALLY ILL ADULTS: A DIMENSIONAL APPROACH

by

Samantha Ingram

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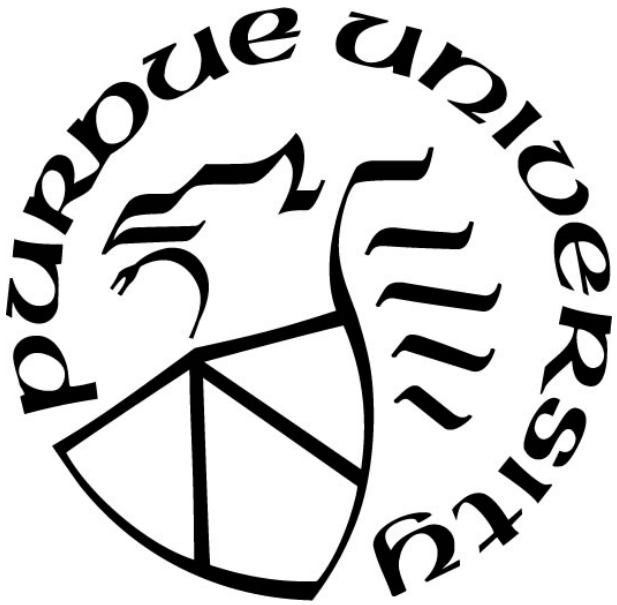

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STATEMENT OF COMMITTEE APPROVAL

Dr. Susan C. South, Chair
Department of Psychological Sciences
Dr. Douglas B. Samuel
Department of Psychological Sciences
Dr. Margo J. Monteith
Department of Psychological Sciences

Approved by:
Dr. David Rollock
Head of the Graduate Program

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ABSTRACT

Author: Ingram, Samantha. MS
Institution: Purdue University
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Committee Chair: Susan C. South

The internalizing and externalizing dimensions of psychopathology have been shown to effectively identify groups that are at higher risk for experiencing certain forms of psychopathology. Many studies have shown that chronic physical health conditions are a risk factor for psychological distress, yet there has been very little research examining the association between chronic physical health conditions and dimensional models of psychopathology to date. In the present study we examined the factor structure of internalizing and externalizing symptoms in a sample of adults with postural orthostatic tachycardia syndrome (POTS; n =172) and in a sample of adults without any chronic illness diagnoses (n = 199). Confirmatory factor analyses suggested that psychological distress in individuals with POTS can be effectively characterized by an internalizing dimension composed of distress and fear subcomponents as well as an externalizing dimension. Tests of measurement invariance allowed for the examination of latent means, which showed that individuals with POTS tend to have higher scores on the internalizing dimension and lower scores on the externalizing dimension than healthy controls. Regression analyses suggested that within the sample of people with POTS, those who were more accepting of their illness and had higher health related quality of life tended to have lower scores on the internalizing dimension. Findings suggest that individuals with POTS are at heightened risk for experiencing internalizing symptoms of

psychopathology. A dimensional conceptualization of psychopathology seems like an effective way to identify symptoms of psychopathology that are separate from symptoms of autonomic nervous system dysfunction.

INTRODUCTION

Chronic illnesses result in physical, psychological, and social consequences that necessitate many life changes, including substantial psychological adjustment (Stanton, Revenson, & Tennen, 2007). Indeed, chronic illness appears to be a risk factor for the development of psychopathology (Egede, 2007). Despite a rich literature devoted to the association between physical and mental health disorders, our current understanding in the area is lacking in a number of ways. Much of the current literature focuses on single mental health diagnoses in a piecemeal fashion, failing to assess for symptoms of psychopathology more comprehensively in chronically ill individuals. Furthermore, the current literature generally ignores chronically ill individuals experiencing subthreshold levels of psychological distress (i.e., symptoms of psychopathology that do not meet criteria for a diagnosis of a psychological disorder). Finally, much of the existing literature has focused mainly on commonly known physical illnesses such as cancer, diabetes, and asthma, while some illnesses are largely ignored. The current study aimed to address the limitations with the current literature through the application of a dimensional model of psychopathology in individuals with Postural Orthostatic Tachycardia Syndrome (POTS)[1], a largely understudied population.

[1]It is important to note that many POTS patients have been mistakenly told that their physical symptoms are due to psychopathology. Professionals working with this population must take care to avoid perpetuating the idea that the physical symptoms associated with dysautonomia are caused by psychological symptoms, as many studies have shown that this is not the case. Even so, the examination of symptoms of psychopathology in this population is warranted, as chronic illness is a risk factor for psychological distress.

Overlap Between Physical and Mental Health Conditions

The relationship between physical and mental health is complex and likely bidirectional in nature (Katon, 2003). Physical health conditions, chronic conditions in particular, may be risk factors for the development of psychological disorders (Egede, 2007). For example, the prevalence of depression has been shown to increase with the number of chronic illness diagnoses: In any given year about 5% of people without any chronic illnesses meet criteria for a major depressive disorder, while about 8% of those with one chronic illness, 10% of those with two chronic illnesses, and 12% of those with more than two chronic illnesses meet criteria (Egede, 2007). Factors related to chronic illness, such as symptom burden, disease prognosis, functional impairment, pain, and changes in physical appearance may contribute to the risk of psychological distress (Katon, 2011; Sharpe et al., 2017; Stanton et al., 2007). Conversely, psychological conditions may be risk factors for the development of chronic illnesses (Katon, 2003). This association is likely at least partially due to the fact that psychological disorders, such as depression, have an adverse effect on health behaviors, such as smoking, eating habits, and physical activity, that put people at risk for developing chronic physical health conditions (Katon, 2003). Chronic illnesses and psychological disorders also share a number of risk factors, including genetic vulnerabilities, stress, low socioeconomic status, and childhood adversity (Black, 2006; Harper & Lynch, 2007; Honkalampi et al., 2005; Katon, 2003).

Regardless of the directionality of the association, it is clear that those with chronic illnesses are at heightened risk for the development of psychopathology. Many individuals with chronic illnesses adjust to their diagnosis following a grieving process,

while other individuals experience prolonged distress that often results in symptoms of psychopathology and the development of psychological disorder (Turner & Kelly, 2000). Mood disorders such as depression have been implicated as both a cause and a consequence for a number of physical illnesses (Evans & Charney, 2003). Studies have linked depression to cardiac disease, cancer, HIV, Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, and more (see Benton, Stabb, & Evans, 2007 for a review). Studies have also linked a number of physical illnesses to symptoms of anxiety. One meta-analysis found that at least one third of individuals who had survived a critical illness exhibited anxiety symptoms for at least one year following the critical illness (Nikayin et al., 2016). Individuals who developed arthritis, asthma, cancer, heart disease, cystic fibrosis, diabetes, or epilepsy in childhood have also been found to be at increased risk for adult depression and anxiety (Secinti, Thompson, Richards, & Gaysina, 2017). Some studies have also found connections between chronic physical illnesses and childhood behavioral issues that are typical of externalizing disorders such as ADHD (Barlow & Ellard, 2006; Pinquart & Shen, 2011). Importantly, the psychological well-being of chronic illness patients predicts health related outcomes. For example, depression has been linked to decreased adherence to self-care practices, higher utilization of health services, higher numbers of perceived physical symptoms, greater functional impairment, and increased risk of death in a number of physical illnesses (Katon, 2011; Benton, et al., 2007).

The vast majority of the current literature on the co-occurrence of physical and mental health conditions focuses on individual diagnoses of psychopathology. In order to

obtain a more complete picture of the psychological well-being of chronically ill individuals, a broader approach to measuring psychopathology is necessary.

The Internalizing and Externalizing Spectra

Categorical systems of diagnosing psychopathology are largely problematic for a number of reasons (Krueger & Eaton, 2010). Comorbidity amongst psychological disorders is exceedingly common (Eaton, South, & Krueger, 2010; Trull & Durrett, 2005; Watson, 2005). In fact, more than half of individuals meeting criteria for a psychological disorder also meet criteria for at least one other disorder (Kessler, Wai, Demler, & Walters, 2005). These high rates of comorbidity suggest that the categorical diagnostic system does not accurately capture distinctions between disorders. Furthermore, categorical approaches fail to capture individuals who experience significant psychological distress but do not meet the diagnostic criteria for a disorder. In order to address these problems, researchers have been moving towards a dimensional model of classifying psychopathology. Growing evidence suggests that psychological disorders cannot be accurately conceptualized as their own categories; instead, it seems that all levels of functioning exist on a continuum. In other words, we can conceptualize psychological functioning as a spectrum that includes both “normal” levels of functioning and psychopathology (Carragher et al., 2014; Widiger & Samuel, 2005; Wright et al., 2013). The internalizing and externalizing spectra are a well validated and supported dimensional model of psychological disorders that help to account for comorbidities amongst categorically defined psychological disorders.

