2016

The Role of Illness Intrusiveness and Personal Control in Mediating the Relationship between the Intravenous Immunoglobulin Treatment Experience and Quality of Life in Neurological Autoimmune Patients

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Abstract

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by

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MA, Walden University, 2011

BS, Valparaiso University, 1969

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Health Psychology

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Abstract

Intravenous immunoglobulin (IVIG) is a common treatment for the neurological autoimmune diseases multiple sclerosis, multifocal motor neuropathy, myasthenia gravis, and chronic inflammatory demyelinating polyneuropathy. However, there is scant literature regarding the psychological effects of this treatment on quality of life (QOL). Using illness intrusiveness theory and personal control theory, this correlational, cross-sectional study examined the relationship between the IVIG treatment experience and QOL in neurological autoimmune patients. Surveys were employed to collect data from 79 patients at a neurological infusion center in Phoenix, AZ. Quantitative analyses included correlation, multiple regression, and mediation analyses to determine whether (a) IVIG treatment experience predicted QOL measured by 10 Neuro-QOL scales, (b) illness intrusiveness mediated the relationship between IVIG treatment experience and QOL, and (c) personal control mediated the relationship between illness intrusiveness and QOL. IVIG treatment experience predicted QOL in 1 Neuro-QOL subscale; illness intrusiveness mediated 9 of the Neuro-QOL subscales using bias-corrected bootstrapping for statistical significance; and personal control did not mediate the relationship between illness intrusiveness and QOL. These results may affect social change by increasing the understanding of physicians, nurses, and patients regarding the psychosocial impact of IVIG treatment. Results from the study may provide insight for interventions to assist patients in adjusting to this form of treatment.

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Dedication

I dedicate this dissertation to my husband, Rick, who has been my constant supporter and encourager through this journey. You have believed in me and the end goal especially during those times when I was exhausted and discouraged. Thank you to our four sons, Joshua, Ian, Joel, and Jonathan who have been excited their mother would attempt such a major project and are proud of me. Your love has reinforced me. I would be remiss not to include my parents in this dedication who taught me the importance of continual lifetime learning. I also dedicate this endeavor and new body of knowledge to the patients suffering from neurological autoimmune disorders who continue to battle challenges every day of their lives.

Finally, and most important I dedicate this dissertation to my Lord and Savior, Jesus Christ. I am grateful for His help to sustain me through the challenging writing process.

Acknowledgments

This dissertation would not have been possible without the continual guidance and direction of my chairperson, Dr. Silvia Bigatti. Thank you, Dr. Bigatti, for the timely reviews of my writing, meaningful suggestions which motivated me to look beyond the obvious, and inspiration to think creatively. You gave me courage when needed especially regarding statistically analyzing my own data. Your words "own your dissertation" constantly played in my mind until one day it finally happened!

Thank you, Dr. Rachel Piferi, for your suggestions, questions, and willingness to serve as my committee member. Dr. Susan Marcus, your critiques, counsel, and advice helped to move me in the right direction in order to write a meaningful dissertation.

Thank you to Dr. Todd Levine, Neurologist and Kathie Clarke, Neuroscience Clinical Nurse Specialist and Clinical Operations Director at Phoenix Neurological Associates for their continual support and assistance during the past three years. They believed in the importance of this research to examine the relationship between IVIG treatment experience and quality of life and for this faith I am eternally grateful.

To my family and friends, thank you for your patience, understanding, and love during this journey.

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Chapter 1: Introduction to the Study

Introduction

Autoimmune neurological disorders such as multiple sclerosis (MS), multifocal motor neuropathy (MMN), myasthenia gravis (MG), and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) affect millions of people in the United States. The National Institutes of Health (NIH), part of the United States Department of Health and Human Services (USDHHS), considers only the diseases that have sound epidemiology studies in their 23.5 million estimated autoimmune disease statistics (NIH, 2005). These autoimmune diseases often physically disable people through loss of function, mobility, and weakness, while decreasing the individual's quality of life (QOL) through psychological factors such as depression, anxiety, frustration, inconvenience, lost interest in surroundings, fatigue, and intrusion into daily life activities (Padua, Sabatelli, Evoli, Pazzaglia, & Tonali, 2005).

Neurological autoimmune diseases affect the central or peripheral nervous system (Appenzeller, Shoenfeld, & de Carvalho, 2012). Included in the neurological autoimmune disease family are the four diseases which were examined in this study. MS is a disease resulting in demyelination of the central nervous system often producing lasting neurological impairment (Padua et al., 2005). MMN is an uncommon, progressive demyelinating disorder producing distal and upper limb weakness, conduction block in the motor nerves, difficulty in walking, and poor dexterity and affects 1–2 people in 100,000 (Nobile-Orazio, Cappellari, & Priori,. 2005). MG affects an estimated 14–20 people per 100,000 (Myasthenia Gravis Foundation of America, 2012), is often

progressive with long-term disability (Leonardi et al., 2010), and is characterized by weakness in muscles and extreme fatigue (Maggi & Mantegazza, 2011). CIPD is a progressive disease often displaying weakened reflexes and sensory loss (Patel, Bhanushali, & Muley, 2010) along with diminished muscle strength in both upper and lower extremities often affecting balance and mobility (Hughes, 2009; Westblad, Forsberg, & Press, 2009) with tendon reflexes often reduced (Hughes, 2010). More detailed descriptions of these four diseases are provided in Chapter 2.

Although there are several treatments used in autoimmune disease, a select treatment for the four diseases examined in this study was intravenous immunoglobulin (IVIG; Dalakas, 2004) which is immunoglobulin obtained from healthy individuals (Bick et al., 2013). It was important to examine the effect of IVIG treatment experience since the impact of treatment may contribute to an intrusion or interruption of lifestyle and activities of enjoyment for patients while at the same time benefiting the physical symptoms of the disease. This disruption to life activities and patient interests is defined as illness intrusiveness and is hypothesized to compromise QOL (Devins, 2010; Poochikian-Sarkissian, Sidani, Wennberg, & Devins, 2008a). Illness intrusiveness was a mediator variable between the IVIG experience and QOL in this study.

QOL was the outcome variable in this study. While considerable research exists concerning the compromising effects of chronic neurological disease symptoms on QOL, there is limited research on the influence of the potential intrusion of treatment on QOL for these diseases. Examining the treatment experience and its effect on QOL may contribute to current research in understanding patient experiences with regard to IVIG.

The current study examined the relationships between this particular treatment (IVIG), the predictor variable, and QOL in a population of MS, MMN, MG, and CIDP patients.

Background

Although the NIH considers only the diseases which have sound epidemiological studies in their prevalence estimates of 23.5 million autoimmune disease, the American Autoimmune Related Diseases Association (AARDA) and the National Coalition of Autoimmune Patient Groups (NCAPG) report researchers have identified 80 to 100 chronic potentially life threatening diseases making the estimation closer to 50 million individuals in the United States affected by autoimmunity diseases (AARDA & NCAPG, 2011; USDHHS, NIH, 2005). Living with one of these autoimmune diseases is challenging, from coping with disease symptoms to the consequences associated with the prescribed treatment. Autoimmune diseases treated with IVIG include (but are not limited to) Kawasaki disease, idiopathic thrombocytopenic purpura (ITP), guillain-barré, dermatomositis, stiff person syndrome, and the four diseases focused on in this study.

A common treatment for the four autoimmune diseases is IVIG. IVIG is developed from the plasma of 1,000 to 10,000 individuals forming a "unit" of the purified blood product and is used for treatment in a variety of neurological diseases (Phoenix Neurological Associates [PNA], 2015). IVIG consists of antibodies which serve to impede the attack on the individual's immune system (Dalakas, 2004).

Numerous research articles have been published regarding the efficacy of IVIG with autoimmune neurological disorders. For example, IVIG is thought to delay progression in some forms of MS and offers safe and efficacious treatment in relapsing-

remitting MS (Katz, Kishner, Magalashvili, Shoenfeld, & Achiron, 2006; Pöhlau et al., 2007). Moreover, IVIG mollifies exacerbations in moderate to severe MG patients (Gajdos & Chevret, 2008; Zinman & Bril, 2008), and improves disease specific QOL in MG patients (Bril, Barnett-Tapia, Barth, & Katzberg, 2012). IVIG promotes rapid improvement in 80% of MMN patients (Padua et al., 2005) and is deemed customary for this diagnosis (van Schaik et al., 2006). Furthermore, the efficacy of IVIG has been demonstrated in seven randomized controlled studies with CIDP (Patel et al., 2010) as well as the Immune Globulin Intravenous For Chronic Inflammatory Demyelinating Polyneuropathy (ICE) trial that reported both short and long-term effectiveness (Hughes et al., 2008; Patel et al., 2010). IVIG has also demonstrated high tolerability with few reported serious side effects in neuromuscular diseases (Nadeau, Bhibhatbhan, McDougall, & Toth, 2010).

How IVIG is administered varies by patient and disease, but in general, requires 4 to 6 hours, usually a dose of 2 GMs/kg which may be divided into two doses administered over a period of 2 days (PNA, 2014). It is possible to give the dose on alternate days or over a period of 5 days with treatment typically repeating every 4 to 6 weeks (PNA, 2014). The treatment experience typically complicates patients' lives regarding scheduling, travel time, high medical costs, and the time commitment of the treatment itself. Thus, the treatment experience may negatively influence QOL.

