EXAMINING NEUROLOGICAL AND PSYCHOLOGICAL SYMPTOMS OF GULF WAR ILLNESS USING THE MINNESOTA MULTIPHASIC PERSONALITY INVENTORY-2

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DEDICATION

I would like to thank the members of my Graduate Committee, family, and friends.

# EXAMINING NEUROLOGICAL AND PSYCHOLOGICAL SYMPTOMS OF GULF WAR ILLNESS USING THE MINNESOTA MULTIPHASIC PERSONALITY INVENTORY-2

by

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Abstract

BACKGROUND: Gulf War Illness (GWI) reflects a constellation of symptoms that affect a large number of veterans from the 1990-1991 Gulf War. Reported ailments include a variety of cognitive, musculoskeletal and psychological complaints. Whereas many symptoms were originally attributed to psychological causes, chemical exposures resulting in neurological damage have since been reported. The purpose of the study was to examine self-reported psychological symptoms and profiles in GWI, with an emphasis on symptoms that may have a neurological basis.

SUBJECTS: Groups were comprised of 65 Gulf War veterans with GWI ("cases") and 31 healthy age-matched veteran controls recruited from a National Survey. The case group was divided into one of three GWI syndromes: syndrome 1 (Impaired Cognition), syndrome 2 (Confusion-Ataxia), and syndrome 3 (Central Pain).

METHOD: Participants completed the Minnesota Multiphasic Personality Inventory-2 (MMPI-2), a common self-report psychological diagnostic inventory, including the standard clinical scales, a set of restructured scales which eliminates item overlap, and a set of scales designed to assess neurologic symptoms, across cases, controls, and syndromes.

RESULTS: GWI subjects displayed higher scores across all MMPI-2 scores compared to controls. Additionally, those with GWI who endorsed a larger percentage of neurological items displayed higher elevations on all other MMPI-2 scales. Within GWI syndromes, syndrome 2 (Confusion-Ataxia) endorsed the highest percentage of neurological ailments and scored higher than the other groups on all additional scales examined.

DISCUSSION: Veterans with GWI displayed a nonspecific, generalized pattern of distress on the MMPI-2. While specific neurological and psychological processes were not identified, results highlight the range and severity of symptoms reported in veterans with GWI.

*Keywords:* Gulf War Illness, MMPI-2, Veterans, GWI syndromes, Restructured Clinical Scales, Cripe's Neurological Symptoms

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## LIST OF ABBREVIATIONS

GWI – Gulf War Illness

PTSD – Post-traumatic stress disorder

MMPI – Minnesota Multiphasic Personality Inventory

MMPI-2 – Minnesota Multiphasic Personality Inventory-2

Hs - Hypochondriasis

D - Depression

Hy - Hysteria

Pd - Psychopathic Deviate

Mf - Masculinity/Femininity

Pa - Paranoia

Pt - Psychasthenia

Sc - Schizophrenia

Ma - Hypomania

Si - Social Introversion

RC - Restructured Clinical

RC d - Demoralization

RC 1 - Somatic complaints

RC 2 - Low Positive Emotions

RC 3 - Cynicism

RC 4 - Antisocial Behavior

RC 6 - Ideas of Persecution

RC 7 - Dysfunctional Negative Emotions

RC 8 - Aberrant Experiences

RC 9 - Hypomanic Activation

CNS - Cripe's Neurological Symptoms

# CHAPTER ONE

## Introduction and Review of the Literature

### Understanding Gulf War Illness Symptoms

**Gulf War Illness and the Minnesota Multiphasic Personality Inventory-2.** Gulf War Illness (GWI) is comprised of a wide range of ailments that are reported by numerous veterans of the 1991-1992 Gulf War. One way of exploring this complex set of symptoms is through the use of detailed questionnaires that evaluate a wide array of psychological and neurological dimensions. Research using the Minnesota Multiphasic Personality Inventory (MMPI & MPPI-2) has suggested that GWI is associated with elevated levels of generalized psychological distress, with specific symptoms including cognitive, psychosocial, and musculoskeletal complaints, with fatigue, increased distress, memory loss, difficulty concentrating, difficulty with speech, sleep disturbances, and mood swings (Axelrod & Milner, 1997; Binder et al., 2000; Storzbach et al., 2000).

The MMPI-2 is a popular self-report inventory that assesses multiple dimensions of self-reported psychological functioning. This inventory consists of 567 true-false items that are computed into T-scores for ten clinical scales: (1-hypochondriasis, 2-depression, 3-hysteria, 4-psychopathic deviate, 5-masculinity/femininity, 6-paranoia, 7-psychasthenia, 8-schizophrenia, 9-hypomania, 0-social introversion). Collectively, these scales comprise a psychological profile for assessing the presence of various aspects of psychopathology (Graham, 1996). Scores are presented in T-score format, with scale elevations considered clinically significant if the T-score is 65 or greater. The MMPI also includes several validity scales to evaluate unusual response bias.

Evaluations of MMPI-2 profiles among veterans suffering from GWI has led to conclusions that the illness is associated with post-traumatic stress disorder (PTSD), anxiety, somatoform and/or depressive disorders (PACGWVI, 1996; Axelrod & Milner, 1997; Binder et al., 2000; Glenn et al., 2002; Storzbach et al., 2000). (Axelrod & Milner, 1997) found scale elevations on the original MMPI (T-scores > 70) on clinical scales 1-hypochondriasis (T=66), 2-depression (T=67), and 8-schizophrenia (T=66), which is indicative of having heightened concerns about health, generalized distress, depressive symptoms, and disturbances in thinking, mood, and behavior. In further MMPI research, elevated scores on clinical scale 1-hypochondrias was also observed by (Storzbach et al., 2000), and significant differences were additionally found between cases and controls on clinical scales 2-depression, 3-hysteria, 7-psychoasthenia, and 8-schizophrenia. These elevations lead the authors to conclude that generalized distress was a predominant basis of GWI symptoms.

(Binder et al., 2000) observed similar differences between veteran controls and GWI cases on MMPI-2 clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychoasthenia, and 8-schizophrenia and reported that cases exhibited elevations on clinical scales 1 and 2, endorsing depressive and somatic symptoms. Furthermore, the GW case group's mean T-scores on clinical scales 3-hysteria, 7-psychoasthenia, and 8-schizophrenia were close to being significantly elevated relative to controls at (T=64), (T=63), and (T=64), respectively. Often interpreted as having psychological causes for endorsed symptoms, the observed scale differences and specific elevations have led many studying GWI to conclude that the reported ailments do not have underlying physiological causes, but instead reflect a psychological etiology (PACGWVI, 1996).

In examining possible psychological causes, (Glenn et al., 2002) compared the MMPI-2 clinical scale profiles of Gulf War veterans with severe PTSD to a group comprised of Vietnam veterans who also presented with severe PTSD. Gulf War veterans showed significant T-score elevations on clinical scales 1-hypochondriasis (T=81), 2-depression (T=79), 3-hysteria (T=77), 4-psychopathic deviate (T=66), 6-paranoia (T=75), 7-psychoasthenia (T=75), 8-schizophrenia (T=84), and 0-social alienation (T=66), reflective of generalized distress and somatic concerns that have similarly been observed on the MMPI-2 in veterans with GWI. Additionally, Gulf War and Vietnam veterans displayed significant differences on clinical scales 2-depression and 7-psychoasthenia, with reported ailments including symptoms of anxiety, depression, heightened somatic concerns, sleep disturbances, problems with concentration, confused thinking, and memory difficulties. This pattern of observed elevated clinical scales led these researchers to conclude that the any illness specific to Gulf War veterans was psychological in etiology.

**Revised MMPI-2 Scales.** A main concern with the clinical scales of the MMPI is that some items load onto several scales. This is problematic because it creates the possibility for a single endorsement to affect scores across multiple scales. To address this issue, a revised set, the restructured clinical (RC) scales, was created that eliminated overlapping items, with each scale intending to represent a *core* measurement of the original clinical scales (Graham, 1996; Tellegen et al., 2003). The following comprise the scales: RC d-demoralization, RC 1-somatic complaints, RC 2-low positive emotions, RC 3-cynicism, RC 4-antisocial behavior, RC 6-ideas of persecution, RC 7-dysfunctional negative emotions, RC 8-aberrant experiences, and RC 9-hypomanic activation. These restructured clinical scales have lower inter-correlations compared to the clinical scales (Graham, 1996; Tellegen et al., 2003), providing evidence that the restructured clinical scales offer more unique measurements of the respective constraints than the

standard clinical scales. Thus, these revised scales provide the opportunity to further examine the specific types of symptoms that are also found in the standard clinical scales, but in a more precise manner.