The internalizing and externalizing dimensions were first identified in studies of child psychopathology (Achenbach, 1966; Achenbach et al., 1991), and have been

replicated in adult samples (Achenbach & Rescorla, 2003; K. T. Forbush & Watson, 2013; Krueger, Markon, Patrick, Benning, & Kramer, 2007; Vollebergh et al., 2001) and in various cultures (Kessler et al., 2011). They have also accounted for disparities in psychopathology across gender (Kramer, Krueger, & Hicks, 2008), age (Eaton, Krueger, & Oltmanns, 2011), ethnic groups (Eaton et al., 2012), and sexual minorities (Eaton, 2014). The internalizing spectrum encompasses sexual dysfunctions, obsessive compulsive disorder (OCD), depressive and anxiety disorders, posttraumatic stress disorder (PTSD), and eating disorders (Kotov et al., 2017). Comorbidities amongst substance use disorders, attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder, intermittent explosive disorder (IED), and adult antisocial behavior can be accounted for by the externalizing dimension (Kotov et al., 2017). More recently, researchers have expanded this dimensional model to include a thought disorder spectrum that includes psychotic disorders, bipolar I disorder, and cluster A personality disorders (Kotov, Chang et al., 2011; Wright et al., 2013), and some research suggests the existence of a somatoform spectrum (Kotov, Ruggero et al., 2011)

A growing body of research has investigated the utility of using a dimensional approach of classifying psychopathology. The internalizing and externalizing spectra effectively characterize the development, course, and treatment of mental health disorders. Twin studies have found that both genetic vulnerabilities and environmental risk factors underlie the spectra (see Kotov et al., 2017 for a review). Furthermore, the spectra can capture the course of psychological illnesses by more effectively capturing change in symptomology over time than is possible with a categorical model (Eaton et al., 2011). The dimensional approach can also help to guide intervention and treatment

efforts, and explain the efficacy of treatments. For example, the internalizing spectrum has been shown to explain impairment associated with the symptoms of depression and anxiety (Markon, 2010), and to explain why the symptoms of these disorders are often effectively treated using the same interventions (e.g., pharmacologic interventions and cognitive behavioral therapy) (Goldberg et al., 2011).

The internalizing and externalizing spectra are also effective in identifying groups that are likely to experience certain forms of psychopathology. Profiles of mental disorders provide essential information about groups of people that are likely to experience different psychological disorders that can guide the development of intervention and prevention strategies (Slade, 2007). While categorical approaches to creating such profiles have been effective, the internalizing and externalizing spectra have been found to do so more effectively. For example, a number of studies have found mean level differences in internalizing and/or externalizing between men and women, between sexual majority and minority populations, between married and single individuals, between individuals who were employed and unemployed, and between individuals who received different levels of education (Carragher et al., 2014; Nicholas R. Eaton, Keyes, Krueger, Balsis, et al., 2012; Slade, 2007). Researchers have also identified stressors that predict the severity of internalizing and externalizing symptoms for certain populations (e.g., Eaton, 2014).

A handful of studies, particularly those in the child literature, have used a dimensional approach to examine psychopathology in chronically ill individuals. A meta-analysis of the child literature found that childhood chronic illnesses were associated with higher mean levels of internalizing and externalizing. More specifically, chronic fatigue

syndrome showed the strongest relationship with the internalizing dimension while migraines and epilepsy were the most strongly associated with elevated levels in externalizing (Pinquart & Shen, 2011). Fewer studies have looked at adults, but those that have find similar results. One study of adults found that chronic physical illness was strongly related to both the internalizing and externalizing dimensions such that the presence of a chronic illness was associated with higher scores on both dimensions (Slade, 2007). Another study found that several chronic health conditions were related to higher mean levels of the internalizing factor. Specifically, asthma, stroke, and arthritis were associated with higher mean levels on the fear dimension (i.e., part of the internalizing dimension that encompasses panic disorder, social anxiety disorder, agoraphobia, and OCD) and the distress dimension (i.e., part of the internalizing dimension that encompasses depression, dysthymia, generalized anxiety, and PTSD). The authors of this study concluded that the associations between individual chronic illnesses and psychopathology are better accounted for with a dimensional approach rather than a categorical approach (Pavert et al., 2017)

Finally, a study by Eaton and colleagues (2013) found associations between both chest pain and stomach ulcers and elevated mean levels of both the distress and fear dimensions. To our knowledge, no other studies have looked at the association between the internalizing and externalizing dimensions and chronic physical illnesses. The present study focused on conducting this investigation with a unique population of chronically ill individuals.

Chronic Illness and Psychopathology: The Case of Dysautonomia

What is Dysautonomia?

The autonomic nervous system (ANS) is involved in the regulation of most automatic processes of the body. Since these processes are so diverse, dysregulation of the ANS can manifest as a variety of seemingly unrelated symptoms (Grubb & Karas, 1999). People with autonomic dysfunction (i.e., dysautonomia) may experience a multitude of physical symptoms, including abnormal heart rate, dizziness, fainting, blurred vision, nausea, vomiting, fatigue, numbness, tingling, and pain. Some forms of dysautonomia occur as a primary disorder while others occur secondarily to other medical conditions, such as diabetes, celiac disease, lupus, and Parkinson's disease. While these disorders are not widely known, it is estimated that over 70 million people suffer from some form of dysautonomia worldwide (Dysautonomia International, 2012).

What is POTS?

Postural Orthostatic Tachycardia Syndrome (POTS) is one of the most common forms of dysautonomia[2]. It is estimated that somewhere around 500,000 people in the United States suffer from POTS (Robertson, 1999). POTS can occur in people of any age or gender, however it is most common in women between the ages of 15 and 50. Similar to other forms of dysautonomia, POTS presents with a wide variety of symptoms (Goldstein, 2016). In order to be diagnosed with POTS, a person must have an abnormal increase in heart rate upon standing (Grubb & Karabin, 2008). However, many other

[2]While we allowed people with any form of dysautonomia to participate in our study, the vast majority of participants reported a diagnosis of POTS. Therefore, we limited our analyses to individuals who endorsed a diagnosis of POTS in order to keep the sample homogeneous.

symptoms are associated with POTS including the symptoms listed above, chest pain, shortness of breath, and more (Grubb & Karabin, 2008; Raj, 2006).

Why Study POTS?

As detailed above, there is a clear association between chronic illnesses and psychopathology. However, most studies focus on commonly known and commonly diagnosed physical illnesses such as cancer, asthma, and heart disease (e.g., Pavert et al., 2017; Slade, 2007; Stanton et al., 2007). Understanding the link between these commonly known physical illnesses and various symptoms of psychopathology has resulted in a multitude of mental health resources targeted to help individuals and families experiencing these illnesses cope with associated psychological distress. Far fewer resources are available for individuals with lesser known or undiagnosed physical health conditions, despite the number of illness related stressors that they are likely to experience.

Individuals with POTS experience a large number of illness related stressors that are likely to increase the chances of psychological distress. For example, because dysautonomia can have a number of causes, people with autonomic disorders such as POTS often have comorbid physical disorders (Gazit, Nahir, Grahame, & Jacob, 2003; Grubb & Karabin, 2008; Kanjwal, Karabin, Kanjwal, & Grubb, 2010; Raj, 2006). As mentioned above, previous research has shown that the risk of having a psychological disorder increases with each additional comorbid physical disorder (Egede, 2007). Furthermore, POTS patients face a lifetime of managing their condition: currently there is no treatment for POTS or other forms of dysautonomia, but symptoms can be managed with a combination of lifestyle changes and medications. Even with treatment, some

studies have observed functional impairment in POTS patients comparable to that seen in chronic obstructive pulmonary disease (COPD) and congestive heart failure (Grubb & Karabin, 2008). Furthermore, because the condition is relatively lesser known than other health conditions, individuals with POTS often experience a long wait for successful diagnosis. For example, a survey of POTS patients found that on average it took over four years to receive a diagnosis of dysautonomia (Raj et al., 2016). Furthermore, many dysautonomia patients are told that their physical health problems are "all in their head" or are diagnosed with a psychological disorder as an explanation for their physical symptoms prior to receiving an accurate diagnosis (Raj et al., 2009). This common response is likely to have the unfortunate effect of acting as a barrier to seeking mental health treatment for individuals who finally receive a diagnosis, even though a diagnosis of a lifelong health condition is a life changing event likely to result in at least some psychological distress. Given that adjustment to chronic illness is associated with the management of illness related stressors (see Stanton et al., 2007 for a review), it seems likely that populations under increased illness related stress, such as individuals with POTS, would be at risk for experiencing at least some symptoms of psychopathology.