The World Health Organization Quality of Life Group (1995) defined QOL as "individuals' perception of their position in life in the context of the culture and value systems in which they live in relation to their goals, expectations, standards and

concerns" (p. 405). A person's goals, expectations, and standards for their future may be altered and changed because of a diagnosis of a neurological autoimmune disease which may in turn influence QOL. Keles, Ekici, Ekici, Bulcun, and Altinkaya (2007) found that negative effects of chronic disease bring about profound psychological distress in patients. They concluded psychological distress in itself may impact QOL similarly to the presence of several chronic diseases.

Although many articles report on the physical improvements with IVIG treatment in neurological autoimmune diseases, little research addresses the problem of the QOL of patients who require lengthy treatments of IVIG to manage or improve their condition (Padua et al., 2005). Emotional and psychological consequences may occur as patients face the ramifications of the IVIG treatment experience, such as side effects, complex schedules, lengthy treatment times, and strain on financial resources (Patel et al., 2010). The few studies do not cover psychological aspects of QOL or describe patients' responses to the intrusiveness of illness and treatment. Gerschlager and Brown (2002) conducted a study with patients diagnosed with stiff person syndrome receiving IVIG and found improved health-related QOL. However, this study had a small sample of six patients. Additionally, Padua et al. (2005) conducted a pilot study assessing quality of life in 25 autoimmune patients receiving IVIG. Using the SF-36, the authors' findings revealed less pain, better upper limb functioning, and improved physical functioning after IVIG therapy, but did not indicate reduced psychological distress. In fact, this is the only study that examined psychological issues related to IVIG and autoimmune disease.

Padua et al. (2005) suggested the necessity of more research on the influence of IVIG on the health-related and psychological QOL to extend previous research. The authors suggested that there may be several treatment experience factors (direct and indirect) affecting patients. My study attempted to fill that gap by examining (a) the direct and indirect effects of the IVIG treatment experience on QOL, and (b) the influence of illness intrusiveness and personal control as potential mediators of this relationship.

Illness intrusiveness has been demonstrated to be a determining factor in the psychosocial effect of chronic disease and treatment (Devins, 1994) as well as a mediator of QOL indicators (Poochikian-Sarkissian et al., 2008a). Levels of illness intrusiveness in the patient's life can determine outcomes in QOL. Elevated levels of illness intrusiveness were found to associate with low QOL in a study of epilepsy treatment groups (Poochikian-Sarkissian et al., 2008a). In fact, illness intrusiveness was found to be significantly associated with all aspects of QOL in MS patients (Shawaryn, Schiaffino, LaRocca, & Johnston, 2002). Included in the construct of illness intrusiveness are the stressors brought about by treatment of chronic disease such as financial pressure, complex schedules, economic or employment hardship, possible side effects, diminishing recreational activities, and dependency on medicine and/or medical personnel (Devins, 2010), all of which may be caused by IVIG treatment. These findings suggest the value of investigating illness intrusiveness as a potential mediator between disease treatment (IVIG) and QOL.

Personal control refers to a person's expectations regarding their own ability to influence results through their own behavior (Rotter, 1990). According to the illness intrusiveness theory, personal control over desirable outcomes in life is reduced when treatment and disease interruptions affect lifestyle and normal activities (Devins, 2010). Personal control may be an important factor in QOL of neurological autoimmune patients. For example, Poochikian-Sarkissian et al. (2008a) found that patients who perceived control over their disease and treatment reported a better QOL than persons who did not perceive control. Gruber-Baldini, Ye, Anderson, and Shulman, (2009) found that the relationship between Parkinson's disease (PD) disability was increased in patients exhibiting less internal locus of control. Rotter (1966) suggested that an individual can change behaviors if they believe they are controllable. Gruber-Baldini et al. (2009) found that patients who believed they could control their behaviors may have implemented strategies to maintain optimal function. The authors also suggested that this higher level of personal control may have modified the progression of the individual's disability.

It is possible that control may influence how a person responds to a chronic disease or illness or how they interpret the impact of the disease on their life style. Bishop (2005) found that personal control mediated the relationship between impact of chronic illness and disability and QOL in a study incorporating a modified illness intrusiveness approach with college students with chronic disabilities. Additionally, Bishop, Frain, and Tschopp (2008) found the impact of MS symptoms was partially mediated by personal control when testing the illness intrusiveness model. The study also suggested a positive

relationship between self-management of chronic illness and personal control which could suggest the importance of control supporting a patient's ability or motivation to intervene for their treatment or communication with physicians (Bishop et al., 2008). Personal control may also have an important role in the relationship between illness intrusiveness and QOL in MS, MMN, MG, and CIDP patients warranting examining it as a potential mediator in my study.

Studying the relationship of the IVIG experience on QOL is important for a number of reasons. The current study provided information regarding the QOL encountered by autoimmune patients receiving immunotherapy. Insight into the relationship of IVIG with QOL may guide medical personnel in service to these patients as they gain a deeper understanding of some of the psychological issues which may result from illness intrusiveness potentially mediating the relationship of IVIG on QOL. Gaining knowledge about the consequences of illness intrusiveness may aid IVIG nurses and medical teams in planning physical or emotional patient interventions to improve QOL while a patient is receiving IVIG immunotherapy. Finally, the current study contributed to closing the knowledge gap and extending previous limited research regarding IVIG and QOL.

Problem Statement

Although research demonstrates IVIG is the treatment of choice for the four neurological autoimmune diseases examined here, studies are limited and do not reflect the possible social and psychological experience of IVIG treatment on QOL for those patients receiving this therapy. Although IVIG is common, the high cost of the therapy,

complicated schedules, and long hours of infusions may cause disruptions to the lives of the neurological autoimmune patients who receive it. Therefore, it was necessary to assess the relationship of this particular treatment experience on QOL for patients with autoimmune diseases that are treated with this approach (MMN, MG, MS, and CIDP patients). Further, it was reasonable to consider illness intrusiveness as a mediating factor between the IVIG experience and QOL since research has shown the IVIG treatment may mean interruption in activities, schedules, and life plans (Devins, 2010), and it has been shown to be a mediator in other chronic diseases (Dancey, Hutton-Young, Moye, & Devins, 2002; Devins et al., 1993; Shawaryn et al., 2002).

Some patients may not be as affected by the potential illness intrusiveness of IVIG as others. Considering whether control may be a mediator between illness intrusiveness and QOL may shed significant light on why some patients may view treatment as intrusive and other patients may not. Personal communication with neurologists and IVIG specialist nurses has indicated a need for more in-depth insight into the IVIG experience for patients receiving this treatment (C. L. Gooch, personal communication, December, 3, 2013; T. Levine, personal communication, June 7, 2012; S. McBride, IVIG RN, personal communication, June 18, 2014; K. Clarke, IVIG RN, personal communication, May 20, 2014). This study was needed to enhance the limited literature regarding the relationship of IVIG and QOL with neurological autoimmune patients receiving this treatment. I hypothesized that the study would provide IVIG nurses, patients, and physicians a deeper understanding of the psychological aspects of the IVIG experience and its effects on QOL.

Purpose of the Study

The purpose of this survey research study was to examine the relationship between the IVIG treatment experience (predictor variable) and QOL (outcome variable) in neurological autoimmune patients. Illness intrusiveness was investigated as a possible mediator between the IVIG treatment experience and QOL in this patient population. Additionally, personal control was studied as a potential mediator between illness intrusiveness and QOL. There have been no previous studies considering the role of these mediators in the relationship between IVIG treatment and QOL. This study was an attempt to fill that gap.

Research Questions and Hypotheses

This study used a predictive model to examine the strength of the IVIG treatment experience in explaining the variance in QOL and to test the mediating influence of illness intrusiveness and personal control. Data were collected from a convenience sample of MS, MMN, MG, and CIDP patients from PNA who were currently receiving IVIG treatment. The following research questions (RQ) and hypotheses were proposed:

RQ1: Is the IVIG treatment experience (as measured by the Visual Analogue Scale) a significant predictor of QOL (as measured by 10 Neuro-QOL scales) in patients with autoimmune disorders who receive IVIG treatment?

$H_1$1: IVIG treatment experience (as measured by the Visual Analogue Scale) is a significant predictor of QOL (as measured by 10 Neuro-QOL scales) in patients with MS, MMN, MG, and CIDP who receive IVIG treatment.

$H_0$1: The IVIG treatment experience (as measured by the Visual Analogue Scale) is not a significant predictor of quality of life (as measured by 10 Neuro-QOL scales) in patients with MS, MMN, MG, and CIDP who receive IVIG treatment.

RQ2: Does illness intrusiveness mediate the relationship between IVIG treatment experience and QOL (as measured by -10 Neuro-QOL scales) among individuals with autoimmune disease who received IVIG treatment?

$H_1$2: Illness intrusiveness mediates the relationship between IVIG treatment experience and QOL (as measured by 10 Neuro-QOL scales) among individuals with MS, MMN, MG, and CIDP.

$H_0$2: Illness intrusiveness does not mediate the relationship between IVIG treatment experience and QOL (as measured by 10 Neuro-QOL scales) among individuals with MS, MMN, MG, and CIDP.

RQ3: Does personal control mediate the relationship between illness intrusiveness and QOL (as measured by 10 Neuro-QOL scales) among individuals with autoimmune disease who receive IVIG treatment?

$H_1$3: Personal control mediates the relationship between illness intrusiveness and QOL (as measured by 10 Neuro-QOL scales) among individuals with MS, MMN, MG, and CIDP.