In addition to having no overlap between scales, the RC scales include a specific somatic complaints category, RC 1. With regard to categorizing symptoms using the MMPI-2, it has also been concluded that the RC scales provide a better description of ailments than the corresponding clinical scales (Graham, 1996). Elevations on the RC 1-somatic complaints scale suggest that reported ailments, which are often considered somatic in etiology, could be related to neurological damage, similar to what has been observed in other studies of veterans with GWI (Haley et al 1997b; Haley, 1997c; Haley et al., 2000; Haley et al., 2002; Haley et al., 2009). As with the other RC scales, the RC 1-somatic complaints scale could provide further understanding into GWI with a clearer categorization of complaints reported by ill veterans. (Sellbom, Ben-Porath, Graham, Arbisi, & Bagby, 2010) reported that compared to the Clinical scales, the RC scales produced a more focused measurement of the core clinical constructs of symptoms and exhibited lower inter-correlations. For GWI, investigating these scales could aid in understanding the range of symptoms and also lead to a better characterization of specific categories of endorsed items within GWI cases. However, a possible problematic issue with examining the revised RC scales in GWI is that reported symptoms, which may be neurological in etiology, are commonly identified as being somatic (i.e., grouped into the corresponding scale such as RC 1-somatic complaints scale), leading interpretations toward a psychological explanation that has often been observed on the MMPI-2 in previously discussed studies.

**Cripe's Neurological Symptoms (CNS) Scales.** (Cripe, 1988; Cripe, 1995; Cripe, 1996) developed a set of neurological symptoms subscales from the MMPI and later the MMPI-2,

which were specifically comprised of 111 items: Attention/Mental Control, Biobehavioral, Emotional/Behavioral Control, Fatigue/Lack of Energy, General Cognitive, Headaches, Health, Memory, Motor, Pain, Seizure/Blank Episodes, Sleep Disturbances, Sensory, Speech/Language, Social, Vertigo/Nausea, and Vocational (Greene, 1999). Cripe used these subscales to investigate the endorsement of items that were considered somatic in nature but were products of neurological causes. Commenting on the use the MMPI-2 in individuals with neurological illnesses, Cripe also pointed out that the overlapping of items across clinical scales creates the possibility that single items might have undue influence on the overall clinical profile (Cripe, 1996). An additional benefit of utilizing these scales is the ability to categorize reported neurological symptoms and gain a better understanding of how to interpret the clinical and RC scales profiles that may be elevated by such endorsements. Further, the symptoms addressed by the CNS scales seem to correspond to symptoms reported by GWI patients (Haley et al., 1997a; Haley, Kurt, & Hom 1997d; Haley, Hunt, & Richardson, 1999; Haley et al., 2000; Hom, Haley, & Kurt, 1997) and CNS scale measurements could discern which neurological symptoms are associated with GWI and each separate syndrome.

**Past and Current understanding of GWI.** GWI presents as a multi-symptom illness that is now generally recognized as being a result of neurological damage experienced by numerous veterans during deployment to the 1990-1991 Gulf War (RACGWVI, 2008). Ailments associated with the illness include fatigue, headache, joint pain, memory difficulties, dizziness, muscle aches, gastrointestinal problems, anxiety, depression, sleep disturbances, numbness, limb weakness, and difficulties with cognition (PACGWVI, 1996). Health complaints were originally attributed to psychological causes such as stress, and veterans were often diagnosed with PTSD, while mounting research has suggested that it may be due to neurotoxic exposure to pesticides,

biological and chemical warfare agents, vaccines, pyridostigmine bromide, depleted uranium, infectious diseases, petroleum products, and oil-well fires (RACGWVI, 2008).

A number of studies have focused on defining a case definition for GWI (Haley, 1997a; Haley et al., 1997b; Haley et al., 2000; Haley, Hunt, & Richardson, 1999; Haley & Kurt, 1997c; Haley, Kurt, & Hom, 1997d; Haley, Luk, & Petty, 2001; Fukuda et al., 1998; Spencer et al., 1998; Spencer et al., 2001; Steele, 2000; Steele, 2001; Kang, Mahan, Lee, Magee, & Murphy 2000). Through various assessments and research, these authors concluded GWI to present with multiple, long-lasting, chronic symptoms consistent with those previously identified by the Presidential Advisory Committee in 1996. Specifically, such maladies affecting Gulf War veterans were found to include fatigue, cognitive, gastro-intestinal, and musculoskeletal ailments. While they did not arrive at a uniform case definition of GWI or the illness's exact cause(s), these authors provided essential understanding into the varying symptoms reported and the scope of the illness across a wide range of Gulf War veterans.

Following a 1996 U.S. government assessment of GWI and the proposed underlying pathology of GWI, many studies examined symptoms from a psychological perspective (PACGWVI, 1997). (Haley, 1997a; Haley et al., 1997b; Haley et al., 2000; Haley, Maddrey, & Gershenfeld, 2002; Haley et al., 2009) in contrast, found evidence that symptoms reported in GWI were a result of toxic exposure to nerve agents that caused damage to the central, peripheral, and autonomic nervous systems. In 2008, the Research Advisory Committee on Gulf War Veterans' Illnesses changed their stance and officially recognized that psychological disorders, particularly those caused by stress, were not solely the cause of GW-related symptoms (RACGWVI, 2008). Instead, neurological damage was considered a cause of GWI in veterans.

Although early MMPI and MMPI-2 research has indicated the presence of psychopathology in veterans with GWI, other studies have provided evidence of neurological damage due to various toxic exposures in certain individuals (Haley et al., 2000; Haley, Maddrey, & Gershenfeld, 2002; Haley et al., 2009; Hom, Haley, & Kurt, 1997), for example, using photon magnetic resonance spectroscopy found abnormalities in the basal ganglia and brainstem in those with GWI compared to controls. Additionally, neuroimaging and epidemiological studies involving analysis of genotypes and blood levels have identified physiological differences among GWI sufferers thought to be related to exposure to organophosphates such as sarin, soman, and diazinon (Haley et al., 2009). With regard to animal studies, through an examination of rodent brains exposed to chlorpyrifos, an insecticide and organophosphate used by service members during the Gulf War, Cao (2011) observed neuronal damage in the locus coeruleus, an area of the brain involved in the processes of regulating anxiety and stress. Additional research examined hens after exposure to the anti-nerve agent pyridostigmine bromide, the insect repellant DEET, and insecticide permethrin, and found evidence of nerve tissue damage (Abou-Donia, 1996). Further, (Abou-Donia et al., 2010) examined rats and found that exposure to pyridostigmine bromide and DEET or permethrin resulted in sensorimotor deficits. Also observed in rats, a combination of stress and the organophosphates pyridostigmine bromide, DEET, and permethrin caused neurological damage in the cingulate cortex, dentate gyrus, thalamus, and hypothalamus, with decreased acetylecholinesterase activity across parts of the brain (Abdel-Rahman, Abou-Donia, El-Masry, Shetty, & Abou-Donia, 2004). Evidence of physiological damage related to toxic exposure has been demonstrated in animal models and GWI veteran studies. The presence of neurological symptoms associated with GWI may affect clinical symptoms and MMPI-2 results through the

endorsement of such neurologic- related items. As a result of these findings, a closer examination of MMPI-2 responses may aid in understanding the reports of clinical symptoms in patients with GWI.

**Neurological Symptoms and the MMPI-2.** Since there is a possibility for individuals with a neurological illness to display heightened MMPI-2 clinical elevations, an examination of CNS items could provide a better illustration of affected veterans' symptoms and further categorize the specific types of MMPI-2 neurological endorsements associated with GWI. While developments to the MMPI-2, such as the CNS scales, have helped to increase understanding of how a range of neurological symptoms present themselves on this inventory, examining only MMPI-2 Clinical and RC scale profiles of GWI depicts a pattern of significant psychological distress and general ill health. CNS scale items are often used more than once in the construction of clinical scales that GWI cases have commonly displayed significant elevations on. Comprising 27 of 32 items (clinical scale 1-hypochondriasis), 24 of 57 items (clinical scale 2-depression), 25 of 60 items (clinical scale 3-hysteria), and 22 of 27 items (RC 1-somatic complaints), such a large percentage of CNS scale items across the clinical scales allows for the endorsements of neurological items to potentially result in elevated T-scores for individuals with a neurological illness and may potentially influence the interpretation(s) of the assessment itself (Cripe, 1988; Cripe, 1996). While it is important to investigate CNS endorsements that may lead to clinical scale elevations, it is additionally critical to examine how these specific subscales can better identify the neurological symptoms of GWI so the illness can be more accurately characterized and interpreted when using the MMPI-2.

## Aims

1. To examine the MMPI-2 Clinical scales and profiles of veterans with GWI and a similar-age healthy control group.
2. To examine the MMPI-2 Restructured Clinical scale profiles (specifically RC d-demoralization, RC 1-somatic complaints, and RC 2-low positive emotions) of veterans with GWI and healthy controls.
3. To examine the Cripe's Neurological Symptoms (CNS) scales of veterans with GWI and healthy controls.
4. To examine the Clinical, Restructured Clinical, and Cripe's Neurological Symptom scales in the three Haley GWI syndromes (Haley et al., 1997): 1 (impaired cognition), 2 (confusion/ataxia), and 3 (central pain).

## Hypotheses

I. GWI cases will exhibit significant differences on MMPI-2 Clinical scales that assess physical symptoms, depression, somatization, anxiety, and disordered thinking (1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia) compared to controls.

   a. GWI cases will exhibit a higher frequency of significant elevations on the aforementioned MMPI-2 Clinical scales compared to controls.

II. GWI cases will exhibit significant differences on the MMPI-2 Restructured Clinical 1-somatic complaints scale compared to controls.

III. Endorsed items from Cripe's Neurological Symptoms scales will be associated with significant elevations in the Clinical scales that assess physical symptoms, depression, somatization, anxiety, and disordered thinking (Clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia and Restructured Clinical scale 1-somatic complaints) for GWI cases.