Finally, some autonomic researchers have suggested that dysautonomia is more of a "mind-body disorder" than many other illnesses (Goldstein, 2016). In other words, mental health may be more strongly associated with dysautonomia than other disorders since both are directly associated with nervous system processes and regulation. Thus, autonomic nervous system disorders such as POTS may uniquely exacerbate mental health issues that could be expected in most chronic health conditions, making it a good model for studying the association between chronic illness and psychopathology.

Historically, researchers believed that autonomic disorders such as POTS were psychosomatic, especially since the physical symptoms associated with POTS are similar to those associated with anxiety disorders. While many studies have shown that POTS is not psychosomatic (Khurana, 2006; Masuki et al., 2007), individuals with these disorders have a number of risk factors for experiencing psychological distress.

POTS and Psychopathology

The literature on dysautonomia and psychopathology is limited, and the relationship between the two seems unclear. Some research suggests that individuals with autonomic dysfunction such as POTS may have higher rates of some forms of psychopathology, while other studies suggest that they experience lower rates of psychopathology than is seen in the general population. One issue with studying the association between dysautonomia and psychopathology seems to be the misattribution of physical symptoms to psychological distress[3]. Indeed, over 83% of POTS patients were diagnosed with at least one psychological disorder prior to receiving their POTS diagnosis (Raj et al., 2016). However, many of these diagnoses are likely the result of misattributing physical symptoms to psychological distress. For example, many of the physical symptoms in POTS are also somatic symptoms of anxiety (Raj et al., 2009). In one study, POTS patients reported significantly higher rates of heart pounding and racing, feeling dizzy, numbness and tingling, and feeling unable to relax on the Beck Anxiety Inventory (BAI) than healthy controls. However, when using a measure of anxiety that did not rely heavily on somatic symptoms of anxiety, anxiety scores were found to be

[3]Historically, researchers believed that autonomic disorders such as POTS were psychosomatic or that such disorders were caused by psychological distress. While many studies have shown that this is not the case (Khurana, 2006; Masuki et al., 2007), that does not mean that individuals with the disorder do not experience psychological distress at all.

only mildly elevated in comparison to control groups (Raj et al., 2009). These misattributions have a number of negative effects on quality of care for individuals with dysautonomia. For example, misdiagnoses result in patients having to wait longer to receive an accurate diagnosis and treatment. Such experiences may also discourage dysautonomia patients from seeking mental health treatment.

Despite this issue, some studies have focused on understanding the association between dysautonomia diagnoses and psychological distress. In addition to moderate levels of anxiety, one study found that individuals with POTS did not have an increased lifetime prevalence of depression, but that they did score as mildly depressed using the Beck Depression Inventory (BDI). Furthermore, individuals with POTS had significantly higher scores on the BDI than healthy controls (Raj et al., 2009). Individuals with POTS also reported symptoms of inattention that were more severe than those reported by healthy controls but less severe than physically healthy individuals with a diagnosis of ADHD. Interestingly, these symptoms were not present during childhood for the individuals with POTS, suggesting that POTS may cause attention difficulties (Raj et al., 2009). Other studies have found significantly higher rates of depression and anxiety in patients with dysautonomia than healthy control groups. For example, Anderson and colleagues (2014) found that the majority of their patients with POTS presented with major depressive disorder and had elevated levels of anxiety when assessed by a psychologist. A number of studies have also suggested that individuals with dysautonomia are at a heightened risk for suicidal ideation than healthy controls, possibly due to an increased incidence of sleep disturbances and decreased quality of life (Bagai et al., 2011; Pederson & Blettner Brook, 2017).

CURRENT STUDY

Despite a rich literature regarding the shared risk for physical and mental health conditions, there has been very little research examining the association between chronic physical health conditions and dimensional models of psychopathology to date. Further, very little research has examined the mental health profile of individuals with lesser known chronic illnesses. The current study builds on the existing literature in three ways: (1) the use of a dimensional model of psychopathology to investigate both the internalizing and externalizing spectra, (2) recruitment of a sample of individuals with dysautonomia, and (3) the investigation other factors that may be related to the development and treatment of psychopathology in individuals with POTS.

Hypotheses

Hypothesis 1

We expected that the internalizing and externalizing factor structure would be replicated in a sample of individuals with diagnoses of dysautonomia.

Hypothesis 2

Individuals with dysautonomia would have higher mean levels on the internalizing factor than a physically healthy control group. Due to limited research on externalizing disorders in individuals with chronic illnesses, we were agnostic about how individuals with dysautonomia would compare to a healthy group on the externalizing factor.

Hypothesis 3

Among individuals with dysautonomia, those with higher levels of illness related acceptance, lower levels of illness related helplessness, or lower health related quality of

life (i.e., higher functional impairment) would have higher mean levels on the internalizing factor. We also expected that individuals who had been told that their physical illness was all in their head would have higher mean levels on the internalizing factor.

Method

We recruited individuals for two separate samples: a sample of individuals with an autonomic nervous system disorder and a sample of individuals free of any chronic physical health diagnoses. Participants in both groups had to be at least 18 years of age and live in the United States to be eligible. Participants in the dysautonomia sample had to report at least one current dysautonomia related diagnosis to participate[4]. Individuals in the healthy control group could not report diagnoses of any chronic physical health conditions. Ninety-eight percent of the dysautonomia sample was recruited through online support groups and researchmatch.org, while the other 2% was recruited through the introductory psychology pool at a large Midwestern University. 78% of the healthy control group was recruited through the introductory psychology pool at a large Midwestern University, 15% was recruited through researchmatch.org, and 7% was recruited through Amazon Mechanical Turk.

A total of 513 individuals met criteria for one of the samples and completed at least part of the survey. After removing incomplete and invalid survey responses, 381 individuals remained. Ten responses were removed from the final dysautonomia sample because they did not endorse a diagnosis of POTS[4]. The final dysautonomia sample included 172 individuals (93% female, 95% white) with a mean age of 36.83 (*SD* =

[4]Over 98% of individuals with dysautonomia who took the survey reported a diagnosis of POTS. Therefore, we limited our analyses in this paper to those individuals.

12.94). Seventy percent had completed at least some college education and 40% reported being employed outside the home. The final healthy control group included 199 individuals (67% female, 80% white) with a mean age of 25.09 (*SD* = 14.18). 80% reported completing at least some college education and 36% reported being employed outside the home[5].

All data were collected through an online questionnaire that could be saved and completed in segments. Before beginning the survey, all participants were given information about the study and provided informed consent. Participants recruited through online support groups and researchmatch.org were given the option to enter a drawing for one of six $25 Amazon gift cards upon completion of the survey, participants recruited through Amazon MTurk were paid $3 for their participation, and participants from the introductory psychology pool received course credit for their participation.

Measures

Internalizing. The Inventory of Depression and Anxiety Symptoms II (IDAS-II; Watson et al., 2012) is a 99-item expanded version of the original scale that is designed to assess basic symptom dimensions of depression and anxiety disorders. The scale assesses symptoms of general depression, dysphoria, suicidality, insomnia, appetite changes, panic, social anxiety, trauma related disorders, obsessive-compulsive disorder, and bipolar disorder. The IDAS-II has been found to be sufficiently reliable and valid (Watson et al., 2012), and scale alphas ranged from 0.77 and 0.92 in the current sample.

[5]Estimated sample size requirements were determined based on guidelines set out by Wolf and colleagues (2015). Based on previous research with factor loadings ranging from .50 to .80 (e.g. Forbush et al., 2010), we based our estimated sample size requirement on guidelines for CFAs with factor loadings of .50. The guidelines indicate that for CFA analyses involving 2 or three factors with 8 indicators, just above 150 participants should be sufficient for adequate power (Wolf et al., 2015). Thus, we will aim to recruit between 200 and 250 participants for each of our study groups.

Since many symptoms of dysautonomia overlap with symptoms of internalizing disorders, the scale was modified for the dysautonomia sample. Participants were instructed to choose a response option as usual and to select an option indicating that a symptom was also a symptom of their physical health condition when pertinent.

Eating disorder symptoms were assessed using the Eating Pathology Symptoms Inventory (EPSI; Forbush et al., 2013). This is a 45-item self-report measure designed to assess symptoms of eating pathology. The EPSI has eight subscales that assess both cognitive and behavioral aspects of eating disorder pathology such as body dissatisfaction, binge eating, negative attitudes towards obesity, and excessive exercise (Forbush et al., 2013). Alphas for the final scales ranged from .72 to .91 in our sample.

Externalizing. The 160-item Externalizing Spectrum Inventory-Brief Form (ESI-BF; Patrick, Kramer, Krueger, & Markon, 2013) is a shortened version of the full 415-item measure. The ESI-BF is a self-report questionnaire scored on a 4-point scale that is recommended for use in research regarding risk-taking, delinquency, aggression, and substance abuse (Patrick et al., 2013). The ESI forms a total scale ($\alpha = 0.90$), three factor scales (α ranged from 0.83 to 0.88), and 23 facet scales (α ranged from 0.61 to 0.90).