$H_0$3: Personal control does not mediate the relationship between illness intrusiveness and QOL (as measured by 10 Neuro-QOL scales) among individuals with MS, MMN, MG, and CIDP.

Theoretical Framework for the Study

The illness intrusiveness framework guided this research. The framework posits disease and/or treatment factors affect illness intrusiveness which then directly affects QOL. Illness intrusiveness is the intervening variable between the disease treatment and QOL (Devins, et al., 1983; Poochikian-Sarkissian et al., 2008a). According to this theory, QOL is compromised when the disease treatment interferes with goals, interests, and enjoyable activities. When treatment interferes with positive experiences, the perception of personal control is also diminished (Devins, 1994). Ultimately, illness intrusiveness directly influences QOL by reducing pleasurable experiences and indirectly by decreasing the patient's personal control (Devins, 2010).

The illness intrusiveness theory has been supported in various studies of different patient populations. Overall, research indicates more illness intrusiveness occurs in patients with severe disease symptoms (Cina & Clase, 1999; Devins, 2010; Devins et al., 1996; Devins et al., 1990; Devins, Edworthy, & ARAMIS Lupus State Models Research Group, 2000). Furthermore, regarding treatment factors, research shows increased illness intrusiveness is correlated with interrupting treatment schedules and side effects (Bettazzoni, Zipurski, Friedland & Devins, 2008; Devins et al, 1990; Devins et al., 1983; Poochikian-Sarkissian et al., 2008a). Personal control has been found to partially mediate the impact of illness intrusiveness on subjective well-being (Poochikian-Sarkissian et al., 2008a). Finally, evidence supports the premise that disease and treatment impact psychosocial results through the indirect effect on illness intrusiveness (Bloom, Stewart, Johnston, & Banks, 1998; Devins, 1994; Devins, Beanlands, Mandin, & Paul, 1997;

Devins, Edworthy, Guthrie, & Martin, 1992; Mullins et al., 2001). Using the illness intrusiveness framework here was appropriate due to potential mediating effects of illness intrusiveness on the relationship between IVIG treatment and the outcome QOL. The illness intrusiveness framework will be explained in more detail in Chapter 2.

Nature of the Study

I selected a non-experimental, correlational survey research design for the current study as this was appropriate to assess the relationship between two or more variables (Stangor, 2011). The predictor or independent variable was the IVIG treatment experience and illness intrusiveness. The dependent or outcome variable was QOL. Additionally, mediation analyses were employed to examine if the relationship between the predictor variable, IVIG experience and QOL, was mediated by illness intrusiveness and personal control. Data were collected from MS, MG, CIDP, and MMN patients receiving IVIG treatment at PNA in Phoenix, Arizona. I distributed surveys to those patients willing to participate in the study. Data were analyzed using regression analysis to assess the direct and indirect effects of illness intrusiveness and personal control on the relationship between the treatment experience and QOL. Bootstrapping was used as a robust test to measure indirect effects. A correlational, cross-sectional design was the best choice for assessing the relationship of the proposed variables as an experimental design would be impossible to conduct with this population receiving treatment on different schedules and time periods (Trochim, 2006). Disadvantages and limitations associated with this type of design are discussed later in this chapter.

Definitions

Autoimmune disease: Autoimmune disease occurs when the immune system (autoantibodies) in the body attacks healthy immune cells. It is a chronic disease that targets tissue and organ systems, and occurs due to the loss of immune tolerance (Anaya, 2010).

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): CIDP is a chronic autoimmune disease which is progressive or relapsing. Characteristics may be fatigue, muscle weakness, loss of balance and reflexes, and sensory dysfunction (Dalakas, 2010; Mathey & Pollard, 2012).

Illness intrusiveness: Illness intrusiveness is a construct derived from disease or treatment interruptions of desirable interests and activities (Devins, 2010). It is a mediating variable of chronic disease and/or treatment and QOL (Poochikian-Sarkissian et al., 2008a).

Intravenous immunoglobulin (IVIG): IVIG is a product of the blood developed from the serum of 10,000 to 15,000 donors per each lot. It is the select treatment for people with antibody deficiency and is given in a variety of neurological, autoimmune, and inflammatory diseases because of the immunomodulatory and anti-inflammatory properties (Hartung et al., 2009; Jolles, Sewell & Misbah, 2005).

Multifocal motor neuropathy (MMN): MMN is a progressive immune-mediated disease identified by asymmetric weakness in the arms and legs without sensory loss. It usually affects the upper limbs more than the lower limbs with neuropathy (Nobile-Orazio, 2001).

Multiple sclerosis (MS): MS is a progressive neurological inflammatory demyelinating disease. Functional impairment may include loss of balance, walking ability, muscle spasticity, and overall mobility problems (Pike, Jones, Rajagopalan, Piercy, & Anderson, 2012).

Myasthenia gravis (MG): MG is an antibody-mediated autoimmune disease of the neuromuscular junction (Dalakas, 2010). It is characterized by muscle weakness and fatigability with involvement of the central nervous system (Sitek, Bilińska, Wieczorek, & Nyka, 2009).

Neurological autoimmune disease: An autoimmune disease affecting the central or peripheral nervous system (Kamm & Zettl, 2012).

Personal control: Personal control is also referred to as locus of control. For the purpose of the current research study personal control refers to the individual's expectations regarding their own ability to influence outcomes by their own behavior (Rotter, 1990).

Quality of life (QOL): QOL is defined for the purposes of this study as the "individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectation, standards and concerns" (The World Health Organization Quality of Life Group [WHOQOL], 1995, p. 405).

Assumptions

Since the data in this study were collected through a self-report questionnaire, I assumed the participating patients were honest in their responses. I described the

procedures to protect the confidentiality and anonymity of the patient responses, so that they felt more encouraged to respond honestly. Additionally, all participants were volunteers and had the ability to withdraw from the study at any time. It was assumed the four autoimmune diagnoses examined in this study were representative of neurological patients who receive IVIG treatment (Padua et al., 2005). An underlying assumption in this study was that QOL will continue to be an important factor to patients receiving medical treatment and to the medical staff serving them. This assumption was supported by the current research literature examining QOL in patients with chronic disease.

Currently, many neurological patients with the medical diagnoses being examined in this study receive IVIG treatment. Another assumption of this study was that IVIG will continue to be a medical treatment for these diseases, and therefore, such an examination of this experience in the patient's lives was relevant. I also assumed that the neurological autoimmune patients involved in the study considered their entire IVIG experience when answering the questionnaires rather than just one daily event. This was taken into consideration in the forming of the single-item IVIG experience visual analogue scale. The single-item question has been used at length for assessing QOL and health related QOL (Bowling, 2005).

Limitations

The study design had inherent limitations that threaten external validity. Given that the source of the accessible population is the PNA in Phoenix, Arizona, the sample may be representative of the accessible population, while not necessarily being representative of the national neurological autoimmune population. Additionally, the

sample was selected using patient volunteers between the ages of 18 and 80 who fulfilled the criteria of the study based on having one of the four diseases (MS, MMN, MG, or CIDP) and were not randomly selected, further limiting external validity. However, I reported the demographic characteristics of the sample, so that descriptive comparisons to the published literature reporting on patients with the same diagnosis receiving IVIG treatment. Proximal similarity is discussed by Trochim (2006) as another approach to *generalizability* which was a relevant consideration after the data was analyzed. It would involve thinking of other settings, clinics, or facilities which may have similar IVIG treatment infusions centers with similar patients and then developing a theory as to whether proximal similarity might exist between persons, settings, or times.

Regarding internal validity, a limitation of correlational studies is that a causal relationship conclusion cannot be drawn among the variables (Stangor, 2011). Although the study may observe a relationship between the measured variables, cause cannot be concluded without question. It is also possible that reverse causation can occur when using mediation since both the mediator and the outcome variable are not manipulated (Kenny, 2014). Additionally, spurious relationships are possible due to a common-causal variable which may be relevant but is usually unknown to the researcher (Stangor, 2011). One method of weakening reverse causation would be to use longitudinal research, which was not feasible in my study given my time and resource limitations. On the other hand, correlational research is worth doing as it often provides useful information regarding the relationships among the variables and directions for future longitudinal research (Stangor, 2011).

Construct validity relates to how well the theoretical concepts are measured by the measuring instrument (Frankfort-Nachmias & Nachmias, 2008). Evidence (described in detail in Chapter 3) supports the construct validity of the illness intrusiveness instrument and its use across a large range of conditions (Devins, 2010; Shawaryn et al., 2002). However, discriminative validity across disease stages has not been supported. The underlying factor structure supports the invariance of the Illness Intrusiveness Rating Scale (IIRS) Confirmatory factor analysis supports the IIRS three factor structure of the subscales showing invariance across eight patient groups (Devins, 2010).

The Neuro-QOL, used to measure the outcome variable, was tested across five adult chronic illness samples and two pediatric samples and demonstrated good construct validity (Cella et al., 2011). The Multidimensional Health Locus of Control scale (MHLC), which will be used to measure control, has shown substantial construct and concurrent validity (Wallston, Stein, & Smith, 1994). Psychometric support of these measures is also detailed in Chapter 3.

Delimitations

The patients selected for the current study were restricted to MS, MMN, MG, and CIDP patients between the ages of 18 and 80. The participants were receiving IVIG treatment at PNA in Phoenix, AZ. Some patients fitting the criteria may have chose not to participate, which would affect how well the final sample of the participating IVIG patients represented those who typically attend the treatment facility. Data were collected using self-report questionnaires written in English requiring respondents to be proficient in reading and understanding English.