*Exploratory Analysis:* Haley's GWI Syndrome groups (Impaired Cognition, Confusion-Ataxia, Central Pain; Haley, Kurt, & Hom 1997d) will be examined for differences on the MMPI-2 Clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, 8-schizophrenia, Restructured Clinical 1-somatic complaints scale, and Cripe's Neurological Symptoms scales.

# CHAPTER TWO

## Method

Participants were comprised of two groups. The first consisted of 65 Gulf War veterans with GWI, and the second contained 31 healthy similar-age veteran controls. Subjects were recruited from a National Survey conducted by the Department of Veterans' Affairs in 2008 and screened for the illness, with cases defined by factor analysis into one of three GWI syndromes: Syndrome 1 (Impaired Cognition): problems with attention, memory, depression, and sleep abnormalities; distractibility, middle and terminal insomnia, fatigue (excessive daytime sleepiness), slurring of speech, confused thought process, migraine-like headaches; syndrome 2 (Confusion-Ataxia): problems with thinking and getting confused, disoriented, problems keeping balance; and syndrome 3 (Central Pain): joint and muscle pains, fatigue (excessive muscle exhaustion after exertion, but not sleepiness), tingling/numbness of extremities, increased difficulty lifting heavy objects, with each diagnosis of GWI made by a physician (Robert W. Haley, M.D.) through a semi-structured diagnostic interview. The control group were comprised of similar-age Gulf War veterans that were not found to have GWI. Participants provided written informed consent according to the protocol approved by University of Texas Southwestern Medical Center's Institutional Review Board. All subjects underwent a week long, multi-modal evaluation that included neuropsychological, neuro-imaging, and biomarker assessments that included the MMPI-2. As recommended by (Graham, 1996), MMPI-2 data were screened for the exclusion criteria of the True Response Inconsistency scale (TRIN) score $\geq$ 100, Variable Response Inconsistency scale (VRIN) score $\geq$ 80, and/or a Cannot Say score $\geq$ 15, with the L, F, and K scales also assessed for acceptable scores (Graham, 1996). Statistical Analysis Software was used to run analyses related to each hypothesis. Descriptive statistics were generated for

each group across the clinical, RC, and CNS scales, with the validity scales TRIN, VRIN, L, F, and K all found to be within acceptable ranges for further analysis of data. ANOVAs (controls vs. syndromes 1, 2, and 3) and T-tests (controls vs. cases; controls vs. syndromes 1, 2, and 3) were run to examine differences between groups.

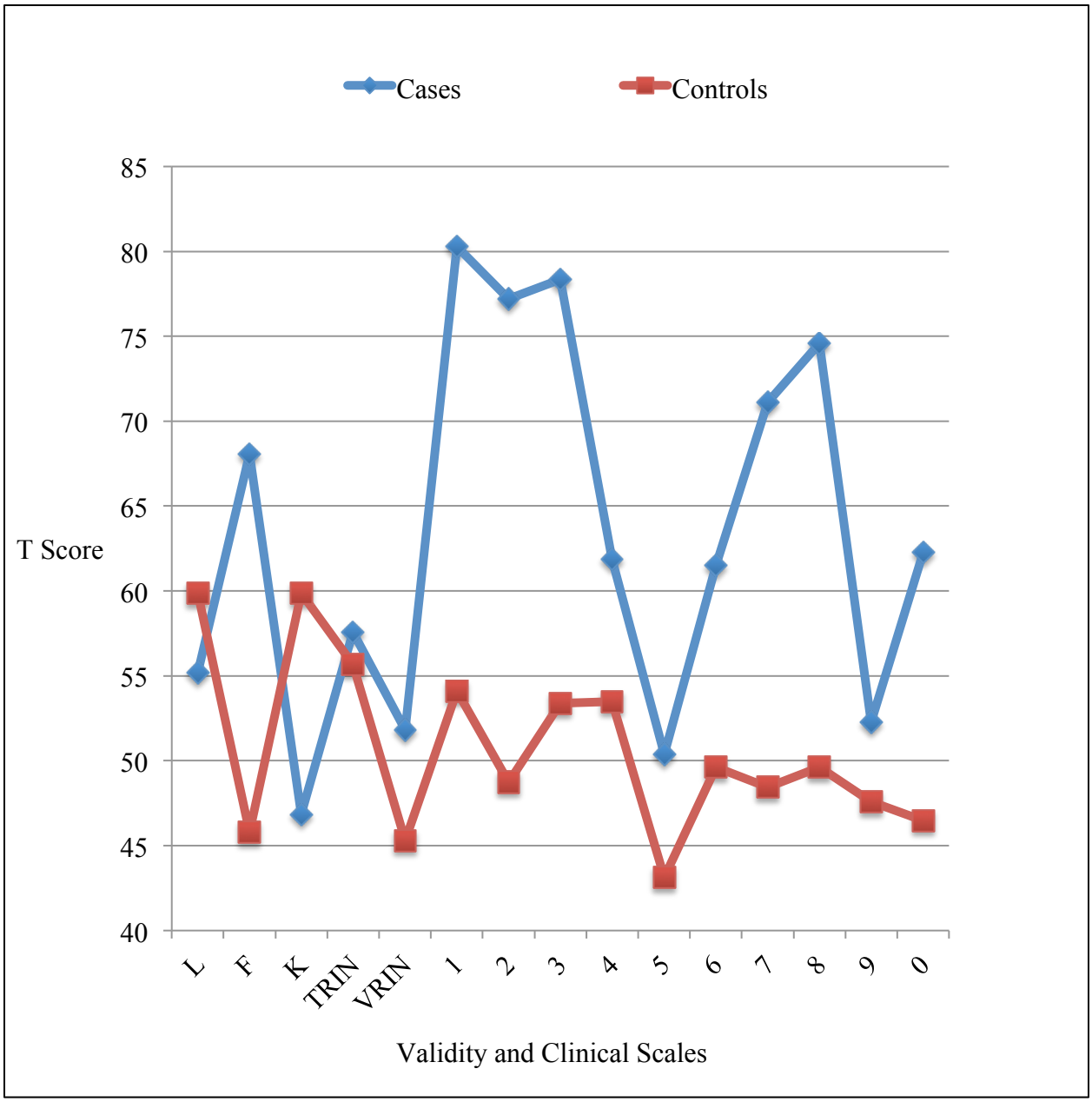
# CHAPTER THREE

## Results

Veterans with GWI were found to display similar L, F, and K validity scale elevations and patterns as observed in previously discussed studies (Axelrod & Milner, 1997; Binder et al., 2000; Storzbach et al., 2000), indicating an approach towards answering questions that can be indicative of symptom exaggeration, malingering, or the actual reporting of serious psychological and/or physical problems. While cases, particularly the syndrome 2 group, displayed a pattern of elevations on validity scales that are similar to what is observed in a symptom exaggeration profile, neither the case group nor any individual syndrome group reached levels that would cause the test results to be considered invalid (Graham, 1996).

The first set of analyses focused on examining differences between GWI cases and controls on validity and clinical scales (1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia) that assess physical symptoms, somatization, anxiety, and disordered thinking. Cases displayed significant mean T-score elevations on all clinical scales including the hypothesized clinical scales 1-hypochondriasis (T=80), 2-depression (T=77), 3-hysteria (T=78), 7-psychasthenia (T=71), and 8-schizophrenia (T=75), while the control group did not display significant mean T-score elevations on any of the clinical scales (Figure 1).

Figure 1. MMPI-2 Validity and Clinical Scale Profiles of GWI Cases versus Controls




When examined by GWI syndrome, groups 1, 2, and 3 showed significantly elevated T-scores on all of the scales except scale 7-psychasthenia (T=64) for syndrome 3, while syndrome 2 was the only group to show a significant elevation on scale 0-social alienation (T=67). ANOVAs further revealed that the four groups (controls, syndromes 1, 2, and 3) differed

significantly across clinical scales, with the largest differences on scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia (Table 1).

Table 1. MMPI-2 Clinical Scales: Group Means and ANOVA Results (Controls, Syndromes 1, 2, and 3).

| Clinical Scales | Group Means | | | | F | p-value |
|---|---|---|---|---|---|---|
| | Controls | Syndrome 1 | Syndrome 2 | Syndrome 3 | | |
| 1 (Hs) | 54.097 | 76.095 | 85.000 | 79.333 | 44.058 | <.001 |
| 2 (D) | 48.742 | 78.095 | 82.913 | 70.048 | 55.520 | <.001 |
| 3 (Hy) | 53.387 | 74.952 | 82.304 | 77.429 | 27.370 | <.001 |
| 4 (Pd) | 53.484 | 63.381 | 64.565 | 57.381 | 6.658 | <.001 |
| 5 (Mf) | 43.129 | 50.619 | 52.261 | 48.048 | 4.334 | <.05 |
| 6 (Pa) | 49.613 | 62.429 | 63.043 | 58.952 | 7.990 | <.001 |
| 7 (Pt) | 48.452 | 73.857 | 75.174 | 63.857 | 28.148 | <.001 |
| 8 (Sc) | 49.613 | 74.286 | 82.826 | 65.810 | 29.013 | <.001 |
| 9 (Ma) | 47.581 | 52.143 | 55.174 | 49.238 | 3.787 | <.05 |
| 0 (Si) | 46.484 | 60.476 | 67.217 | 58.667 | 16.421 | <.001 |

When comparing overall case and control groups, *t*-tests showed significant differences across all MMPI-2 clinical scales (Table 2).