Given elevated levels of ADHD symptoms in previous research with dysautonomia patients (Raj et al., 2009), we assessed ADHD symptoms through the use of the Adult ADHD Self- Report Scale (ASRS; Adler et al., 2006). The ASRS is an 18-item measure that is used to evaluate the presence of ADHD symptoms in adults ($\alpha = 0.90$).

Personality. The Big Five Inventory 2 (BFI-2; Soto & John, 2017) is a 60-item scale designed to measure the personality domains of extraversion ($\alpha = 0.86$),

agreeableness (α = 0.83), conscientiousness (α = 0.88), negative emotionality (α = 0.91), and openness (α = 0.87). The BFI-2 also provides fifteen facet scores associated with the five domains (α ranged from 0.67 to 0.85).

The Personality Diagnostic Questionnaire 4+ (PDQ-4+; (Hyler, 1994) is a 99-item true-false measure that assesses personality disorders through content that corresponds directly to the personality disorder criteria in section two of the DSM 5. Given that symptoms of some personality disorders (e.g., antisocial personality disorder) have been shown to be associated with the externalizing spectrum of psychopathology (Kotov et al., 2017), we included the PDQ-4+ in our study. The antisocial personality disorder scale had an alpha of 0.55 in this sample.

Heath related quality of life. Health related quality of life was assessed using the Short-Form Health Survey (SF-36; Ware & Sherbourne, 1992). This is a 36-item self-report measure that assesses eight health related outcomes: physical functioning (α = 0.96), limitations due to physical health problems (α = 0.82), limitations due to emotional problems (α = 0.85), physical pain (α = 0.91), fatigue (α = 0.88), emotional wellbeing (α = 0.82), social functioning (α = 0.91), and overall perceptions of health (α = 0.90). The survey was designed for use in individuals ages 14 and above and is widely used in the medical field (Ware & Sherbourne, 1992).

Illness cognitions. The Illness Cognition Questionnaire (ICQ; Evers et al., 2001), is an 18- item questionnaire intended to measure how individuals with chronic illnesses think about their medical conditions. The questionnaire measures three illness cognition factors, helplessness (α = 0.88), acceptance (α = 0.87), and perceived benefit (α = 0.88), all of which have been associated with adjustment to chronic disease (Evers et al., 2001).

The measure has demonstrated acceptable reliability and validity across chronic illness populations (Lauwerier et al., 2010).

Statistical Analyses

All factor analyses were conducted using the M*plus* software Version 8 and maximum likelihood estimation (Muthén & Muthén, 2017). The psychopathology indicators (i.e., scale and subscale scores as listed below) were entered into a series of confirmatory factor analyses (CFA). We selected indicators for the internalizing and externalizing factors based on suggested factor structure laid out by Kotov and colleagues (2017). The dysphoria, social anxiety, panic, traumatic intrusions, traumatic avoidance, checking, ordering, and cleaning symptom scales from the IDAS II served as observed indicators for the internalizing factor. The eight symptom scales on the EPSI (muscle building, restricting, body dissatisfaction, purging, excessive exercise, binge eating, negative attitudes toward obesity, and cognitive restraint) and the neuroticism domain of the BFI-2 also served as observed indicators for the internalizing factor. Observed indicators for the externalizing factor included ADHD symptom counts from the ASRS, the antisocial personality disorder symptom scale on the PDQ-4+, and the callous aggression, disinhibition, and substance use problem scales from the ESI-BF. For CFA models that included internalizing subfactors, the dysphoria, traumatic intrusions, traumatic avoidance, and BFI neuroticism scales served as indicators for the distress subfactor; the panic, social anxiety, checking, ordering, and cleaning scales served as indicators for the fear subfactor, and the eight symptom scales on the EPSI served as indicators for the eating factor. Fit of each model was determined according to standard

guidelines (Hu & Bentler, 1999): RMSEA < .08 and CFI > .95. Nested models were compared using chi-square difference testing and change in CFI.

Regression analyses were conducted in SPSS using simultaneous linear regression models. The physical functioning, physical limitations, pain, and perceptions of general health scales from the SF-36 were used as predictors representing functional impairment. Other predictors included the helplessness and acceptance scales from the ICQ and participants' responses about whether or not they had been told their physical health conditions were all in their head[6]. Internalizing, distress, and fear factor scores from the final factor model were used as the dependent variables.

Results

Descriptives

Means and standard deviations for all factor indicators are reported in Table 1[7]. We also conducted *t*-tests to compare mean scores on the scales between the sample of individuals with POTS and the healthy control sample. Individuals with POTS reported significantly lower scores on the traumatic intrusions, traumatic avoidance, callous aggression, substance abuse, and antisocial personality disorder scales than healthy controls. Individuals with POTS reported experiencing significantly more dysphoria, panic, and social anxiety symptoms[8]. 81% of participants in this sample reported that a

[6]We were also interested in measuring the time since the onset of symptomology, since people with a longer time to adjust to physical symptoms may theoretically have less distress. However, over half of our sample did not provide sufficient information to measure this variable and we did not include it in analyses.
[7]We also conducted these *t*-tests limiting our sample to women only (see Table 10) and limiting our sample to individuals under 26-years-old (see Table 11).
[8]We adjusted the wording of the IDAS-II such that individuals with POTS were asked to indicate whether specific items were symptoms of their physical health condition. We recalculated scores on the IDAS scales by removing items for which more than ¼ of the sample indicated the item was measuring a symptom of their physical health condition. After doing so, only one of the items on the panic scale remained. However, *t*-tests for the other recalculated scales did not change the effects found with the full scales (see supplemental Tables 8 and 9).

health professional had told them that their physical symptoms were “all in their head”. The mean number of physical health diagnoses reported by individuals with POTS was 3.21.

Model Estimation and Comparison

The first step was to confirm that the internalizing and externalizing factor structure would hold in our sample of individuals with POTS. We began by testing three models that were specified a priori. First, we tested a model that allowed all indicators for internalizing (i.e., dysphoria, traumatic intrusions, traumatic avoidance, checking, ordering, cleaning, social anxiety, panic, neuroticism, and the eight symptoms scales from the EPSI) to load onto one factor, all indicators for externalizing (i.e., ADHD, antisocial personality disorder, callous aggression, disinhibition, and substance use problems) to load onto one factor, and the two factors to covary. The metric of the factors was set by fixing the factor variance to 1.0 and allowing the factor loadings of the indicators to be freely estimated. All other residual variances were freely estimated and no residual covariances were specified. The fit indices indicated poor fit of this model (i.e., $X^2(208) = 702.65$, $p < .001$, RMSEA = .12, CFI = .67; see Model 1, Table 2). Next, we tested a model in which the indicators for the internalizing factor loaded on distress (i.e., dysphoria, traumatic intrusion, traumatic avoidance, and neuroticism), fear (i.e., social anxiety, panic, checking, ordering, and cleaning), and eating pathology subfactors (i.e., muscle building, restricting, body dissatisfaction, purging, excessive exercise, binge eating, negative attitudes towards obesity, and cognitive restraint), which in turn all loaded onto an internalizing factor, all indicators for externalizing (i.e., ADHD, antisocial personality disorder, callous aggression, disinhibition, and substance use problems)

loaded onto one factor and the internalizing and externalizing factors covaried. Again, the metric of the factors was set by fixing all factor variances to 1.0 and allowing the factor loadings of the indicators to be freely estimated. Factor loadings for the lower order factors were held equivalent to one another. All other residual variances were freely estimated, and no residual variances were specified. The fit indices also indicated poor fit for this model (i.e., $X^2(205) = 570.05$, $p < .001$, RMSEA = .10, CFI = .75; see Model 2, Table 2). Third, we tested a model in which a higher-order internalizing factor was comprised of lower-order depression, anxiety, PTSD, and OCD subfactors; all indicators for externalizing (i.e., ADHD, antisocial personality disorder, callous aggression, disinhibition, and substance use problems) loaded onto one factor; and the internalizing and externalizing factors covaried. Again, the metric of the factors was set by fixing all of the factor variances to 1.0 and allowing the factor loadings for the indicators and the lower-order factors to be freely estimated. All other residual variances were freely estimated and no residual covariances were specified. Model fit for this model was improved, but still unsatisfactory (i.e., $X^2(77) = 223.19$, $p < .001$, RMSEA = .11, CFI = .87; see Model 3, Table 2).