An experimental or quasi-experimental design was not feasible. Therefore, there may have been a selection bias of the participant pool which could be a threat to internal validity, particularly given that there was no comparison group (i.e., patients receiving another form of treatment). A cross-sectional design was justifiable, given that (a) there was an accessible population meeting the sampling criteria, (b) this particular medical treatment is being used more often with these diagnoses, and (c) that there has been no research assessing the relationship between the IVIG treatment experience and QOL (PNA, 2014). One of the theoretical frameworks that might be related to this area of study in the future is coping theory (Folkman et al., 1986) as patients may indeed require coping skills and abilities while undergoing this often on-going medical treatment. This was considered during the design of the study but was eliminated as it would expand the scope and length of the dissertation.

Significance

I examined MS, MMN, MG, and CIDP in this study, and they fall into the four distinct general categories for neurologic autoimmune diseases (Dalakas, 2004). The loss of immune tolerance characterizing these diseases results in changes in mobility and life styles. Research shows people living with these four neurological autoimmune diseases indicate a lower QOL than healthy individuals (Benito-León, Morales, Rivera-Navarro, & Mitchell, 2003; Cocito et al., 2006; Mitchell, Benito-León, González, & Rivera-Navarro, 2005). These conditions, once thought to be untreatable, are now being treated with IVIG on a short and long term basis. IVIG has shown positive effects on the physical aspects of neurological autoimmune disease, but there is not research

illuminating the psychological effects of the treatment experience. This study provides information useful to the providers regarding the IVIG experience as it relates to the psychological aspects and health related QOL. While shown to be beneficial, IVIG is costly and may or may not be covered by insurance companies. This in turn can contribute to psychological stress for the patient.

As a result of the findings of the study, interventions might be planned based on the understanding about some of the patient's perceptions of their IVIG experience and how this experience has affected their daily lives (K. Clarke, personal communication, May 21, 2014). It is very possible that results of this study would be of interest to an IVIG nurse association and could be disseminated through writing or public addressing such a group (C. Gooch, K. Clarke, & S. McBride, personal communications, December, 2013 through May 2014). Presenting the results of this research might very well provide needed data to assist the medical staff in accommodating some patient related needs for scheduling, etc. Both nurses and neurologists have expressed interest in results from such a study, and so I plan on presenting the work after completing the study.

Implications on Social Change

The results of this study could contribute to positive social change by providing knowledge of IVIG and QOL and subsequently influencing policy makers to evaluate and increase the availability of this medical treatment. The nursing staff and physicians I have interviewed maintain there are many rules and regulations as well as availability which make infusions sometimes challenging (C. Gooch, K. Clarke, & S. McBride, personal communications, December, 2013 through May 2014). Part of the problem according to

staff is that there is little research available documenting the relationship of IVIG experience to QOL.

It is not unreasonable to assume that even pharmaceutical companies may be interested in the results of this study. For example, Biofusion, a pharmaceutical distribution company employs a patient advocate who travels to various locations assisting patients needing this treatment (S. McBride, personal communication, May 18, 2014). Understanding the relationship between IVIG and QOL, particularly the role of illness intrusiveness in this relationship, could provide information needed for a medical staff to develop interventions which might have an effect on the patient's ability to cope with those life interruptions. For example, perhaps such knowledge would guide the medical team to adjust schedules to decrease the intrusion on employment or leisure activities or provide counseling to assist patients in coping with the life changes.

The study has positive implications for social change for both patients and medical personnel. Social change may occur when medical teams, families, physicians, and insurance companies have a deeper understanding of the relationship of this treatment on QOL in neurological autoimmune patients and act on that understanding. Walden University (2013) deems "positive social change results in the improvement of human and social conditions" (p. 13). This study has the potential of positive social change by contributing to the dignity and understanding of the effects of IVIG treatment on the QOL in the lives of MMN, MG, MS, and CIDP patients through making results available to various stakeholders. Results of this study will be distributed to the staff at PNA where the nursing staff, physicians, and research coordinator have been supportive

and are anticipating results. Members of the IVIG infusion nurses' association have also expressed a desire for a presentation of results through speaking at their yearly meeting held at different locations in the United States (K. Clarke, personal communication, May 20, 2014; S. McBride, personal communication, June, 2014). It may be possible that Gamunex (one of the types of IVIG) may be interested in having me present the results of the study (T. Levine, personal communication, May 20, 2012). Biofusion, a pharmaceutical distribution company which provides IVIG across the United States for those receiving IVIG at home, may be interested in the results of the study as well as they have shown concern for the well-being of IVIG patients by providing a patient advocate for assisting patients in coping with the IVIG experience.

Summary

Literature has established the neurological autoimmune diseases are debilitating physically and psychologically. Research has demonstrated MS, MMN, MG, and CIDP experience a lower QOL compared to healthy individuals (Erdmann, Lindeman, Cats & van den Berg, 2010; Kargiotis et al., 2010; Leonardi et al., 2010; Westblad et al., 2009). Consequences from neurological autoimmune disease usually mean problems in the central and/or peripheral nervous system. Although many of these diseases can be effectively treated with IVIG, the high cost of medicine and interruption to life style can negatively impact the patient's ability to participate in social events, family interactions, and employment. The effect of this treatment experience may in turn lead to illness intrusiveness which may negatively impact a patient's QOL. The fact that only one study exists examining IVIG and QOL with these four neurological autoimmune diseases

(Padua et al., 2005) and no studies exist examining the relationship between IVIG, illness intrusiveness and QOL in these diseases leaves a serious gap in the literature that causes medical staff to speculate rather than make informed decisions regarding treatment plans and care in the effort to maximize this medical treatment. It was imperative that the relationship of illness intrusiveness, IVIG treatment, and QOL was examined in hopes of better understanding neurological autoimmune patients. This study hypothesized that illness intrusiveness plays an important role in the relationship between IVIG treatment and QOL in neurological autoimmune patients with MS, MMN, MG, and CIDP.

In Chapter 2, I provide a review of current literature regarding neurological autoimmune diseases, QOL, IVIG treatment, and Illness Intrusiveness. In Chapter 3, I explain the method and research design and the research questions and hypotheses. I also discuss data collection, sampling method, instrumentation data analysis, and ethical protection of participants.

Chapter 2: Literature Review

Introduction

It is estimated that 23.5 million individuals in the United States endure autoimmune disease, and the prevalence is increasing (USDHHS, NIH, 2005). Autoimmune diseases can be viewed as a group of related disorders with common characteristics that can be studied together or separately. They are a burden to individuals and society, reducing QOL and increasing medical costs (NIH, 2005). The study focused on autoimmune diseases.

Currently, there is no known cure for most autoimmune diseases, such that large numbers of patients face a life of chronic disease and treatments. Autoimmune diseases can lead to loss of mobility, sensory and nerve loss, pain, and damage to tissues or cells, which may lead to interferences in the individual's interests and activities (Devins, 2010). This interference may lead to illness intrusiveness (Devins et al., 1990; Poochikian-Sarkissian et al., 2008a). Illness intrusiveness is the result of a chronic disease interfering with valued goals and activities; it can compromise (QOL) through diminishing positive outcomes from valuable or gratifying experiences and by restricting one's ability to avoid negative outcomes (Devins, 2010).

Antibodies are proteins which help an individual to resist infections, but when an antibody becomes directed to a person's own tissues it is referred to as an autoantibody (USDHHS, NIH, 2012). IVIG is common in the treatment of autoimmune diseases (i.e., diseases where antibodies have become autoantibodies) (Dalakas, 2004). Although the

medical efficacy of IVIG has been established (Dalakas, 2008; Hughes, 2008; Hughes et al., 2009), there is little research regarding the effects of the IVIG treatment experience on QOL. IVIG will be discussed in depth in this chapter.

In this chapter, I review IVIG treatment in autoimmune neurological disorders, QOL and illness intrusiveness in autoimmune diseases, and explore the role of the variable personal control on the relationship between illness intrusiveness and QOL. My review will include information regarding the physical, mental, and social domains of QOL as indicated in the Neuro-QOL instrument which was used in this study. The review will also include information on IVIG and the four autoimmune diseases being compared: MS, MMN, CIDP, and MG. Although there are several studies relating to illness intrusiveness, QOL, and (Devins, Seland, Klein, Edworthy, & Saary, 1993; Shawaryn et al., 2002), there have been no studies examining the relationship of illness intrusiveness and IVIG treatment experience with this population. Furthermore, there have been no studies found examining illness intrusiveness and IVIG in MG, CIDP, or MMN patients.

The search strategy included the following search engines: PubMed, the Walden Library dissertation database, ProQuest Dissertations, Thoreau Walden University Discovery Service, PsycARTICLES, Google Scholar, and EBSCOhost Academic Search Complete. Topics researched included: *illness intrusiveness, autoimmune diseases, intravenous immunoglobulin treatment in autoimmune diseases, chronic disease, multiple sclerosis, multifocal motor neuropathy, chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, depression, social support,* and *perceived control*. Although the majority of the research focused on articles from 2002–2012, in some cases

seminal articles relevant to major concepts or variables were reviewed. Early illness intrusiveness research studies from 1990–2002 were important in establishing seminal findings related to the construct of illness intrusiveness and some chronic illnesses. Although there were articles relating to IVIG and the medical components of QOL, there was a scarcity of research on IVIG and QOL. Therefore, studies were examined that looked at depression, social support, and control often associated with chronic disease in general.