Table 2. MMPI-2 Clinical Scales: Group Means and T-tests (GWI Cases versus Controls).

| Clinical Scales | Group Means | | t-value | p-value |
|---|---|---|---|---|
| | Cases | Controls | | |
| 1 (Hs) | 80.292 | 54.097 | 10.827 | <.001 |
| 2 (D) | 77.200 | 48.742 | 11.422 | <.001 |
| 3 (Hy) | 78.354 | 53.387 | 8.774 | <.001 |
| 4 (Pd) | 61.862 | 53.484 | 3.655 | <.001 |
| 5 (Mf) | 50.369 | 43.129 | 3.322 | <.05 |
| 6 (Pa) | 61.523 | 49.613 | 4.743 | <.001 |
| 7 (Pt) | 71.092 | 48.452 | 8.169 | <.001 |
| 8 (Sc) | 74.569 | 49.613 | 7.769 | <.001 |
| 9 (Ma) | 52.277 | 47.581 | 2.446 | <.05 |
| 0 (Si) | 62.277 | 46.484 | 6.308 | <.001 |

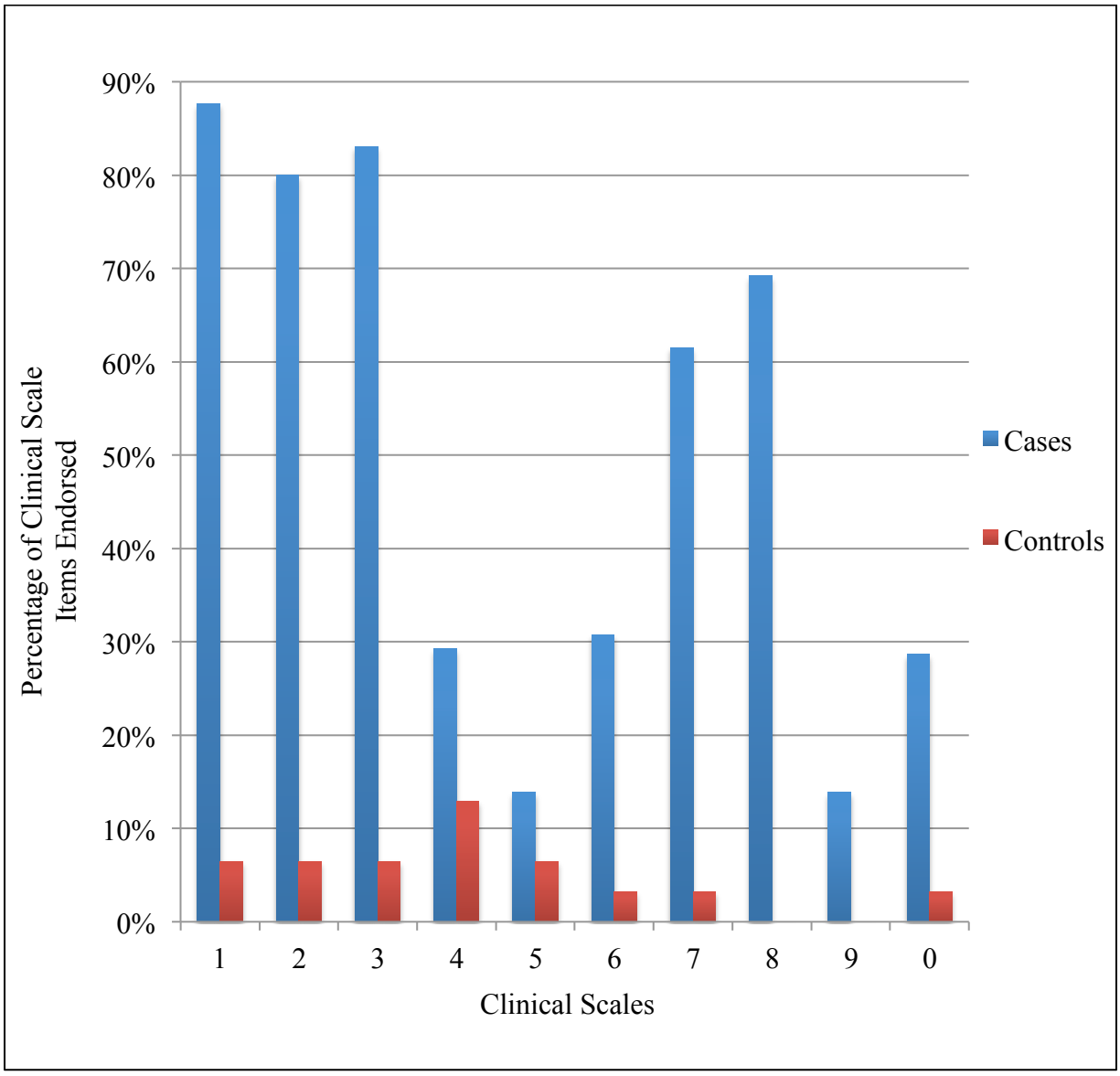
Additional analyses, examining group differences on clinical scales across controls and all three syndromes revealed significant differences across all clinical scales except for controls vs. syndrome 3 on clinical scales 4-psychopathic deviate, 5-masculinity/femininity and 9-hypomania, and between controls and syndrome 1 on scale 9-hypomania (Table 3).

Table 3. MMPI-2 Clinical Scales: Group Means and T-tests (Controls versus Syndromes 1, 2, and 3).

| Clinical Scales | Controls vs. Syndrome 1 | Controls vs. Syndrome 2 | Controls vs. Syndrome 3 | Controls vs. Syndrome 1 | Controls vs. Syndrome 2 | Controls vs. Syndrome 3 |
|---|---|---|---|---|---|---|
| | t-value | | | p-value | | |
| 1 (Hs) | 7.414 | 12.524 | 11.022 | <.001 | <.001 | <.001 |
| 2 (D) | 10.300 | 13.561 | 8.048 | <.001 | <.001 | <.001 |
| 3 (Hy) | 6.447 | 10.891 | 7.384 | <.001 | <.001 | <.001 |
| 4 (Pd) | 3.704 | 3.926 | 1.550 | <.001 | <.001 | 0.1 |
| 5 (Mf) | 2.662 | 3.148 | 1.842 | <.05 | <.05 | 0.1 |
| 6 (Pa) | 3.970 | 4.678 | 3.502 | <.001 | <.001 | <.001 |
| 7 (Pt) | 8.343 | 8.895 | 5.521 | <.001 | <.001 | <.001 |
| 8 (Sc) | 9.178 | 9.025 | 5.065 | <.001 | <.001 | <.001 |
| 9 (Ma) | 1.780 | 3.435 | .820 | 0.1 | <.05 | 0.4 |
| 0 (Si) | 5.009 | 6.821 | 4.228 | <.001 | <.001 | <.001 |

Another way to examine MMPI-2 profiles is to explore the frequency of significant scale elevations. The percentage of participants showing significant elevations on all clinical scales was found to be higher in cases versus controls. Clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia exhibited the largest differences between the two groups in terms of the percentage of significant scale elevations (Figure 2).