Given that none of the models hypothesized a priori fit well in the sample according to standard fit guidelines, we next looked at the correlations among the variables and standardized residuals from the CFAs to determine if we might be able to specify a better fitting model. The standardized residuals showed that each of our three models were underestimating the correlation between ADHD symptoms and the internalizing factor. We looked at the means of the items on the ASRS measure of ADHD symptoms that we used and hypothesized that the ASRS seemed to be measuring

symptoms of anxiety rather than problems with attention and hyperactivity as expected. Thus, we decided to drop the indicator from future models. Scales from the EPSI also did not fit well in this sample. Compared to loadings, means, and residuals in previous studies (e.g., Forbush et al., 2013), it appeared that the EPSI was not an adequate measure of eating pathology in this study's population. Therefore, we decided to drop the EPSI from further analyses as well. We re-ran our models without the scales from the ASRS and EPSI. Model fit improved but was still unsatisfactory (i.e., $X^2(64) = 313.77$, $p < .001$, RMSEA = .15, CFI = .76; $X^2(63) = 222.29$, $p < .001$, RMSEA = .12, CFI = .84; and $X^2(65) = 163.56$, $p < .001$, RMSEA = .09, CFI = .91; see Model 1B, Model 2B, and Model 3B, Table 2).

We then looked at scale correlations and parceled the checking, ordering, and cleaning scale to form an OCD scale and we parceled the traumatic intrusions and traumatic avoidance scales to form a PTSD scale. We tested our adjusted models (now without the EPSI eating pathology scales and ASRS ADHD scale) using the parceled OCD indicators and the parceled PTSD indicators. Model fits for these models were improved (i.e., $X^2(34) = 102.39$, $p < .001$, RMSEA = .11, CFI .90; $X^2(33) = 96.97$, $p < .001$, RMSEA = .11, CFI .90; see Model 1C and Model 2C, Table 2). However, the RMSEA values in these adjusted models were still higher than the standard of .08, so we looked at standardized residuals from our two best fitting models (Model 3B and Model 2C) to determine if adding paths might improve the model fit for subsequent analyses. Standardized residuals and modification indices for Model 3B suggested adding paths that did not make theoretical sense. Those that did make sense would essentially form distress and fear subfactors resembling Model 2C. Therefore, we decided not to pursue

the model for subsequent analyses. After looking at the standardized residuals for Model 2C, we added three residual covariances, improving the fit for this model in the POTS sample (i.e., $X^2(30) = 50.31$, $p = .01$, RMSEA = .06, CFI = .99; see Best-Fitting Model, Table 2). In order to pursue subsequent analyses, we also tested all nine of the models in the healthy control sample to determine if both samples had the same best fitting model. Fit indices for the healthy control sample can be found in Table 3[9]. The best fitting model was the same for both samples and was selected for subsequent analyses. A conceptual version of the best-fitting model is shown in Figure 1. Factor loadings are in Table 5.

Physical Health Measurement Invariance

Having established the best fitting confirmatory factor model in both the POTS and healthy control samples, we turned to examining measurement invariance of the factor structure across these two groups. Measurement invariance across the two groups was tested by using multiple group modeling, progressively constraining parameters across the two physical health groups consistent with procedures described by Meredith (1993) and Muthén, & Muthén (1998-2017). We first tested configural invariance to determine if the same latent variable structure was present for both healthy individuals and individuals with POTS by constraining the pattern of fixed and free loadings across the two groups. In a configural invariance model, the factor loadings, indicator intercepts, residual variances, and factor covariances are freely estimated separately in both groups. Factor and subfactor means were set to 0 and factor and subfactor variances were set to 1.0. Model fit for this analysis was comparable with the fit of the best-fitting model in the overall sample (RMSEA = .07, CFI = .96; Table 6), which suggests that the final model

[9]Note that fit indices for all models in the overall sample can be found in Table 4. The best fitting model was the same for the overall sample, the POTS sample, and the healthy control sample.

does an adequate job of explaining the relation between internalizing and externalizing symptoms of psychopathology for both samples.

To examine whether the relationships between the observed indicators and latent factors in the final model were equal, we tested metric invariance. This level of invariance holds both the factor pattern and factor loadings equal across the two groups. The intercepts, residual variances, and factor covariances were allowed to freely vary, with the exception of the disinhibition indicator which had a negative residual covariance in the healthy control group. Thus, we constrained the residual covariance in this scale to 0[10]. Again, factor and subfactor means were set at 0 and factor and subfactor variances were set at 1.0. Fit indices indicated that this model fit well according to standard guidelines (RMSEA = .072, CFI = .96; Table 6). Further, the chi-square difference test was not significant ($p < .001$) and the change in CFI was less than 0.01 from configural to metric invariance.

We tested scalar invariance by holding the factor patterns, factor loadings, and intercepts equal across the two groups. The fit indices for the scalar model were worse than the configural or metric models and poor according to most fit guidelines (RMSEA = .14, CFI = .80; Table 6). Further, the chi-square difference test was significant and the change in CFI from metric to scalar was far greater than .01, indicating that scalar invariance did not hold across the two groups. To investigate partial measurement invariance, we examined modification indices in Mplus, and based on the highest MI, we allowed the allowed the intercepts of the panic indicator and the disinhibition indicator to vary across groups. This resulted in a negative residual covariance for the disinhibition

[10]Model fit did not change when the residual covariance for this scale was constrained to 0.

scale in the healthy group, so we constrained the value to 0 and tested the model again. This resulted in a well-fitting model (RMSEA = 0.08, CFI = 0.95; Table 6). The chi-square difference test was significant (p = .051), but the change in CFI was less than 0.01 from the metric to partial scalar invariance.

Achieving partial scalar equivalence allowed us to compare the latent symptom means across the two physical health groups. Consistent with our hypothesis, individuals with POTS had significantly higher mean levels of internalizing symptoms that the healthy control sample (*mean difference* = -.49, p < .001). Results also showed that individuals with POTS had significantly lower mean levels of externalizing symptoms than healthy controls (*mean difference* = .79, p < .001).

Variables Related to Internalizing Symptoms in Individuals With POTS

Having determined the best-fitting structural model, we turned to examine the relationships between the higher-order internalizing and lower-order fear and distress factors and external outcome variables. Factor scores for internalizing, fear, and distress factors were extracted from Mplus to use in regression modeling in SPSS. We ran linear regression models to test health related factors that might be associated with higher levels of internalizing symptoms in individuals with POTS. Table 7 shows the results of the final regression models predicting the internalizing factors and subfactors from the final factor model in the dysautonomia sample. All models included illness related helplessness, illness related acceptance, a categorical variable representing whether participants had been told their health symptoms were all in their head, physical functioning, role limitations due to physical health, pain, and general health perceptions as predictors.

The first model predicted factor scores on the internalizing factor. The overall model fit was significant ($F(7, 158) = 4.66$, $p < .001$; Table 7) and the health related predictors explained 18% of the variance in overall internalizing symptoms. Illness related acceptance predicted internalizing level such that individuals who were more accepting of their illness had lower scores on the internalizing factor. Physical functioning was significantly negatively associated with scores on the internalizing factor such that individuals who reported better physical functioning had lower scores on the internalizing factor. Pain was also significantly negatively associated with internalizing factor scores such that individuals who reported fewer pain related problems also had lower internalizing factor scores[11]. None of the other predictors in the model were significant.

The second model predicted factor scores on the distress subfactor of internalizing. The overall model fit was significant ($F(7, 158) = 5.13$, $p < .001$; Table 7) and the health related predictors explained 19% of the variance in distress scores. Illness related acceptance and pain were also significantly related to internalizing factor scores. Again, illness related acceptance predicted distress such that individuals who were more accepting of their illness had lower scores on the distress subfactor and individuals who reported fewer problems with pain had lower distress subfactor scores[11]. Limitations due to physical health were also significantly negatively associated with distress subfactor

[11]Note that scales on the SF-36 are scored such that higher scores represent a more favorable health outcome. Thus, high scores on the pain scale represent *better* pain related quality of life and high scores on the role limitations due to physical health scale represent *fewer* quality of life problems from health-related limitations.

scores such that individuals who reported being less limited by their physical health also had lower distress subfactor scores.

The third model predicted factor scores on the fear subfactor of internalizing. The overall model fit was significant ($F(7, 158) = 3.66$, $p < .001$; Table 7) and the health related predictors explained 15% of the variance in fear scores. Again, illness related acceptance predicted distress such that individuals who were more accepting of their illness had lower scores on the fear subfactor and individuals who reported fewer problems with pain had lower fear subfactor scores. Physical functioning was also negatively associated with scores on the fear subfactor such that individuals who reported better functioning also had lower scores on the fear subfactor.