Autoimmune Disease

The human body is defended against invading pathogens such as viruses, parasites, and bacteria by the immune system (Jäger & Kuchroo, 2010). The ability of the immune system to recognize self from nonself is required in order for unwanted pathogens to be cleared effectively (Jäger & Kuchroo, 2010). Immune cells that are self-reactive and are not eliminated present danger to the individual's health and autoimmunity can develop (Jäger & Kuchroo, 2010). A deficit in immunological tolerance to self-antigens signifies the beginning of autoimmune disease (Anya, 2010). Damage occurs through T cells and B cells in the preclinical stage of the pathophysiology of autoimmune disease (Anaya, 2012). Autoimmune diseases are usually chronic and heterogeneous, directed at organ systems as well as specific organs (Jäger & Kuchroo, 2010). An example of an autoimmune disease attacking a specific organ is found in Type I diabetes, whereas lupus erythematosus is an example of an autoimmune disease in which the self-antigen extends through the body inflaming tissue in many different organs (Jäger & Kuchroo, 2010). There are indications that autoimmune diseases share

common origins as they often have some of the same clinical symptoms, predisposing genetic factors, and similar physiopathological mechanisms (Anaya, 2012). Interestingly, autoimmune diseases attack women disproportionately, and are a significant cause of death in middle-age women (Anaya, 2012). For example, 80% of the 5% who contract autoimmune disease worldwide, are women (Fairweather, Frisancho-Kiss, & Rose, 2008).

Multiple Sclerosis (MS)

Multiple sclerosis (MS) is an inflammatory neurological disease of the central nervous system, with genetic and environmental influences affecting the risk of contracting the disease (Hemmer, Nessler, Zhou, Kieseier, & Hartung, 2006). It has long been accepted that MS has two components, an inflammatory demyelination stage which occurs early in the disease and a neurodegeneration stage which transpires as a result of repeated inflammation (Charil & Filippi, 2007). However, Charil and Filippi (2007) posited that both demyelination and neurodegeneration may occur simultaneously. Regardless of when they occur in MS (early or late in the disease process), they are important aspects of this chronic disease. Demyelination is defined as damage to the myelin with preservation of the axons caused by diseases that destroy the myelin sheath and/or the cells which create them (Love, 2006). Demyelination can occur in the brain, optic nerves, spinal cord, and brain stem in multiple sclerosis (Trapp & Nave, 2008).

The other primary disease process is neurodegeneration which is referred to the progressive loss of neuron function or structure and sometimes neural death (Choudhury, Saytode, & Shah, 2014; Koch, Uyttenboogaart, van Harten, Heerings, & De Keyser,

2008). Chronic progression of the disease may be related to the axonal degeneration where the relapses in MS are most often attributed to the central nervous system (CNS) inflammatory demyelination (Koch et al., 2008). Chronic fatigue often accompanies MS and may be affiliated with the chronic progression in the disease (Koch et al., 2008).

Research has found that individuals living with MS, MG, CIDP, and MMN have a lower QOL than healthy populations (Benito-León et al., 2003; Cocito et al., 2006; Mitchell et al., 2005) and fatigue, pain, personal control, and social support may all play a role in the QOL of these patients. For example, fatigue is a disease outcome of all four diseases which were examined in this study as it relates to QOL in autoimmune patients (Greim, Engel, Apel, & Zettl, 2007; Merkies & Faber, 2012). If the illness intrusiveness from MS, CIDP, MMN, and MG is such that desired activities are diminished, it may follow that patient's QOL might also be negatively influenced. Although Shawaryn et al. (2002) showed illness intrusiveness mediated the QOL and MS relationship, research regarding illness intrusiveness and QOL in CIDP, MMN, and MG has not been presented in the literature. A goal of the present research study was to extend research further by assessing the QOL of MS, MMN, CIDP, and MG patients receiving IVIG and determining whether illness intrusiveness mediated the relationship between IVIG and QOL.

Myasthenia Gravis (MG)

MG is an acquired chronic autoimmune disease characterized by fatigue and weakness with a prevalence of about 200 people per million in the United States (Meriggioli & Sanders, 2009). This neuromuscular junction disease demonstrates

painless voluntary muscle weakness in specific muscle groups, which can include ocular weakness in 85% of individuals with the disease (Maggi & Mantegazza, 2011). Other symptoms may include problems in swallowing and respiration (Kulaksizoglu, 2007). The disease course is unpredictable and diagnosis can be difficult due to similarities to other diseases and variable disease characteristics (Juel & Massey, 2007). MG is a disease which most often appears in women younger than 40 and after age 50 may occur more often in men (Juel & Massey, 2007). Fatigue can change by the hour and/or day and sustained exercise may exacerbate the fatigue (Juel & Massey, 2007). Daily activities may become difficult to sustain, respiratory infections can be lethal, and QOL minimized as a result of MG (Kulaksizoglu, 2007). IVIG provides short term improvement in strength and is used for MG crisis and exacerbations (Juel & Massey, 2007; Maggi & Mantegazza, 2011).

Multifocal Motor Neuropathy (MMN)

MMN is an immune-mediated chronic disease with demyelination of the motor nerve fibers and a prevalence of 1–2 per 100,000 (Nobile-Orazio et al., 2005). Progression is usually slow with a stepwise course with partial conduction block (Nguyen & Chaudhry, 2011). It is characterized by multifocal weakness of limbs without loss of sensation (Erdmann et al., 2010), but has been reported to have more asymmetric weakness in the upper extremities rather than the lower (Erdmann et al., 2010). In addition to limb weakness MMN patients often have activity restrictions and problems with general functioning including difficulty moving and walking, muscle strength problems, and interacting in activities of enjoyment which affect QOL (Erdman et al.,

2005). The majority of MMN patients have problems with dexterity making daily manual jobs challenging (Van den Berg-Vos et al., 2002a). According to Nguyen and Chaudhry (2011), MMN is a treatable disorder which responds well to IVIG and affects men more than women (3:1 ratio). Treatment can sometimes be long-term with IVIG transpiring over years (Van den Berg-Vos, Franssen, Wokke & Van den Berg, 2002b). IVIG is the primary treatment which is effective in this immune mediated disease, but it is expensive and the required frequency of treatments are burdensome for patients to maintain (van Asseldonk, Granssen, Van den Berg-Vos, Wokke, & Van den Berg, 2005).

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

CIDP is an autoimmune disease usually manifesting during the ages of 30 to 60 (Dalakas, 2010). Seminal research indicates CIDP became a recognized medical entity in 1975 when the disease characteristics were originally defined (Dyck et al., 1975). Symptoms are often progressive advancing over a minimum of 2 months and are characterized by sensory dysfunction, progressive muscle weakness usually symmetric, with loss of balance, and absent or reduced tendon reflexes (Dalakas, 2010; Mathey, & Pollard, 2012). Dalakas (2010) indicated the disease can be marked by periods of spontaneous remission causing re-evaluation of treatment. CIDP can cause permanent disability when it occurs in children, although response to treatment may be more favorable than with adults (Dalakas, 2010). Diagnosing CIDP correctly at the outset through electrophysiological testing, cerebrospinal fluid analysis, and/or nerve biopsy is vital to determine responsiveness to immunotherapies and distinguish CIDP from those autoimmune disorders which do not respond to immunotherapies (Dalakas, 2010).

Finally, treatment goals for CIDP include improving motor performance, strength, balance, and QOL which is approached through corticosteroids, IVIG or plasmapheresis (Dalakas, 2010). Since long term therapy is often necessary for CIDP patients, it is reasonable to imagine QOL may be compromised in these individuals. Since this study specifically relates to patients with CIDP who are receiving IVIG treatment, it is important to note that the ICE study suggested IVIG as a first line therapy for CIDP and led to a Federal Drug Administration (FDA) approval of one particular brand of IVIG for CIDP patients (Hughes et al., 2008). The cost and availability of IVIG may limit this potential therapy for some CIDP patients (Mathey & Pollard, 2012).

Intravenous Immunoglobulin (IVIG) as a Treatment for Autoimmune Disease

Antibodies are proteins which help an individual to resist infections, but when an antibody becomes directed to a person's own tissues it is referred to as an autoantibody (USDHHS, NIH, 2012). Autoantibodies are the root of autoimmune disease and of the intrusive debilitating factors and treatments those diseases can bring on the individual. IVIG is a preparation produced from over 5,000 blood donors providing healthy antibodies for treatment in patients with a variety of diseases (Jolles et al., 2005). A large pool of donors provides a larger number of diverse immunoglobulins (IGG) compared to one individual, which may be instrumental in the treatment result (Stangel, Hartung, Marx, & Gold, 1998). It is given as replacement plasma protein therapy to individuals who are lacking and deficient in antibodies (Stangel et al., 1998). IVIG is used as treatment for neurological disorders and autoimmune diseases that impact the peripheral nerves, central nervous system, or neuromuscular junction, including the four diseases

that were the focus of this study, CIDP, MMN, MG, and MS (Dalakas, 2004). The IVIG is administered as replacement treatment every 3 weeks in the amount of 200–400 mg/kg body weight. A high dosage of IVIG (2 g/kg/month) is given to individuals with inflammatory and immune disorders usually in two doses on alternate days or if there is a concern about potential side effects, it may be given over 5 days (Jolles et al., 2005).