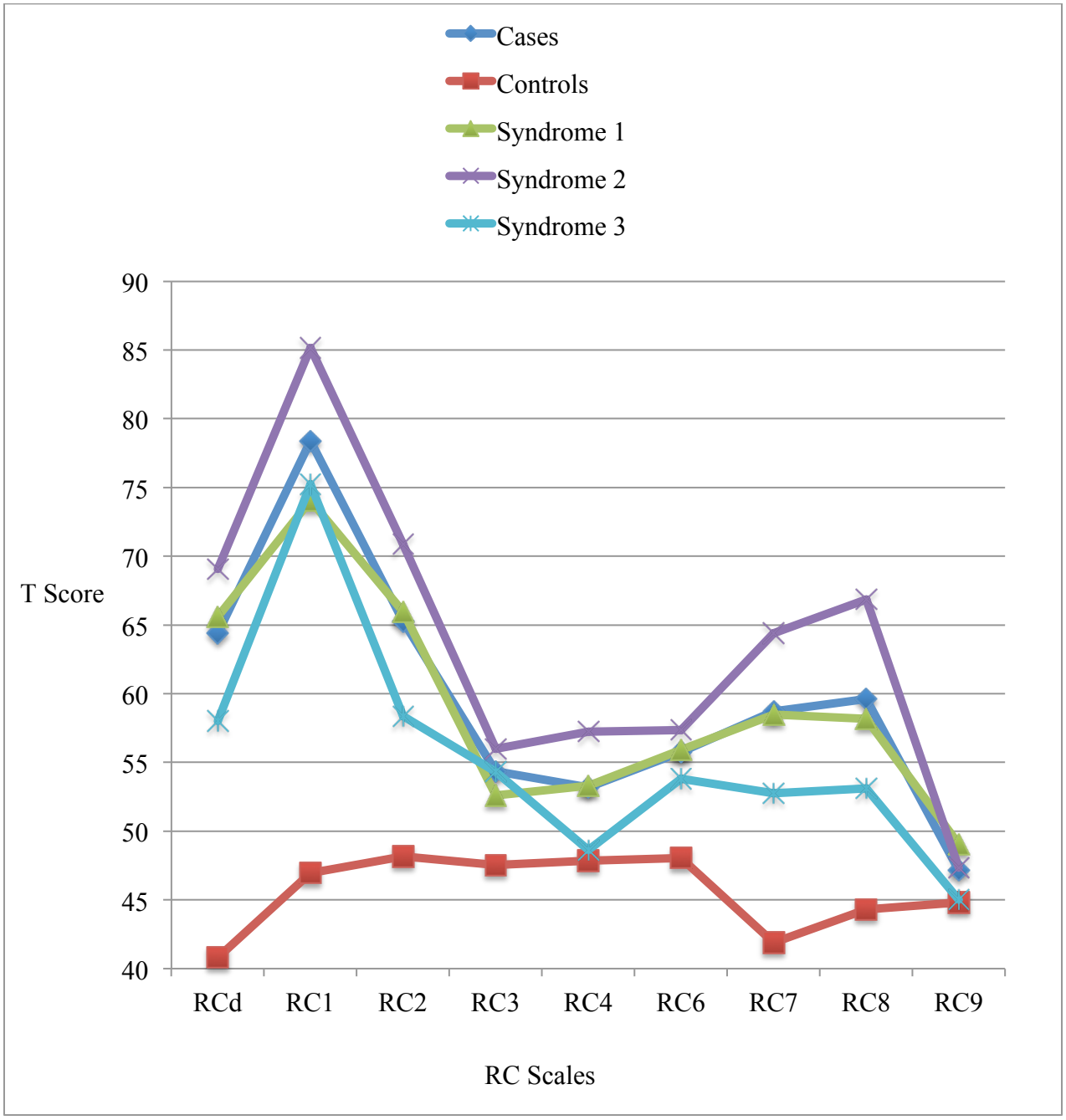
Figure 2. Percentage of Subjects Showing Significant MMPI-2 Clinical Scale Elevations by Group.




The second set of analyses investigated the RC scale profiles of controls and veterans with GWI as outlined in Hypothesis II. Overall, the case group exhibited elevated T-scores on RC 1-somatic complaints scale (T=78) and RC 2-low positive emotions scale (T=65), while controls did not display any clinically significant T-scores. Further, each individual syndrome

group exhibited a mean T-score greater than 65 on RC 1-somatic complaints scale. Further, GWI syndrome 1 was elevated on RC d-demoralization scale (T=66) and RC 2-low positive emotions scale (T=66), while syndrome 2 reached significance on RC d-demoralization scale (T=69), RC 2-low positive emotions scale (T=71), and RC 8-aberrant experiences scale (T=67) (Figure 3).

Figure 3. MMPI-2 RC Scale Profiles of GWI Cases, Controls, and Syndromes 1, 2 and 3.



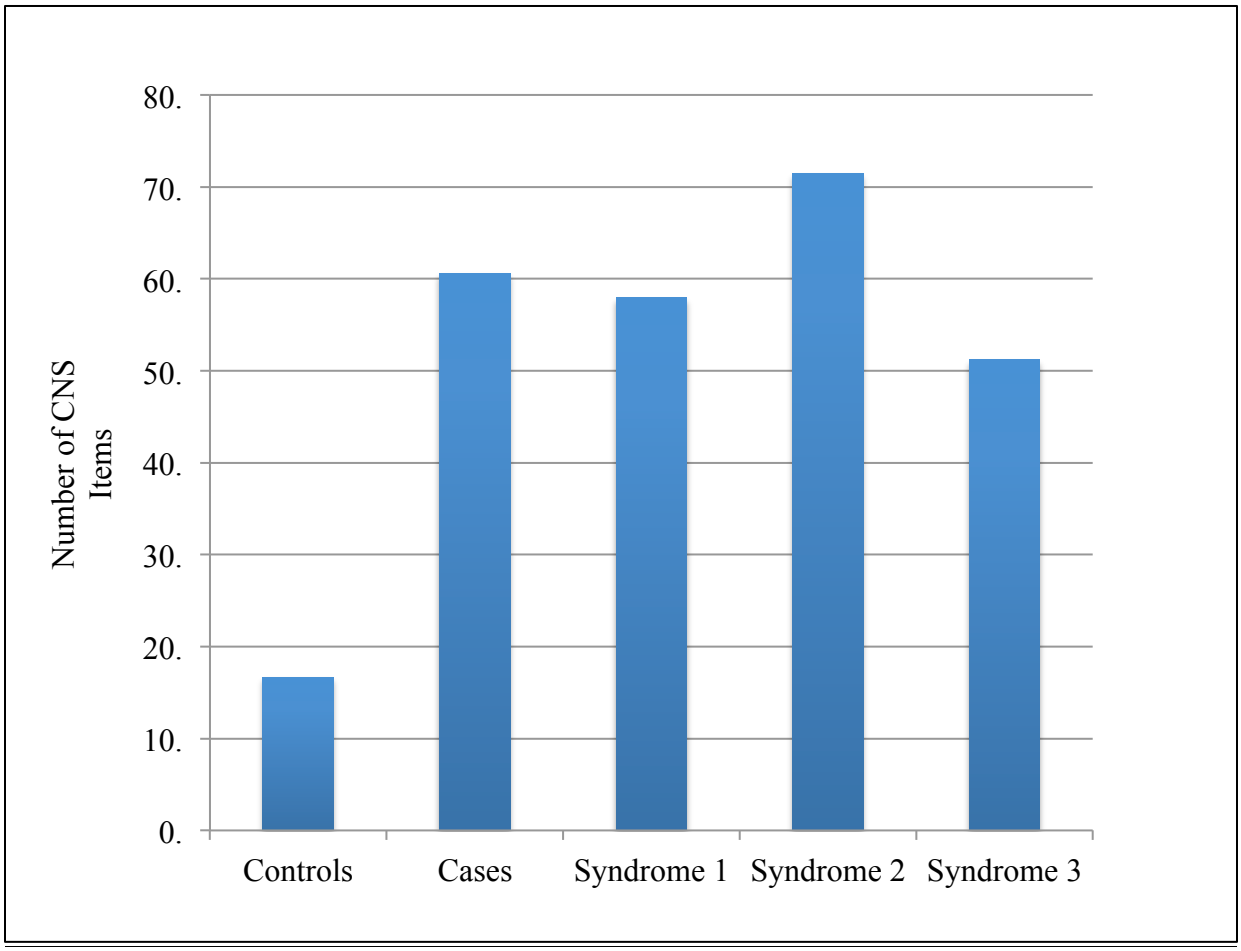
Using ANOVAs to further investigate differences on the RC scales outlined in Hypothesis II, significant differences were observed between the control group and GWI syndromes 1, 2, and 3 on the majority of scales (Table 4).

Table 4. MMPI-2 RC Scales: Group Means and ANOVA Results (Controls vs. Syndromes 1, 2, and 3).

| ANOVA - Controls, Syndromes 1, 2 and 3 | | | | | | |
|---|---|---|---|---|---|---|
| RC Scales | Group Means | | | | F | p-value |
| | Controls | Syndrome 1 | Syndrome 2 | Syndrome 3 | | |
| RCd | 40.806 | 65.619 | 69.087 | 58.000 | 38.102 | <.001 |
| RC1 | 46.968 | 74.048 | 85.174 | 75.238 | 61.131 | <.001 |
| RC2 | 48.161 | 65.952 | 70.870 | 58.381 | 18.177 | <.001 |
| RC3 | 47.548 | 52.619 | 56.000 | 54.333 | 2.528 | 0.062 |
| RC4 | 47.839 | 53.286 | 57.217 | 48.619 | 4.505 | <.05 |
| RC6 | 48.065 | 55.905 | 57.348 | 53.810 | 4.140 | <.05 |
| RC7 | 41.903 | 58.476 | 64.391 | 52.762 | 15.315 | <.001 |
| RC8 | 44.323 | 58.190 | 66.870 | 53.095 | 17.689 | <.001 |
| RC9 | 44.806 | 49.048 | 47.348 | 45.000 | 1.243 | 0.299 |