Discussion

The aim of this study was to expand on the current literature in health psychology by examining the association between chronic physical health conditions and dimensional models of psychopathology in a unique sample of chronically ill individuals (i.e., individuals with POTS). We also aimed to determine how health related outcomes were associated with psychopathology in individuals with POTS. Previous research has found that the internalizing factor structure holds in individuals with chronic illnesses (e.g., Slade, 2007; Pavert et al. 2017), but to our knowledge no studies have looked at the factor structure of externalizing symptoms in the context of chronic physical illness. Findings from our factor analyses suggested that both the internalizing and externalizing factor structure held for individuals with POTS.

Internalizing Factor Structure

Consistent with previous findings about the factor structure of internalizing symptoms in individuals with chronic illnesses (e.g., Pavert et al., 2017), our results supported an internalizing factor comprised of two subcomponents: a distress component made up of depressive and PTSD symptoms and a fear component made up of anxiety and obsessive-compulsive symptoms. However, contrary to emerging work on the factor structure of eating pathology (e.g., Forbush et al., 2017; Kotov et al., 2017), we did not find that symptom scales from the EPSI fit into a larger model of internalizing psychopathology in our sample. Research by Coniglio and colleagues (2018) found support for the factor structure of the EPSI in a clinical sample of individuals with eating disorders, but results suggested that more research is needed on the structural validity of the EPSI across samples and contexts apart from clinical samples. Consistent with their findings, our results indicate that further research is needed to understand the structure of the EPSI in non-clinical samples. In this case, samples of individuals with chronic illnesses.

It may be that measures of eating pathology such as the EPSI detect physical symptoms of disorders such as POTS (e.g., gastrointestinal problems, exercise intolerance, and health or medication related changes in weight) as well as symptoms of eating pathology, which may result in a different structure in these samples. For example, items such as “I pushed myself extremely hard when I exercised” are likely to reflect difficulty with any level of physical exertion for individuals experiencing exercise intolerance, and items such as “I got full after eating what most people would consider a small amount of food” or “I ate when I was not hungry” may reflect gastric dysmotility

and lack of appetite due to gastrointestinal symptoms rather than symptoms of psychopathology, while other items such as “I made myself vomit in order to lose weight” or “If someone offered my food, I felt that I could not resist eating it” are likely to represent disordered eating behavior in the traditional psychological conceptualization. Further research is needed to assess the factor structure of EPSI and determine valid items for assessing eating pathology in samples of individuals with chronic illnesses.

Externalizing Factor Structure

Our results also supported the existence of an externalizing factor composed of antisocial personality disorder symptoms, substance use symptoms, aggressive symptoms, and disinhibited symptoms in individuals with POTS, which is consistent with previous work on the factor structure of psychopathology (e.g., Kotov et al., 2017). However, ADHD symptoms as measured by the ASRS did not fit well in our overall model and loaded better onto the internalizing factor than the externalizing factor, a finding contrary to previous studies of ADHD symptomology in a dimensional framework (Kotov et al., 2017). Some studies have found that individuals with POTS experience symptoms of inattention that are more severe than healthy controls, but would not meet criteria for an ADHD diagnosis as the symptoms were not generally present in childhood (Raj et al., 2009). Therefore, it is possible that inattention experienced by individuals with POTS is conceptually different than that experienced by individuals with ADHD and does not fit well in a traditional internalizing/externalizing framework. However, ADHD symptoms as measured by the ASRS also did not fit well in our healthy control sample, suggesting that the ASRS was not an accurate measure of ADHD in this study. Findings from Gray and colleagues (2014) suggested that while the measure is

reliable for detecting ADHD symptoms, findings are more reliable when the ASRS is conducted as an interview by a clinician and descriptions of specific behaviors can be obtained. It is possible that the self-report version used here detected symptoms of both adult anxiety and adult ADHD resulting in the poor fit of the measure in the overall factor model.

Mean Differences in Internalizing and Externalizing

Since the internalizing and externalizing factor structure held across both of our samples, we were able to test measurement invariance across the two groups in the context of a confirmatory factor analysis.

Internalizing. As hypothesized, individuals with POTS reported significantly higher levels of internalizing psychopathology than did healthy controls. This finding is not surprising, given that chronic illnesses are risk factors for psychological distress and previous studies have shown that individuals with POTS have higher rates of major depressive disorder, anxiety disorders, and are at heightened risk for suicidal ideation than healthy controls (Anderson et al., 2014; Bagai et al., 2011). However, some researchers have suggested that elevated rates of psychopathology in samples of POTS patients are due to overlap between the physical symptoms of POTS and commonly used psychological symptom measures. For example, Raj and colleagues (2009) found that POTS patients had significantly higher scores on the Beck Anxiety Inventory (BAI) than healthy controls, but when using a measure that did not rely heavily on somatic symptoms of anxiety, scores were only mildly elevated in comparison to control groups. Our findings suggest that individuals with POTS still experienced significantly more symptoms of internalizing psychopathology than healthy controls even after removing

items that overlapped with symptoms of POTS (see supplemental Tables 8 and 9). Differences between our results and results of other studies may be explained by a number of factors. First, commonly used screening measures in medical settings, such as the BAI and BDI (e.g., Raj et al., 2009), are shorter than measures such as the IDAS-II and may be more heavily influenced by items measuring somatic symptoms of depression and anxiety as a result. Our findings suggest that a broad assessment of internalizing symptoms, rather than a focus on assessing limited symptoms of categorical diagnoses, allows for the identification of individuals experiencing psychological distress separate from the symptoms of their physical health condition. However, our results also indicate that researchers and medical professionals need to be aware of the overlap between physical and psychological symptoms in samples such as ours, especially when assessing symptoms relating to fatigue, appetite, and panic. A more detailed, in person assessment of such symptoms would likely help discriminate between physical symptoms of POTS and panic attacks, mood related changes in appetite, or mood related changes in energy.

Externalizing. Our results also suggested mean differences in externalizing across the two samples. Interestingly, individuals with POTS had significantly lower scores on the externalizing factor than healthy controls. Looking at results of *t*-tests, it appears that individuals with POTS have significantly fewer callous aggression, antisocial, and substance abuse symptoms than individuals without any chronic illness diagnoses. Since the use of substances such as alcohol can worsen symptoms of chronic illnesses (Dysautonomia International, 2012), it would follow that individuals with POTS might avoid using these substances and report fewer substance abuse issues than healthy controls. Furthermore, substances such as marijuana and opiates are often prescribed to

help manage symptoms of chronic illness, meaning that individuals using these substances as prescribed might be less likely to endorse items measuring their illegal use or problems resulting from their use than individuals without chronic illnesses. However, the finding that individuals with POTS reported less callous aggression and antisocial behavior than healthy controls was surprising. It could be that items measuring callous aggression and antisocial behavior assess behaviors that individuals with POTS are unable to participate in due to physical limitations (e.g., "I get into a lot of physical fights", Hyler,1994). Yet these scales also ask about experiences of empathy and emotional understanding that would likely not be enhanced or hindered by physical limitations. Previous research has found that men tend to experience more externalizing symptoms than women and that younger-adults tend to engage in more externalizing behaviors than older-adults (Kramer et al., 2008; Kotov et al., 2017), so it is possible that the observed differences in externalizing simply reflect the gender and/or age differences between our two samples. However, results of the independent samples *t*-tests suggest that these differences hold in our sample when limited to only women and individuals under 26-years of age. Thus, it is also possible that the findings reflect true health-related differences in externalizing between the two samples. More research is needed to determine if these findings replicate and to explore possible explanations for the observed differences.

Internalizing Levels in Individuals With POTS

Finally, since individuals with POTS face a wide variety of illness related stressors, we were interested in factors that might explain differences in levels of internalizing psychopathology within this group. Consistent with our hypothesis, illness

related acceptance was significantly related to levels of internalizing, distress, and fear, such that individuals who were more accepting of their chronic physical illnesses experienced less internalizing symptomology. Acceptance is a core component of many psychological treatments such as acceptance and commitment therapy, and interventions targeting acceptance have shown promise in encouraging health related behavior change (e.g., Gifford et al., 2004; Roche, Dawson, Moghaddam, Abey, & Gresswell, 2017). Indeed, previous research has shown that acceptance of chronic conditions and abandonment of attempts to change or control them leads to better adjustment, more emotional stability, and less psychological distress (e.g., McCracken, Carson, Eccleston, & Keefe, 2004; Van Damme, Crombez, Van Houdenhove, Mariman, & Michielsen, 2006). Since POTS does not currently have a cure, and most treatments focus on managing symptoms (Goldstein, 2016), it makes sense that accepting the reality of the condition would be associated with decreased psychological distress. However, contrary to our expectations and previous research showing that experiences of helplessness are associated with increased psychological distress (Karademas & Hondronikola, 2010), illness related helplessness was not related to internalizing symptoms in our sample of individuals with POTS. Some research has found that while perceived control has beneficial effects in some cases, in others, such as disease flare ups, it can be detrimental to psychological well-being (Helgeson, 1999). It could be that individuals in our sample were in varying disease states when they participated in the study, preventing detection of a clear effect. Future research should explore whether the effect of illness related helplessness on psychological wellbeing is dependent upon the current disease state of an individual.