The action mechanisms by which IVIG works seems to depend on the disease pathogenesis and the dose of the immunoglobulin given to the patient (Jolles et al., 2005). It is believed IVIG produces therapeutic effects by influencing certain elements of the immune system including macrophages, B-cells, cytokines, T-cells, complement and cellular adhesion molecules (Jacob & Rajabally, 2009). Hartung (2008) explains IVIG contains IgA and IgM antibodies, Th2 cytokines, and cytokine antagonists which may support the therapeutic results. IVIG inactivates auto-reactive T-cells and restores the balance of cytokines (Hartung, 2008). Importantly, IVIG is hypothesized to block auto-immune T-cells from entering the blood-nerve barrier (Hartung, 2008). IVIG is also surmised to prevent harmful activity in production of B-cells and may affect innate immunity. Finally, IVIG results in a down-regulation of the immune response which may be beneficial in neurological immune diseases and neuromuscular disorders (Hartung, 2008).

The benefits of using IVIG in therapy include a broad action range and safety. It is able to block B-cells, T-cells, macrophages, and antibodies at various sites which are particularly useful in neurological inflammatory conditions (Hughes, 2008). IVIG does not have the side effects exhibited by steroids or immunosuppressive therapy but patients

can experience some mild or moderate side effects which may include headaches, fever, or a stiff neck following the infusion (Jolles et al., 2005). According to Jolles et al. (2005), slowing or adjusting infusion time, and giving pre-medications can help to minimize the side effects. Problems that can arise with IVIG treatment include cost and shortage of supply (Hughes, 2008).

Historically, there was a shortage of IVIG worldwide in 1997 due to an interruption in production caused by the more rigorous U. S. Food and Drug Administration regulations (Feasby et al., 2007). A similar shortage of IVIG has not re-ensued but this continues to be a very expensive therapy, and rising costs have caused insurers and hospitals to question the cost effectiveness of the treatment (Jordan, Vo, Peng, Toyoda, & Tyan, 2006). In fact, the cost is considered the major negative aspect of IVIG treatment (Griffin & Hughes, 2009). The cost of IVIG has been on the rise and as of 2010 was approximately $70.22 per gram. The cost of an IVIG infusion (usually divided into two doses over a 2 day period) totaling 2.0 grams per kilogram (g/kg) of the average adult individual's body weight of 70 kilograms, would be about $10,000.00 (Winters, Brown, Hazard, Chainani, & Andrzejewski, 2011.). Private insurance will pay for IVIG in many cases depending on the diagnosis. Medicare will pay for IVIG to be received for some diagnoses, but will allow only primary immune deficiency disease to be covered in the home setting. The at-home coverage is for the medication only and not for the nursing care required. Some IVIG will be covered by Medicare under part D, but again it depends on the plan. Medicare will cover 80% of IVIG in the hospital setting for diagnoses allowed for this treatment and if the physician states it is medically necessary

which means that the patient pays the remaining 20% out of secondary insurance or out of personal resources (Medicare, 2014).

The Effects of IVIG Treatment

Since most autoimmune diseases have the comparable problem of one part of the body immune system attacking another part of the body instead of protecting the body against viruses and bacteria, IVIG is helpful in that it is considered to contain antibodies which seems to block the attack (PNA, 2014). The overall length of treatment with IVIG for neurological autoimmune patients varies with the individual's diagnosis and the response to the therapy. For example, for some autoimmune patients treatment is repeated every 4 to 6 weeks and for others it may be a few weeks or months (PNA, 2014). Usually, for a 2-GMs/kg dose given over a period of 2 days each daily treatment would be approximately 4 to 6 hours in length (PNA, 2015). Each patient is evaluated regularly by the neurologist to determine the effectiveness of the treatment. In some cases, patients continue to receive this IVIG therapy for a lifetime. Immediate physical results of an IVIG treatment also may differ with the individual patient response. For example, some patients experience physical benefits (improved strength or mobility) the same day of the treatment while others may not experience physical improvements for a day or two (PNA, 2015). Benefits from IVIG include less fatigue, improved strength, and increased mobility and less dependency for activities of daily living (PNA, 2014). Potential negative side effects may be headache, chills, and fever with serious side effects such as renal failure and thrombotic events being rare (Hughes & Lunn, 2012).

Measurement of IVIG Treatment Experience

Measurement of IVIG treatment experience/impact was accomplished through a single item question in a Visual Analog Scale. This appeared to be the best option as there is no measurement already created to examine the IVIG experience, and the experience consists of a number of disparate dimensions, such as timing/schedule intrusion, cost and discomfort, in addition to the benefits (decreased symptoms, better mobility, etc.). Using this measurement will allow the patient population to consider their overall IVIG experience after thinking about all these factors. This possibility has been discussed with the medical experts who agreed this would be a feasible alternative to creating a new measurement. Academic experts were consulted who thought this would be the best option since there is not an instrument available (C. Gooch, K. Clarke, & S. McBride, personal communications, December, 2013 through May 2014).

Single item questions have been useful in research especially when there is limited time or the need to reduce patient burden (Davey, Barratt, Butow, & Deeks, 2007). A single item Visual Analog Scale (VAS) was used to measure anxiety with good comparability to a longer STAI instrument (Davey et al., 2007). Patients are able to mark their subjective responses on the VAS A and it is simple and rapidly administered. The VAS-A computerized single-item measure was shown to be a beneficial tool self-rating state anxiety (Abend, Dan, Maoz, Raz, & Bar-Haim, 2014). A different study found a single item VAS to have excellent reliability, good validity and responsiveness compared to multi-item questionnaires when assessing global quality of life (de Boer et al., 2004). Moreover, the single item VAS was found to be the best instrument to assess pain in

fibromyalgia patients (Bigatti & Cronan, 2002). In the light of previous literature, it seemed reasonable to use this approach for the predictor variable, IVIG treatment experience. Recommendations for future research in measurement development are presented in Chapter 5.

Theoretical Foundation

Two theoretical frameworks were selected to guide the proposed research. Illness intrusiveness theory focuses on the extent to which valued interests and activities are disrupted by disease factors and treatment (Devins, 2010; Poochikian-Sarkissian et al., 2008a). Personal control theory focuses on the person's belief in the ability to control the important parts of one's life through their own actions and choices (Rotter, 1966).

The Illness Intrusiveness Model

Chronic disease presents challenges such as disability, pain, and symptoms which may require patients to surrender jobs resulting in economic adversity, reduce ability to participate in enjoyable activities, and institute dependence on medical systems for day to day living. These disruptions are considered stressors which interfere with lifestyles and psychologically meaningful interests and activities (Devins, 2010). The construct is defined as the degree the patient's disease factors and/or treatment interfere with the person's continued activities or social roles which are important to him in life. Although illness intrusiveness is a molar construct, it can have a variety of sources such as loss of function, treatment side effects, financial stress due to treatment requirements, and lifestyle disruptions (Devins, 2010). The construct of illness intrusiveness arising from disruptions caused by illness and treatment interferences in one's lifestyle may result in

compromised QOL. The main tenet of the theory is that aspects of the disease and treatment reduce QOL through two pathways: decreasing accessibility to pleasurable experiences and diminishing the individual's feelings of personal control (Devins, 2010).

Illness intrusiveness refers to ways in which disease and treatment interfere with the individual's daily life (Devins et al., 1983). In particular, illness intrusiveness considers the extent a particular illness or its treatment may impede the patient's routines, opportunities, and goals. Illness intrusiveness arises from functional deficits, anatomical changes, and physical limitations (Devins, 2010; Devins et al., 1992; Shawaryn et al., 2002). Illness intrusiveness may be predicted by physical and psychological factors. Snyder, Foley, Farrell, Beier, and Zemon (2013) found depression, anxiety, and disability each independently predicted illness intrusiveness. Illness intrusiveness has been applied in a variety of chronic disease studies as an important construct (Beanlands et al., 2003; Dancey et al., 2002; Franche et al., 2004; Paukert, LeMaire, & Cully, 2009; Schattner, Shahar, Lerman & Shakra, 2010). Early illness intrusiveness studies indicate Devins (the author of the illness intrusiveness theory) used QOL and subjective well-being interchangeably in the illness intrusiveness model (Bloom et al., 1998; Poochikian-Sarkissian et al., 2008a). However, over the years Devins' viewpoint has evolved. Currently, Devins (personal communication, June 1, 2014) now views subjective well-being as one facet of QOL. Additional factors in QOL might be objective QOL (e.g., education, owning a home,), utilities (importance the individual places on their life as affected by the disease compared to a life free of disease), and health-related QOL (treatment side effects, symptoms and/or social and physical difficulties caused by the

disease; personal communication, June 1, 2014). In the present study, I specifically examined the relationship between the IVIG treatment experience and the health related facet of QOL (how the treatment experience has affected symptoms, social and physical challenges of the treatment) mediated by illness intrusiveness.

The illness intrusiveness model does not suggest that disease and treatment have direct effects on QOL, but rather the factors associated with the disease or treatment such as complicated schedules, side effects, pain, lost time with family, and others impact QOL (Devins, 2010). It is a mediating variable between the disease and treatment factor and the quality of life of the patient. It is viewed as a stressor prompted by the disease and/or treatment experience which endangers QOL. Specifically, disease and treatment experience lead to illness intrusiveness and this in turn leads to changes in QOL (Devins, 1994; Devins et al., 2000; Devins et al., 1990). The theory posits illness intrusiveness is an intervening variable between disease circumstances and quality of life (Devins, 1983, 2010). In other words, Dancey et al. (2002) posited since it mediates between treatment conditions and psychosocial influence, illness intrusiveness is considered a primary element in the determination of chronic disease impact. In the current study illness intrusiveness was assessed as a mediator between the IVIG treatment experience and QOL.