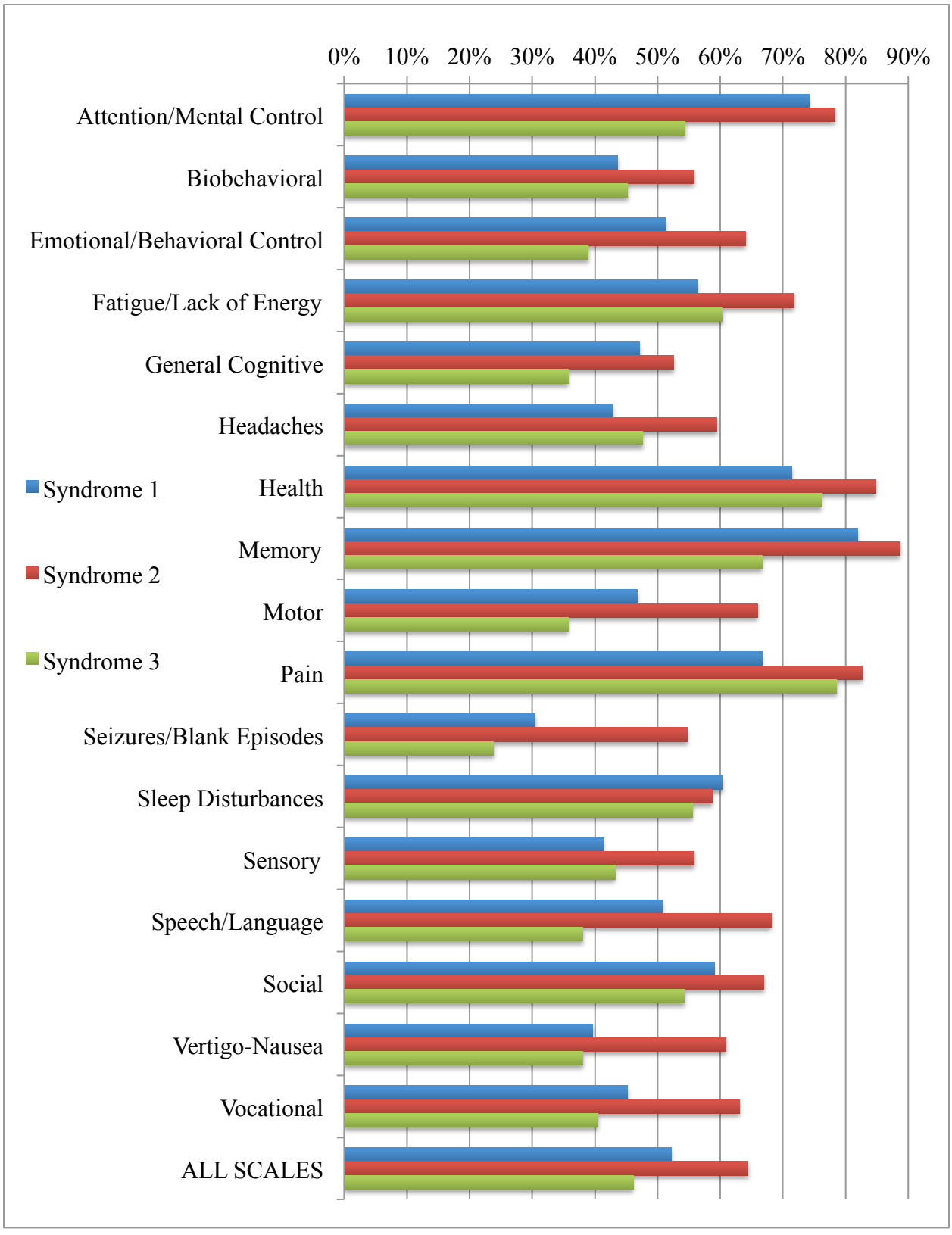
The third set of analyses focused on identifying differences in the endorsements of items on CNS scales and the possible association with significant elevations on clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, 8-schizophrenia, and RC1-somatic complaints scale as stated in Hypothesis III. GWI cases were separated using a median split of the total CNS score into high and low CNS scale endorser subgroups. Additionally in these analyses, compared to controls, the case group displayed a higher total CNS scale score, with syndrome 2 having the highest total CNS scale score (Figure 4).

Figure 4. MMPI-2 CNS Total Item Scores by Group.




As a result of each CNS scale categories being constructed with a varying number of items, comparing individual scale means was not solely appropriate, and thus, the percentages of elevations in each group were chosen for examination (Figure 5). As expected, cases had a higher percentage of significant CNS scale elevations compared to controls, with syndrome 2 showing the largest percentage of endorsements across scales except for the sleep disturbances scale.

Figure 5. Percentage of Endorsement of MMPI-2 CNS Scale Items by Group.



ANOVAs revealed significant differences ($p<.001$) between controls and individual GWI syndrome groups on all of the CNS scales. Through separating the veterans with GWI from healthy controls, T-tests revealed significant differences on all comparisons, except that between syndrome 3 and controls on the social scale (Table 5).

Table 5. MMPI-2 CNS Scales: Group Mean Scores and ANOVA Results (Controls, Syndromes 1, 2, and 3).

| CNS Scales (number of items) | Group Means | | | | F* |
|---|---|---|---|---|---|
| | Controls | Syndrome 1 | Syndrome 2 | Syndrome 3 | |
| Attention/Mental Control (7) | 0.871 | 5.190 | 5.478 | 3.810 | 43.886 |
| Biobehavioral (6) | 0.839 | 2.619 | 3.348 | 2.714 | 20.251 |
| Emotional/Behavioral Control (22) | 4.097 | 11.286 | 14.087 | 8.571 | 22.656 |
| Fatigue/Lack of Energy (6) | 0.581 | 3.381 | 4.304 | 3.619 | 53.105 |
| General Cognitive (10) | 1.129 | 4.714 | 5.261 | 3.571 | 15.945 |
| Headaches (6) | 0.613 | 2.571 | 3.565 | 2.857 | 23.039 |
| Health (4) | 1.258 | 2.857 | 3.391 | 3.048 | 25.310 |
| Memory (5) | 0.806 | 4.095 | 4.435 | 3.333 | 35.935 |
| Motor (6) | 0.452 | 2.810 | 3.957 | 2.143 | 28.242 |
| Pain (2) | 0.258 | 1.333 | 1.652 | 1.571 | 39.556 |
| Seizures/Blank Episodes (5) | 0.323 | 1.524 | 2.739 | 1.190 | 16.942 |
| Sleep Disturbances (6) | 1.226 | 3.619 | 3.522 | 3.333 | 30.095 |
| Sensory (13) | 2.258 | 5.381 | 7.261 | 5.619 | 31.538 |
| Speech/Language (3) | 0.161 | 1.524 | 2.043 | 1.143 | 21.086 |
| Social (5) | 1.613 | 2.952 | 3.348 | 2.714 | 8.792 |
| Vertigo-Nausea (3) | 0.065 | 1.190 | 1.826 | 1.143 | 20.727 |
| Vocational (2) | 0.129 | 0.905 | 1.261 | 0.810 | 18.262 |

*all $p < .001$

In order to examine the association between endorsed neurological items and elevations on the clinical and restructured clinical scales, veterans were divided into two groups, high CNS endorsers (N=32: GWI syndrome 1 N=9, GWI syndrome 2 N=17, GWI syndrome 3 N=6) and low CNS endorsers (N=31: GWI syndrome 1 N=10, GWI syndrome 2 N=6, GWI syndrome 3

N=15) groups, based on the cases' median score of 61 that was derived from the total CNS scales score. Next, each veteran's total CNS scales scores were then compared to their T-scores on the clinical and restructured clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia, and RC1-somatic complaints scale. When comparing veterans in the "low CNS endorser" group, participants in the "high CNS endorser" group were found to have a much larger percentage of significant elevations on all clinical and RC scales (Table 6).

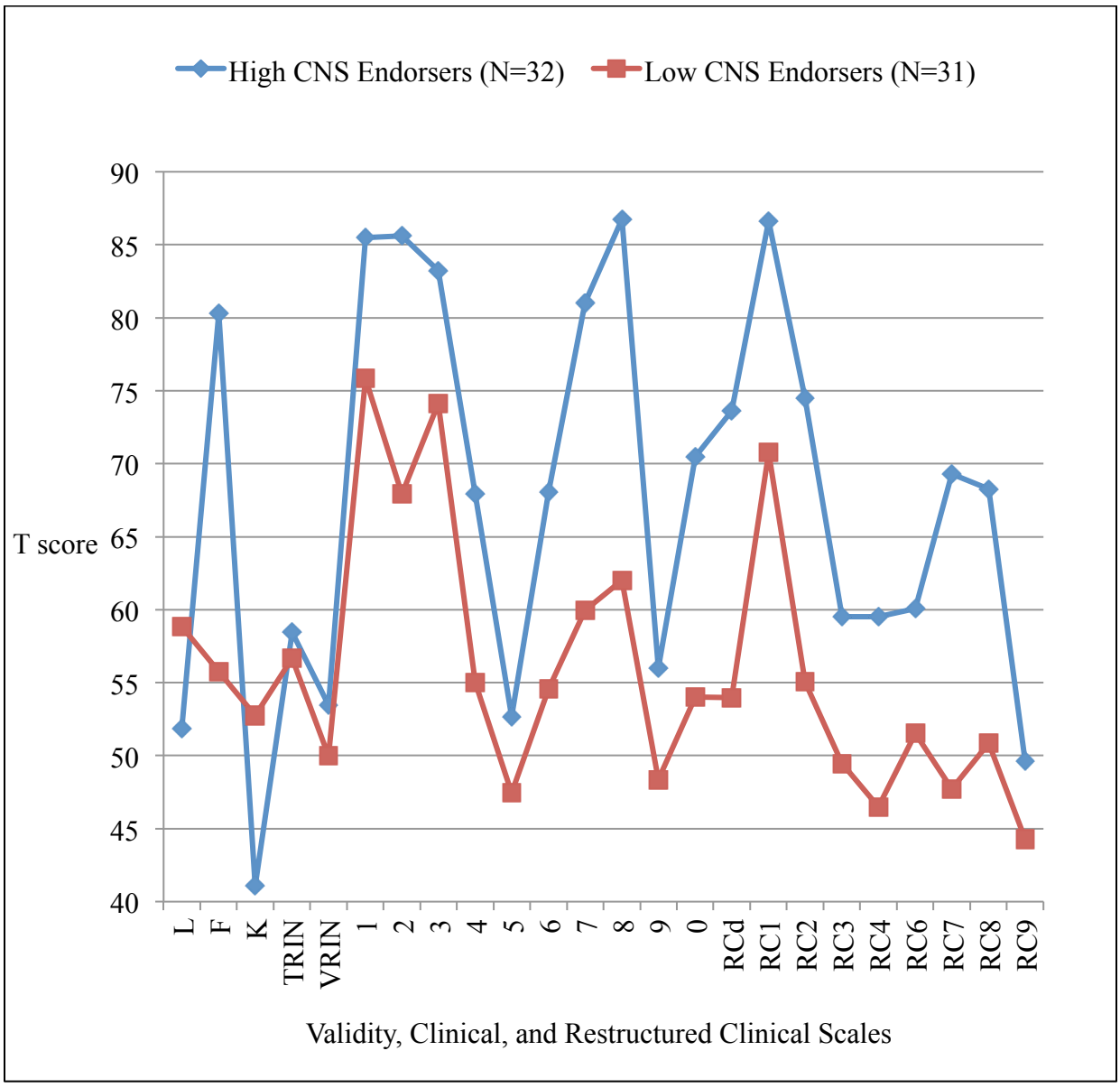
Table 6. Significant MMPI-2 Clinical Scale Elevation Percentages in High versus Low CNS Endorsers