We also expected that health related quality of life would be associated with levels of internalizing in individuals with POTS. As expected, pain related quality of life was associated with scores on the internalizing, distress, and fear dimensions such that those who experienced more functional impairment related to their pain reported more internalizing psychopathology. This finding is not particularly surprising given that pain is consistently associated with increased psychological distress in chronic illness patients both on a moment to moment basis and in long-term follow-ups (e.g., Crombez, Viane, Eccleston, Devulder, & Goubert, 2013; Wells, Murphy, Wujcik, & Johnson, 2007). Physical functioning was associated with scores on the internalizing and fear dimensions, while role limitations due to physical health were associated with scores on the distress dimension, suggesting that individuals with POTS who experience poor physical functioning are more likely to experience symptoms of anxiety while those who experience role limitations are more likely to experience depressive symptoms. It could be that individuals who experience more difficulties in their physical functioning spend more time worrying about their ability to interact with other people and keep up with their responsibilities, whereas those experiencing role limitations may be more likely to feel isolate as a result. Future research should investigate the nature of these differences.

Contrary to our hypothesis, individuals who had been told that their physical symptoms were due to psychological causes did not report higher levels of internalizing symptoms. It seems likely that this experience would be more distressing pre-diagnosis and could be that distress does not persist post-diagnosis. Overall, it seems that pain and levels of functional disability are risk factors for increased symptoms of internalizing in

individuals with POTS and that interventions targeting illness related acceptance may be beneficial in improving psychological distress in these individuals.

Limitations

This study is not without limitations. Our sample of individuals with POTS was largely made up of females, while our healthy control sample was more evenly split between sexes. Given that research has shown that women tend to have higher mean levels of internalizing and men tend to have higher mean levels of externalizing symptoms (Kramer et al., 2008), we cannot rule out the possibility that some of the observed differences in our study were due to gender differences. However, given that POTS is more common in women than in men (Goldstein, 2016) and that women are at higher risk for the development of many chronic diseases than men, the information obtained in our study reflects true population differences and provides valuable information about psychopathology in individuals with POTS. Further, results of the independent samples *t*-tests suggest that observed differences in most of the internalizing and externalizing scales hold when limited to include only the women in our samples. Future researchers could consider limiting their studies to include only women to confirm the finding that women with conditions such as POTS experience differing levels of psychological distress than women without any chronic conditions. Our sample of individuals with POTS was also made up of older individuals that our healthy control sample. Since research has shown that younger adults tend to have higher mean levels of externalizing symptoms (e.g. Kotov et al., 2017), we cannot rule out the possibility that observed differences between our samples are due to age differences. However, results of the independent samples *t*-tests suggest that differences in substance abuse and antisocial

behavior between the two samples hold when the sample is limited to younger adults. Future studies should work to match participants on age in order to replicate these findings. We also assessed all variables using questionnaires rather than clinician interviews, and future research would benefit from multi-method assessments of health status (e.g., physician diagnoses, clinical interviews, self-report, informant-report, and behavioral observation). Furthermore, our results are cross-sectional. Future research should investigate levels of psychopathology and related factors in a longitudinal framework to better understand relationships between the variables examined in this study. Finally, future research is needed to evaluate associations between chronic illness and eating pathology, ADHD symptomology, and externalizing psychopathology to determine whether our findings replicate.

Overall, results of the current study suggest that a dimensional framework is a valid tool for understanding psychopathology in adults with POTS. Findings suggest that individuals with POTS experience higher levels of internalizing and lower levels of externalizing pathology than adults without any chronic illness diagnoses. Among individuals with POTS, illness related acceptance, levels of pain, and level of functional disability appear important in explaining differences in psychological distress. Researchers and medical professionals should be aware of the risk of psychological distress in individuals with POTS and take care to assess for symptoms that do not overlap with symptoms of autonomic nervous system dysfunction. Careful assessment could help to minimize inaccurate diagnoses and invalidation of physical symptoms and encourage integrated physical and mental health care for these individuals. Psychological

interventions that target illness related acceptance combined with pain and symptom management would likely be beneficial.

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APPENDIX A

Table 1

Independent Samples t-Tests Factor Indicators

	POTS		Healthy		
	M	*SD*	*M*	*SD*	*t*
Dysphoria	26.01	8.24	21.03	8.24	5.50**
Traumatic Intrusions	7.75	4.06	6.39	3.10	-3.61**
Traumatic Avoidance	7.56	3.92	8.05	3.77	-1.21**
Panic	21.84	5.92	11.79	4.81	16.67**
Social Anxiety	13.07	5.75	11.19	5.35	3.24**
Checking	5.57	3.09	5.92	2.72	-1.15
Ordering	8.57	4.40	9.01	3.70	-1.02
Cleaning	10.13	5.08	10.26	4.29	-0.27
Disinhibition	9.14	7.47	8.50	6.79	0.85
Callous Aggression	5.12	7.17	8.60	7.47	-4.47**
Substance Abuse	10.30	9.42	13.94	11.73	-3.20**
Antisocial PD	0.58	0.97	1.10	1.24	-4.38**

Note. N = 172 POTS, N = 199 Healthy.

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

Table 2

Fit Indices of the Confirmatory Factor Analysis (CFA) of the Internalizing and Externalizing Symptoms in Individuals With POTS

Model	χ^2 (*df*)	RMSEA	CFI	BIC
Model 1	702.65 (208)	0.118	0.659	20909
Model 2	570.05 (205)	0.102	0.748	20792
Model 3	223.19 (77)	0.105	0.870	13242
Model 1B	313.77 (64)	0.151	0.761	12141
Model 2B	222.29 (63)	0.121	0.848	12054
Model 3B	163.56 (65)	0.094	0.906	11985
Model 1C	102.39 (34)	0.108	0.895	9067
Model 2C	96.97 (33)	0.106	0.902	9066
Best-Fitting Model*	50.31 (30)	0.063	0.969	9035

Note. N = 172, RMSEA = X^2 = chi-square; *df* = degrees of freedom; root mean square error of approximation; CFI = comparative fit index; BIC = Bayesian Information Criterion.

*The best-fitting model is a version of model 2C using parceled OCD indicators and parceled PTSD indicators.

Table 3

Fit Indices of the Confirmatory Factor Analysis (CFA) of the Internalizing and Externalizing Symptoms in the Healthy Control Sample

Model	χ^2 (*df*)	RMSEA	CFI	BIC
Model 1	896.86 (208)	0.129	0.624	24797
Model 2		No Convergence		
Model 3	214.67 (75)	0.097	0.887	15852
Model 1B	267.27 (64)	0.126	0.823	14509
Model 2B	251.57 (63)	0.123	0.836	14499
Model 3B	139.44 (63)	0.078	0.934	14386
Model 1C	100.73 (34)	0.099	0.923	10100
Model 2C	92.69 (33)	0.095	0.931	10997
Best-Fitting Model*	71.00 (30)	0.083	0.953	10991

Note. N = 199, X^2 = chi-square; *df* = degrees of freedom; RMSEA = root mean square error of approximation; CFI = comparative fit index; BIC = Bayesian Information Criterion.

*The best-fitting model is a version of model 2C using parceled OCD indicators and parceled PTSD indicators.

Table 4

Fit Indices of the Confirmatory Factor Analysis (CFA) of the Internalizing and Externalizing Symptoms in the Overall Sample

Model	χ^2 (*df*)	RMSEA	CFI	BIC
Model 1	1490.44 (208)	0.129	0.600	46120
Model 2	1318.17 (205)	0.121	0.653	45966
Model 3	350.23 (75)	0.099	0.880	29378
Model 1B	599.91 (64)	0.150	0.747	27027
Model 2B	545.18 (63)	0.144	0.772	26978
Model 3B	218.95 (63)	0.082	0.926	26652
Model 1C	192.07 (34)	0.112	0.890	20390
Model 2C	187.06 (33)	0.112	0.893	20391
Best-Fitting Model*	96.98 (30)	0.078	0.954	20318

Note. $N = 371$ X^2 = chi-square; *df* = degrees of freedom; RMSEA = root mean square error of approximation; CFI = comparative fit index; BIC = Bayesian Information Criterion.

*The best-fitting model is a version of model 2C using parceled OCD indicators and parceled PTSD indicators.