Illness Intrusiveness as a Mediator. Mediation occurs when the relationship between the predictor variable (IVIG treatment experience) and the outcome variable (QOL) is altered or adjusted by the presence of the mediator variable illness intrusiveness (Kenny, 2014; Shawaryn et al., 2002). Illness intrusiveness has been shown to mediate

patient adjustment to chronic disease (Devins et al., 1990; Devins et al. 1992; Devins et al. 1997). Additionally, Bloom et al. (1998) found illness intrusiveness mediated the relationship between disease and treatment and QOL in a study with 308 young women with breast cancer indicating a relationship between illness intrusiveness and QOL

The correlation between QOL and illness intrusiveness has been demonstrated in a variety of conditions such as patients with MS (Devins et al., 1996; Mullins et al., 2001; Shawaryn et al., 2002; Snyder et al., 2013), young women with breast cancer (Bloom et al., 1998), cancer related stressors (Devins et al., 2013), men and women with irritable bowel syndrome (Dancey et al.,2002), sleep disorders, and patients with chronic dialysis (Mucsi et al., 2004), diabetes patients (Talbot, Nouwen, Gingras, Bélanger, & Audet, 1999), women with systemic lupus erythematosus (Devins et al., 2000), epilepsy (Poochikian-Sarkissian, Sidani, Wennberg, & Devins, 2008b), and end-stage renal disease (Devins et al., 1997).

Measurement of Illness Intrusiveness. Measurement of illness intrusiveness is accomplished through the Illness Intrusiveness Rating Scale (IIRS) which is a short, self-reporting instrument (Devins, 2010). Originally developed for chronic and life-threatening illnesses, it can be used for more moderate conditions as well to gain understanding about the degree of life disruptions. The IIRS is comprised of three subscales: instrumental, intimacy, and relationships and personal development (Devins, Bezjak, Mah, Loblaw, & Gotowiec, 2006). The 13 life domains identified under each subscale include: instrumental (financial situation, heath, work, and active recreation), intimacy (sex life and relationship with spouse), and relationships and personal

development (self-expression/self-improvement, family relations, community and civic involvements, other social relationships, passive recreation, and religious expression). The questions in the 13 life domains request patients to rate the degree the disease and/or treatment impede life domains essential to QOL (Devins, 2010; Devins et al., 2006).

Considering the brevity of the IIRS measure (13 items), Shawaryn et al. (2002) concluded that the IIRS could be a helpful screening tool for physicians and clinics which encounter time constraints evaluating their patients. Additionally, the IIRS might help identify patients who would be in need of additional services due to quality of life challenges or disruptions they experience due to disease and treatment. During a time when physicians are expected to evaluate high numbers of patients, it may be difficult to evaluate all the emotional and physical needs of each patient; therefore, the brief and easily administered IIRS may make problem identification for patients at risk more expeditious. It may serve to elucidate those individuals who may be experiencing life disruptions and intrusiveness from the chronic disease or treatment.

Chronic Disease and Illness Intrusiveness. The relationship of illness intrusiveness and chronic disease has been demonstrated in a number of studies. Previous research has shown increased illness intrusiveness with increased disease severity and symptoms (Devins et al., 1992; Devins et al., 1990; Devins et al., 1996; Goudsmit, Stouten, & Howes, 2009; Musci et al., 2004). Additionally, treatment factors have been shown to be affiliated with increased illness intrusiveness (Bettazzoni et al., 2008; Devins et al., 1990; Poochikian-Sarkissian et. al., 2008a). Assuaging the effects of disease through medical pathways (Poochikian-Sarkissian et al., 2008a, 2008b), or psychosocial

techniques reduces illness intrusiveness effects (Bennet et al., 2005; Carter, Bewell, & Devins, 2008; Edworthy et al., 2003). Research findings have indicated correlations between illness intrusiveness and concepts such as depression, QOL, social support, life domains, and control (Dancey & Friend, 2008; Devins et al., 2006; Neri et al., 2010; Talbot et al., 1999; Shawaryn et al., 2002). Some studies have suggested that psychosocial factors moderated the effects of illness intrusiveness (Beanlands et al., 2003; Devins et al., 1992; Devins et al., 2006; Franche et al., 2004) while other studies indicated that illness intrusiveness is the mediator between the disease and treatment for the individual patient (Bettazzoni et al., 2008; Devins, 1994; Devins et al., 2000; Devins, Edworthy, Leendert et al., 1993; Devins et al., 1990). Furthermore, early research into the construct of illness intrusiveness showed that a significant difference can transpire across treatment modalities as in the case of end-stage renal disease (Devins et al., 1990). Devins et al's (1990) study examined patients receiving dialysis in-center, at home dialysis and post-transplant patients ($N = 200$). Their study revealed a significant lower level of perceived intrusiveness of post-transplant patients compared to the three dialysis groups (continual ambulatory peritoneal dialysis, hemodialysis, and home dialysis). However, the three dialysis groups did not differ significantly in overall perceived intrusiveness. Another significant finding in this early research study on illness intrusiveness was a significant correlation between increased perceived illness intrusiveness and lower QOL. Additionally, increased depression significantly correlated with higher levels of perceived intrusiveness. Differences in treatment modalities showed significant differences in QOL and perceived illness intrusiveness. Life domains most

affected were the physical well-being and the work and finances. Research has also compared race-related differences in illness intrusiveness in chronic disease. Race-related differences have been shown to exist in women with systemic lupus erythematosus (SLE) with Caucasian women showing the highest level of well-being and African Americans the lowest level (Devins et al., 2000).

Illness intrusiveness in chronic diseases such as cancer can become prolonged over time. Sohl, Levine, Case, Danhauer and Avis (2014) found women experienced different levels of illness intrusiveness 2 years after breast cancer diagnosis. They found women with low illness intrusiveness were older, did not have children at home, were less apt to have a mastectomy or chemotherapy and few reported side effects such as pain. Those with higher intrusiveness were identified as having more problems paying for basic treatment and lower psychosocial scores. This study supported findings in previous studies (Bloom et al., 1998; Devins et al., 2006). Interestingly, some of the Sohl et al. (2014) treatment experiences of cancer patients may be similar with IVIG patients, e.g., financial cost of the therapy, and insurance issues. Age was found to play an important role in the illness intrusiveness of breast cancer with younger women showing significantly higher levels of illness intrusiveness affecting sexual relations, pain, and side effects of treatment and the ability to perform household chores (Avis et al., 2012). Furthermore, the IIRS was used to demonstrate illness intrusion in patients with atrial fibrillation (Dorian et al., 2000).

Receiving IVIG May Influence Illness Intrusiveness. Autoimmune disease patients receiving IVIG may experience different treatment modalities such as IVIG in

the hospital setting, neurological clinic, or at home which may affect intrusiveness in the life domains. Treatment for neurological disorders can impact QOL domains of physical, psychological, social, and environmental health (Cella et al., 2012). For example, most treatments for neurological disease aim to improve the physical functioning of the patient, but the nature of the treatment may interfere with valued interests, activities and goals of the patients. Treatments may be painful, time consuming and costly, restricting a patient from employment or social responsibilities.

Requirements of this treatment can change the individual's lifestyle and range of activity participation. For example, IVIG must be administered by medical personnel in most cases requiring special environments such as clinics or hospitals. Administration of IVIG occurs over a period of 3–5 hours and fluctuates from every 4–6 weeks. Sometimes a patient must receive infusions two to three times a week. The frequency of IVIG can interfere with work schedules, family routine or pleasurable activities. Transportation to and from hospitals or clinics and scheduling may become a challenge which in turn interferes with the person's daily routine and family life. Employment and finances may be negatively impacted with IVIG due to interfering infusion schedules (each infusion is about 3–4 hours long, sometimes longer). Home administration of IVIG can pose psychological, insurance and financial challenges as well.

In some cases, individuals have physical reactions to the IVIG which may create medical complications. Patients require monitoring for side effects which may transpire during or after the infusion. Since II is characterized by interference in an individual's

way of life and control of positive outcomes (Devins, 2010), administration of IVIG treatment sets the stage for illness intrusiveness.

Personal Control

The second theoretical framework used in this study was personal control, which refers to the individual's belief in the ability to control the important parts of one's life through their own actions and choices (Rotter, 1966). Control has been studied in the literature at length from links to medical health, substance abuse and psychological issues to correlations with other stress related life issues such as unemployment. Kobasa (1979) described hardiness as characteristic of personality composed of control, commitment and challenge. For example, control is described as one feature of psychological hardiness which may assist the individual in coping with workplace stress by behaving in ways to reduce stress (Lambert, Lambert & Yamase, 2003). Moreover, the personal control component has been found to predict well-being in the workplace (Nayyeri & Aubi, 2011). Additionally, personal control has been found to be a resilience factor in coping with daily stress with higher levels of control correlating with lower reactions to stress (Neupert, Almeida, & Charles, 2007; Ong, Bergeman, & Bisconti, 2005). In another study Diehl and Hay (2010) found perceived personal control acted as a resilience factor in coping with stress as well as buffering reactions to it. Personal control was shown to be a significant predictor of psychological distress for the unemployed second only to the financial strain produced in such life situations (Creed & Bartrum, 2008). In fact, a longitudinal study indicated personal control was an important mediator between job loss and poor health and functioning (Price, Choi, & Vinokur, 2002).