| Clinical Scales | High CNS Endorsers (N=32) | Low CNS Endorsers (N=31) |
|---|---|---|
| 1 (Hs) | 100.00 | 77.42 |
| 2 (D) | 100.00 | 61.29 |
| 3 (Hy) | 96.88 | 70.97 |
| 4 (Pd) | 59.38 | 9.68 |
| 5 (Mf) | 12.50 | 9.68 |
| 6 (Pa) | 53.13 | 12.90 |
| 7 (Pt) | 93.75 | 29.03 |
| 8 (Sc) | 93.75 | 41.94 |
| 9 (Ma) | 25.00 | 3.23 |
| 0 (Si) | 75.00 | 12.90 |
| RCd | 84.38 | 12.13 |
| RC1 | 96.88 | 64.52 |
| RC2 | 71.88 | 12.90 |

**Results Summary.** Each hypothesis was supported, with significant differences observed between the GWI case and healthy control groups on the specified clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia, RC 1-somatic complaints scale, and CNS scales. While the case group displayed significant elevations across most clinical and RC scales, respondents who endorsed over 55% of the items in the CNS scales

were observed as being significantly elevated across all clinical and RC scales. These reports therefore reflect a heightened level of general distress and multifaceted symptom complaints among GWI subjects. While the high CNS scale endorsers displayed heightened neurological endorsements and elevated scores across the majority of the clinical and RC scales, the veterans with GWI who reported a large number of neurologic ailments also appeared significantly elevated across the majority of clinical and RC scales (Figure 6).

Figure 6. High versus Low MMPI-2 CNS Endorser Profiles.



# CHAPTER FOUR

## Discussion

GWI subjects displayed a high level of generalized distress and endorsed a multiplicity of psychological, neurologic, and physical symptoms. As hypothesized, controls and GWI syndromes displayed significant differences on clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia and RC 1-somatic complaints scale. However, GWI cases also exhibited a higher frequency of significant elevations on all clinical scales compared to controls. Further examination of profiles additionally found the largest differences on MMPI-2 clinical scales 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia, with GWI cases displaying clinically significant elevations that are reflective of anxious, depressive, and somatic symptoms, with complaints of difficulty concentrating, experiences of psychological turmoil, fatigue, sleep disturbance, social alienation, and possible symptom exaggeration issues. Such elevations point towards an increased presence of generalized psychological distress reported by veterans with GWI. While these reported ailments have been commonly identified in previous studies of veterans with GWI (Axelrod & Milner, 1997; Binder et al., 2000; Storzbach et al., 2000), observing such significant scale differences and elevations in this group of veterans with GWI provides further evidence of such symptoms being associated with the illness.

In support of Hypothesis II, GWI cases exhibited significant differences compared to controls on the MMPI-2 RC 1-somatic complaints scale, indicating a heightened concern and reporting of physical ailments that have been interpreted in the past as having a psychological basis. However, considering the neurologically relevant item composition of the RC 1-somatic complaints scale (22 of 27 items), the GWI case group also displayed significant elevations that

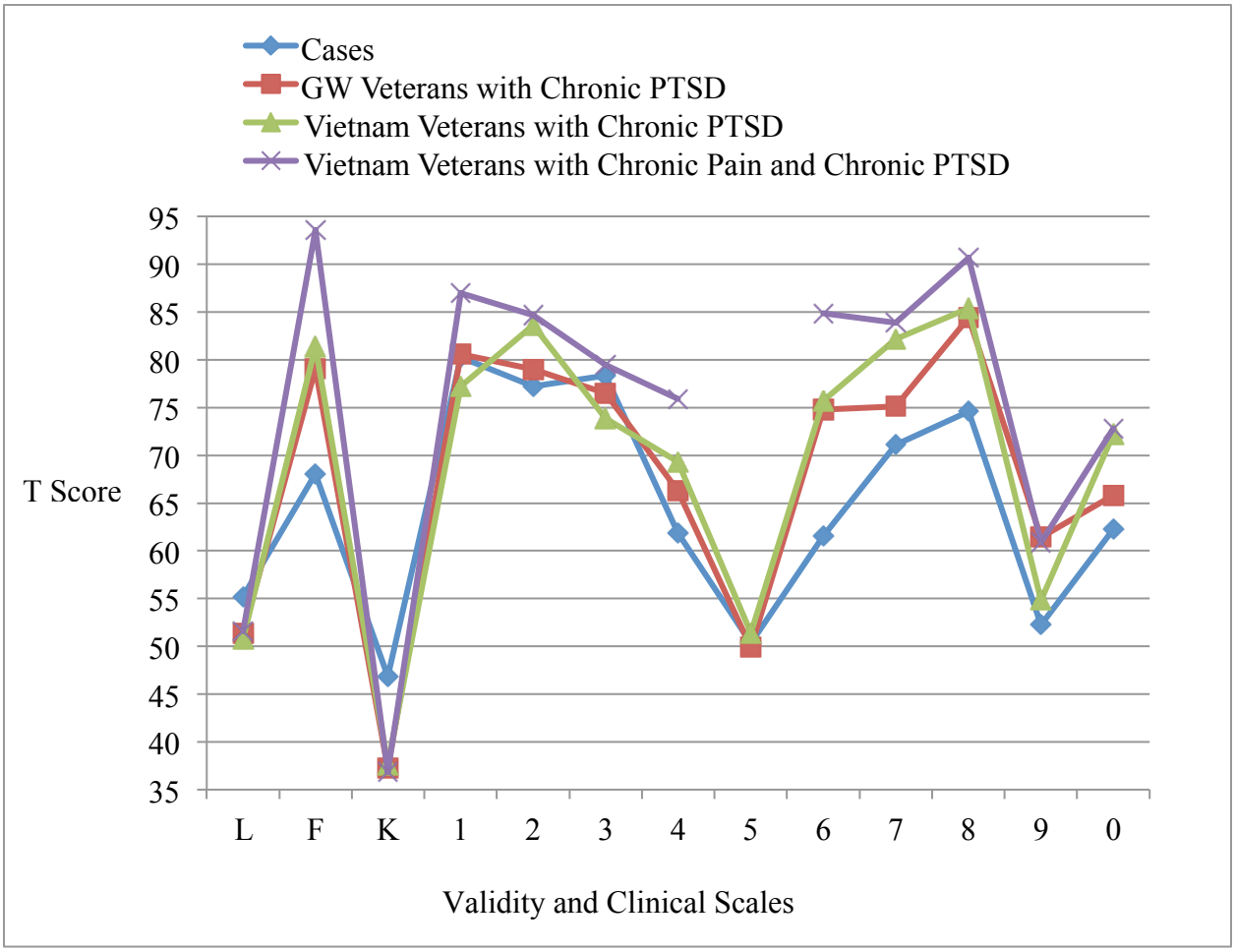
were associated with a large number of CNS item content areas. Additionally, reported symptoms in cases also indicated sensory disturbances, difficulties with cognitive, motor, perceptual functioning, and reports of considerable emotional discomfort. While this provides further evidence of the significant amount of general distress experienced by veterans with GWI, it might also suggest that some of these ailments could be interpreted as somatic in nature.

Hypothesis III stated that the endorsement of items on the CNS scales would be associated with significant elevations on selected clinical scales and RC 1-somatic complaints scale that assess physical symptoms, depression, somatization, anxiety, and disordered thinking. CNS scale endorsements in cases were found to be associated with significant elevations on 1-hypochondriasis, 2-depression, 3-hysteria, 7-psychasthenia, and 8-schizophrenia, and RC 1-somatic complaints scale. However, the GWI and syndrome groups were found to display a higher percentage of item endorsements across the CNS scales compared to controls, suggesting that the predicted differences were part of a nonspecific pattern of generalized symptom complaints among GWI subjects. With regard to the different GWI syndrome groups, syndrome 2 exhibited the highest mean scores and percentage of endorsed items on all CNS scale categories except one, which could suggest that this group might be experiencing the most severe symptoms compared to other GWI syndromes. GWI syndrome 2 veterans also displayed more significant differences across clinical and RC scale sets compared to controls.