Table 5

Factor Loadings From Best-Fitting Model in Both Samples

	POTS		Healthy Control	
	Distress	Fear	Distress	Fear
Dysphoria	2.75***/0.83		2.59***/0.94	
Trauma	0.57***/0.71		0.36***/0.68	
Neuroticism	3.56***/0.82		2.50***/0.75	
OCD		0.64***/0.56		0.41***/0.54
Panic		1.04***/0.44		1.25***/0.79
Social Anxiety		2.03***/0.82		1.52***/0.87
	Internalizing		Internalizing	
Distress	2.27***/0.92		2.86***/0.94	
Fear	2.27***/0.92		2.86***/0.94	

(*table continues*)

	Internalizing	Internalizing
Disinhibition	7.25***/0.97	6.41***/0.95
Aggression	4.17***/0.58	4.27***/0.57
Substance Use	3.69***/0.39	5.61***/0.48
Antisocial Personality	0.61***/0.63	0.73***/0.59

Note. Standardized/Unstandardized.

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

Table 6

Tests of Measurement Invariance Across Physical Health Groups

	Overall Fit Indices					Model Comparison Indices				
	χ^2	*df*	RMSEA	CFI	BIC		$\Delta\chi^2$	Δdf	*p*	ΔCFI
1. Configural	122.28	61	0.07	0.96	20070.46					
2. Metric	140.43	72	0.07	0.96	20023.57	2 vs 1	18.16	11	0.08	.00
3. Scalar	370.40	79	0.14	0.81	20212.14	3 vs 2	229.97	7	<.001	.15
4. ScalarB	159.83	78	0.08	0.95	20004.49	4 vs 2	19.40	1	.05	.01

Note. RMSEA = root mean square error of approximation; CFI = comparative fit index; BIC = Bayesian Information Criterion.

Table 7

Regression Table of Variables Predicting Internalizing Factor and Subfactor Scores

	Beta	Std. Error	Sig.
Model 1- Internalizing, R^2 = .18, F(7, 158) = 4.66, p <.001			
Helplessness	.07	.03	.58
Acceptance	-.31	.02	<.001
Due to psychological cause	.08	.18	.29
Physical Functioning	-.21	.00	.046
Limitations due to Health	-.15	.00	.090
Pain	-.19	.00	.029
General Perceptions of Health	-.18	.01	.062
Model 2- Distress, R^2 = .19, F(7, 158) = 5.13, p <.001			
Helplessness	.06	.06	.62
Acceptance	-.35	.06	<.001
Due to psychological cause	.08	.45	.28
Physical Functioning	-.17	.01	.11
Limitations due to Health	-.17	.01	.047
Pain	-.18	.01	.041
General Perceptions of Health	-.15	.01	.108
Model 3- Fear, R^2 = .15, F(7, 158) = 3.66, p <.001			
Helplessness	.07	.06	.60
Acceptance	-.25	.06	.007
Due to psychological cause	.09	.45	.23
Physical Functioning	-.22	.01	.04
Limitations due to Health	-.10	.01	.24
Pain	-.18	.01	.04
General Perceptions of Health	-.17	.01	.07

Note. High scores on the SF-36 scales (physical functioning, limitations due to health, and pain) represent a more favorable health outcome.

APPENDIX B

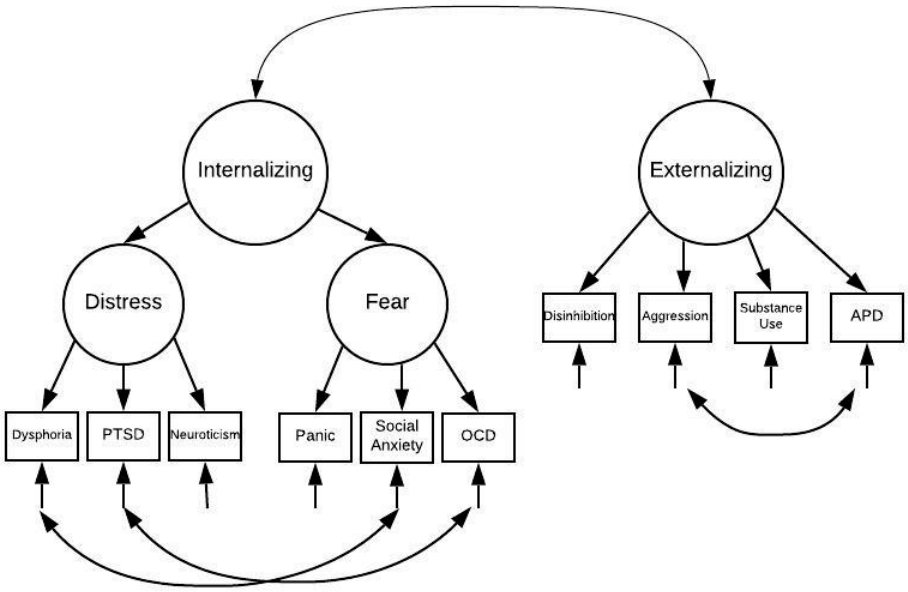

Figure 1. Conceptual image of the best fitting model.

APPENDIX C

Table 8

Independent Samples t-Test With Adjusted IDAS Scales

	POTS		Healthy		
Adjusted IDAS Scale	*M*	*SD*	*M*	*SD*	*t*
Depression	32.84	9.05	27.04	9.11	5.84**
Dysphoria	22.43	7.56	18.73	7.46	4.55*
Panic Item 58	1.57	1.00	1.14	0.57	5.13**

Note. *$p < .05$. **$p < .01$.

Table 9

IDAS Items That Overlap With POTS Symptoms

Item (Percentage of participants who said the item is a symptom of POTS)	Scale(s)
I felt dizzy or lightheaded (83%)	Panic
I felt faint (80%)	Panic
My heart was pounding or racing (80%)	Panic
I felt exhausted (78%)	Depression, Lassitude
I was short of breath (68%)	Panic
I felt drowsy, sleepy (62%)	Lassitude
It took a lot of effort for me to get going (55%)	Depression, Lassitude
I had trouble concentrating (55%)	Depression, Dysphoria
I slept very poorly (49%)	Depression, Insomnia
I was trembling or shaking (49%)	Panic
I did not have much of an appetite (46%)	Depression, Appetite Loss
I slept less than usual (45%)	Insomnia
I felt pain in my chest (44%)	Panic
I had trouble falling asleep (43%)	Depression, Insomnia
I felt much worse in the morning than later in the day (41%)	Lassitude
I woke up frequently during the night (39%)	Insomnia
I had trouble waking up in the morning (38%)	Lassitude
I had a very dry mouth (34%)	Panic
I did not feel much like eating (34%)	Appetite Loss
I woke up early and could not get back to sleep (32%)	Insomnia
I slept more than usual (31%)	Lassitude
I felt like eating less than usual (27%)	Depression, Appetite Loss

Table 10

Independent Samples t-Tests Factor Indicators Women Only

	POTS		Healthy		
	M	*SD*	*M*	*SD*	*t*
Dysphoria	25.68	8.16	21.93	8.66	3.62**
Traumatic Intrusions	7.61	3.97	6.55	3.28	2.45**
Traumatic Avoidance	7.49	3.92	8.39	3.92	-1.94*
Panic	21.78	5.91	12.25	5.11	13.66**
Social Anxiety	12.81	5.65	11.61	5.60	1.81
Checking	5.53	3.10	5.96	2.74	-1.24
Ordering	8.50	4.38	9.21	3.96	-1.42
Cleaning	10.30	5.20	10.60	4.55	-0.52
Disinhibition	9.11	7.61	7.75	5.68	1.71
Callous Aggression	5.05	7.24	6.35	5.69	-1.66
Substance Abuse	9.90	9.23	13.20	10.84	-2.76**
Antisocial PD	0.57	0.99	.99	1.11	-2.52*

Note. N = 172 POTS, N = 199 Healthy.

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

Table 11

Independent Samples t-Tests Factor Indicators Under 26 Years Only

	POTS		Healthy		
	M	*SD*	*M*	*SD*	*t*
Dysphoria	26.18	7.55	22.27	8.10	2.67**
Traumatic Intrusions	8.30	4.23	6.80	3.20	2.53**
Traumatic Avoidance	8.58	4.12	5.59	3.83	-.006
Panic	22.17	4.98	12.30	5.02	9.73**
Social Anxiety	13.95	5.54	11.82	5.49	2.24*
Checking	6.25	3.17	6.47	2.75	-0.45
Ordering	9.32	4.95	9.64	3.82	-0.46
Cleaning	11.27	5.89	10.76	4.45	0.62
Disinhibition	10.49	8.76	8.93	6.56	1.25
Callous Aggression	7.71	11.75	9.46	7.74	-1.15
Substance Abuse	8.71	9.93	11.48	11.48	-2.27**
Antisocial PD	0.98	1.37	1.21	1.21	-1.01*

Note. N = 172 POTS, N = 199 Healthy.

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