Previous comparisons of GWI MMPI and MMPI-2 profiles to PTSD or somatoform disorders reveals similar clinical elevations among the current sample, but to a lesser degree than those other groups. Whereas higher psychological symptoms may be elevating GWI scores, it is worth noting that the pattern of MMPI-2 elevations in these GWI veterans do resemble those seen in other neurologic groups such as multiple sclerosis and fibromyalgia, the latter of which is

an illness with a range of often unexplained symptoms (Nelson, Elder, Tehrani, & Groot, 2010). In particular, clinical scales 1-hypochondriasis, 2-depression, 3-hysteria in GWI veterans displayed similar elevations as observed in neurologically based and unexplained illness groups, with higher T scores being exhibited by psychiatric groups with PTSD and/or chronic pain (Beckham et al., 1997; Glenn et al., 2002) (Figure 7).

Figure 7. MMPI-2 Profile Comparisons: GWI, Chronic PTSD, and Chronic Pain.

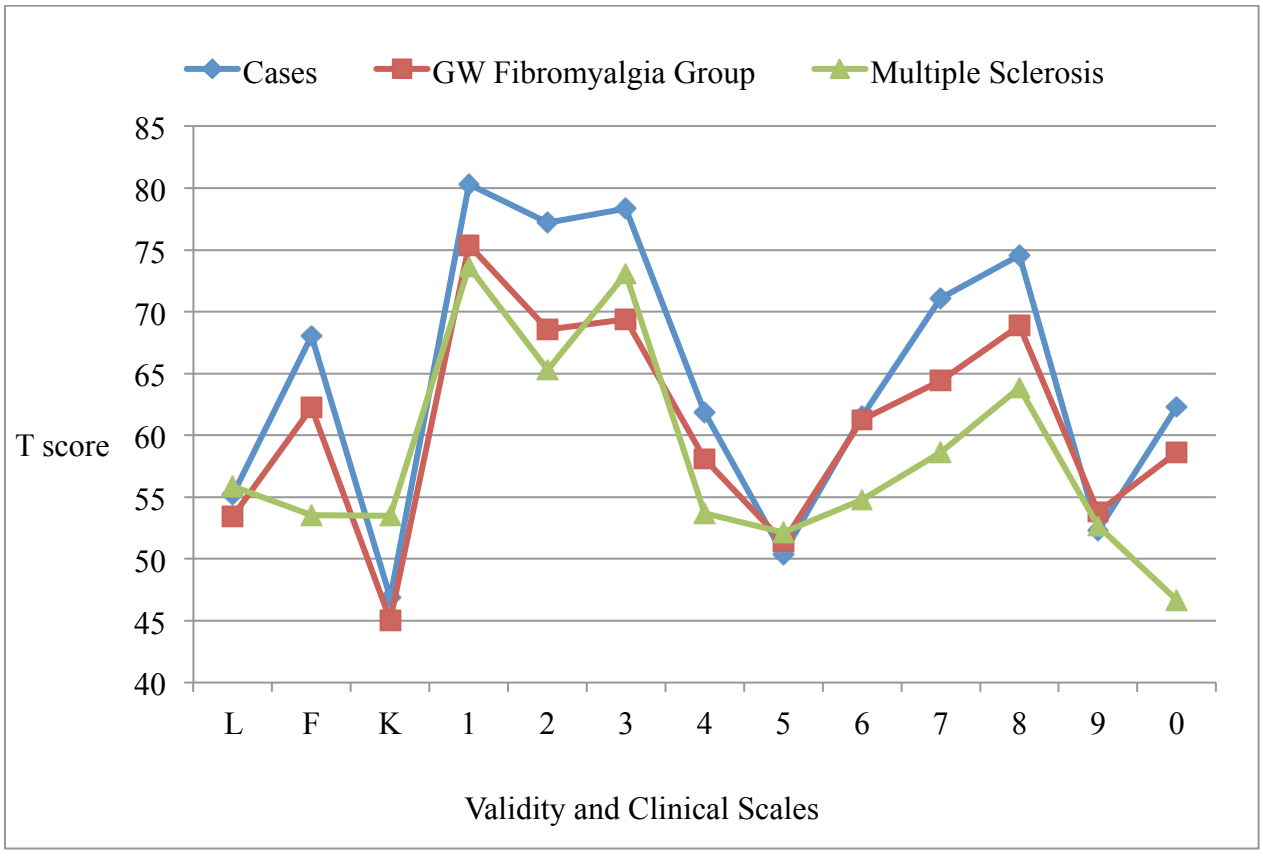



Note. Chronic PTSD and Chronic Pain Vietnam Veterans Group data adapted from "Chronic post traumatic stress disorder and chronic pain in Vietnam combat veterans," by Beckham et al., 1997, *Journal of Psychosomatic Research*, 43(4), p 382. Copyright 1997 by the Elsevier Science Inc.GW Veterans with Chronic PTSD and Vietnam Veterans

with Chronic PTSD groups adapted from "MMPI-2 profiles of Gulf War and Vietnam combat veterans with chronic posttraumatic stress disorder," by Glenn et al., 2002, *Journal of Clinical Psychology*, 58(4), 371-381. Copyright 2002 by the Wiley Periodicals, Inc.

A similar observation was seen on scales 6-paranoia, 7-psychasthenia, 8-schizophrenia, in which the GWI case group exhibited much lower elevations than groups with PTSD and/or chronic pain, yet cases also displayed higher scores than those found in a fibromyalgia group comprised of Gulf War veterans (Johnson et al., 2009) and a separate sample of individuals with multiple sclerosis (Nelson, Elder, Tehrani, & Groot, J., 2002) (Figure 8).

Figure 8. MMPI-2 Clinical Scale Profile Comparisons: GWI Cases, Fibromyalgia, and Multiple Sclerosis.



Note. GW Fibromyalgia group adapted from "MMPI-2 profiles: Fibromyalgia patients compared to epileptic and non-epileptic patients," by Johnson et al., 2009, *The Clinical Neuropsychologist*, (24)2, p. 226. Copyright 2009 by the Psychology Press. Multiple Sclerosis group data adapted from "Measuring personality and emotional functioning in multiple sclerosis: a cautionary note," by Nelson, elder, Tehrani, & Groot, 2003, *Archives of Clinical Neuropsychology*, 18, p424. Copyright 2002 by the National Academy of Neuropsychology.

While the MMPI-2 clinical profiles of cases look similar to those observed in other groups with a neurologically based or unexplained illness, it is impossible to determine the nature of these elevations and whether the scale elevations among GWI subjects reflect anything unique to this population or suggest an array of vague somatic, neurologic, and psychological symptoms.

## Limitations and Future Recommendations

While using the MMPI-2 to investigate symptoms associated with GWI yielded insight into the extensive range of reported ailments in this population, significant elevations across the majority of clinical, RC scales, and CNS scales did not allow for an interpretation of the nature of item endorsements from GWI cases with regard to specific neurological or psychiatric bases. Instead, it must be concluded that these heightened elevations reflect a large number of perceived ailments and generalized distress in GWI veterans. The limited sample size of individuals with GWI syndromes is another limitation, as is the large number of statistical analyses, which may inflate Type I error. Last, as the case definition of GWI was based upon another self-report symptom measure, and the MMPI-2 is also a self-report symptom questionnaire, it is not surprising that the MMP-2 yielded differences between cases and controls. Additional

exploration of the specific complaints of each syndrome across the MMPI-2 and the original case definition questionnaire might be useful in gaining insight into possible differences or unique features across GWI syndromes.

Longitudinal studies should focus on the change or stability of ill veterans' symptoms. Additionally beneficial would be the investigation of possible differences and similarities between illnesses with underlying neurological processes and GWI over an extended time period. While the current results underscore the extent of symptom complaints among GWI and Haley Syndrome subjects, results unfortunately provide little support to the specific hypothesis of underlying neurological processes associated with GWI, although further study is needed to address this complex question.

## Summary

GWI cases exhibited elevations across the hypothesized MMPI-2 scales that might relate to the presence of underlying neurologic symptoms. However, these scale elevations were in the context of numerous other scale elevations, suggesting an overall pattern of generalized distress on the MMPI-2. Among the range of ailments reported by veterans with GWI, symptoms included experiences of anxiousness, depression, difficulty with attention and concentration, disorientation, generalized joint and muscle pain, fatigue, memory problems, numbness, psychological turmoil, sleep disturbances, social alienation, and problems with speech. While conclusions cannot be drawn regarding neurological vs. psychological causes of symptoms, these results underscore the range and severity of symptoms reported by veterans with GWI.

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## PAPERS

Hutchison, J. L., Hubbard, N. A., Brigante, R. M., Turner, M., Sandoval, T. I., Hillis, G. A., Weaver, T. & Rypma, B. (2014) The efficiency of region of interest analysis methods for detecting group differences. *Journal of Neuroscience Methods*, (15)226, 57-65.

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