Personal Control and Chronic Disease. Research has shown personal control is an important construct in many chronic diseases. Control beliefs have been demonstrated to be important when coping with a number of illnesses such as cancer (Bárez, Blasco, Fernández-Castro, & Viladrich, 2007; Henselmans et al., 2010; Henselmans, Sanderman, Baas, Smink & Ranchor, 2009; Ranchor et al., 2010) heart disease (Bosma et al., 2005; Leong, Molassiotis, & Marsh, 2004), inflammatory bowel disease (Cooper, Collier, James, & Hawkey, 2010), parkinson's disease (Gruber-Baldini, Ye, Anderson, & Shulman, 2009), dysphonia (Haselden, Powell, Drinnan, & Carding, 2009) and adolescents with chronic illness (Meijer, Sinnema, Bijstra, Mellenbergh, & Wolters, 2002).

Personal Control as a Mediator in the Illness Intrusiveness Model. One of the implications of the illness intrusiveness theory is that personal control is reduced so that the individual has more difficulty obtaining positive results or averting negative outcomes from experiences (Devins, 2010). The individual's perception of the illness intrusiveness of the IVIG treatment experience as well as the perception of personal control related to that experience was an important consideration in the overall picture of assessment in this study. The illness intrusiveness model suggests that personal control is one of several potential mediators between illness intrusiveness and the outcome variable.

In a cross-sectional study (n = 237) assessing the relationship of diabetes intrusiveness and control to depression in adults results indicated illness intrusiveness, and perceived control mediated the relationship between diabetes and depression (Talbot et al., 1999). Utilizing a cross-sectional design (Poochikian-Sarkissian et al., 2008a)

found perceived control to be a mediator between the impact of illness intrusiveness in epilepsy patients and subjective well-being.

Seminal research examined the importance of a patient's perception of II and control with 35 hemodialysis end-stage renal disease patients (Devins et al., 1983). This research study showed significant correlation of patient perception of illness intrusiveness and limited control of their life with negative mood and diminished positive mood. Control was found to be a mediator in this research study.

Personal control has been examined across populations and with the relationship of disease intrusiveness to the individual. For example, perceived control was shown to decrease before and after diagnosis regardless of prognosis with more psychological distress in a group of cancer patients, but some control was regained after a year post-diagnosis and treatment (Ranchor et al., 2010). Additionally, perceived control has been shown to affect the reported number and severity of disease symptoms across a variety of illnesses such as hereditary heart disease (Hoedemaekers, Jaspers, & van Tintelen, 2007), posttraumatic stress disorder after myocardial infarction (Doerfler, Paraskos, & Piniarski, 2005), osteoarthritis (Rivard & Cappeliez, 2007), women suffering from hot flashes and night sweats (Pimenta, Maroco, & Ramos, 2011), and withdrawal symptoms from nicotine (Schnoll, Martinez, Tatum, Glass, & Bernath, 2011). Perceived control regarding the intrusiveness of a chronic disease is also vulnerable to change with age (Kempen et al., 2005) and educational level (Bailis, Segall, Mahon, Chipperfield, & Dunn, 2001). Ranchor et al. (2010) concluded perceptions of control vary according to environmental influence.

Previous research demonstrated that psychosocial well-being was related to illness intrusiveness and increased personal control in MS patients (Devins et al., 1993). Poochikian-Sarkissian et al. (2008a) also found better psychosocial outcomes and QOL when patients believed they had control in the different life domains. Poochikian-Sarkissian et al. showed patient's perceived control over the three life domains measured by the Illness Intrusiveness Rating Scale (IIRS; relationships and personal development, instrumental, and intimacy) positively correlated with psychosocial outcomes and QOL. Poochikian-Sarkissian et al. used the IIRS scale to test the illness intrusiveness theoretical framework with epilepsy and to measure all three life domains in epilepsy patients who had received surgical and pharmacological treatment. Results showed a significant correlation with increased illness intrusiveness and decreased QOL but, at the same time, depression increased. Importantly, patients who perceived they had control over their life domains showed optimistic QOL and stronger psychosocial effects. The author's path analyses supported the influence of illness intrusiveness theory with epilepsy. Certainly, this study lends support to the illness intrusiveness theory which posits feelings of personal control are reduced when illness intrusiveness is increased. Although the authors indicated their study might have been open to compromise with a self-report measure, they surmised the study provided more support of illness intrusiveness as a mediator in QOL and a determinant of the psychosocial impact of this chronic disease (Poochikian-Sarkissian et al., 2008a).

In other words, when a person believes they have the ability to control their valued experiences or life goals, there appears to be fewer negative intrusive

consequences from the disease factors (loss of function, fatigue, etc.) or treatment in the life of patient. An individual's perception of whether control lies with themselves or with others (health professionals, family, etc.) affects coping with chronic disease as well as adhering to treatment regimens (Fioravanti, Casale, Mantegazza, Leonardi, & Raggi, 2010; Gençöz & Astan, 2006).

Unpredictable changes in a chronic medical condition can lead to feelings of a lack of control in one's life domains. A different study, Poochikian-Sarkissian et al. (2008b) examined the relationship of illness intrusiveness and QOL on seizure controlled and non-seizure controlled epilepsy patients utilizing the illness intrusiveness framework. Low illness intrusiveness and better QOL associated with the seizure free group regardless of treatment type while the uncontrolled seizure group associated with a lower QOL (Poochikian-Sarkissian et al., 2008b). This study was yet another example supporting the illness intrusiveness theory that personal control is diminished with more intrusiveness.

Similarly, autoimmune patients experience unforeseeable physiological variations from day to day which may interrupt their life routine or habits (fatigue, difficulty with mobilization, pain) thus, diminishing personal control in the three life domains; intimacy, relationships and personal development and instrumental. Since autoimmune patients receiving IVIG must potentially encounter long hours of infusions, interrupted schedules, a generally restrictive therapy environment and loss of valuable activities, it is suggested that the patients who experience illness intrusiveness also feel less personal control and a detrimental effect on their QOL. Thus, it is clear that the theoretical framework of

personal control has been studied in the context health and illness. Since research seems to support fewer reported symptoms with increased personal control seemed reasonable to surmise personal control may be related to the IVIG treatment experience of neurological autoimmune patients.

Measures of Personal Control. The current study measured the control variable with the Multidimensional Health Locus of Control Form C (MHLC). The 18-item form C of the MHLC was developed as a condition specific scale which could be adapted to various medical conditions (Wallston et al., 1994). It assesses the extent to which an individual believes health-related outcomes are the result of chance or luck, their own action or behavior of professionals or family (Wallston et al., 1994). Wallston's (1992) modification of Rotter's (1954) social learning theory posited locus of control indirectly influences the individual's health standing (Wallston, 1994). The MHLC-Form C was developed from Rotter's early work. It was developed so researchers could compare patients with two different diseases; a condition-specific scale for locus of control suitable for use with any medical condition.

The factor structure, reliability and validity of the four subscales was established from information gained from 588 patients with chronic pain, diabetes, rheumatoid arthritis and cancer. The chance and internal subscales are comprised of six items whereas the other people and doctors' subscales have three items. Items are arranged on a 1 to 6 Likert with 1 representing strongly disagree and 6 representing strongly agree. Internal consistency on the four subscales have alpha levels of 0.70-0.71 for powerful others, 0.79- 0.822 for chance, 0.85-0.87 for internal and 0.71 for doctors' subscale

(Wallston et al., 1994). A recent study examining the relationship of locus of control in patients with sickle cell disease found alpha levels of 0.87 (internal), 0.78 (chance), 0.56 (doctors), and 0.77 (other people) for the four subscales in the MHLC- Form C (Gibson, 2014). Concurrent validity was demonstrated for Form C with a sample of rheumatoid arthritis patients. Form B and C of the MHLC showed the two chance scales correlated *r* = .65, the Internality subscales *r* = .59, the Form B Powerful Others *r* = .55 and Doctors *r* = .38 (Wallston, 2005). Form C also showed concurrent validity with modest correlation with Levenson's scales with chance, other people, and internality (Wallston et al., 1994).

The MHLC has been utilized with different groups of medical patients. For example, the MHLC was used to predict quality of life in Chinese patients with epilepsy indicating the importance that patients believe they have a sense of control over their medical condition (Au et al., 2002). Waldron et al. (2010) assessed adjustment to spinal cord injury and found well-adjusted spinal cord injured patient exhibited more internal control using the MHLC. Variants of the MHLC scales have been developed focusing on certain health issues but direct comparisons with other scales were not possible since scales differed in selected items or wording. Thus, the MHLC-Form C was developed specifically as a condition-specific scale adaptable to any health condition. Earlier scales such as Levenson's general Locus of Control I, P, and C scale and Rotter's I-E scale did not include items dealing specifically with health expectations and focused more on situational illness beliefs (Wallston, 2005; Wallston & Wallston, 1981). For these reasons, the MHLC-Form C is the most appropriate instrument to assess the relationship

of personal control in examining the IVIG experience in neurological autoimmune patients.

Quality of Life

QOL is a multidimensional construct encompassing many domains. For persons with chronic disease, these domains may be differentially experienced (Centers for Disease Control [CDC, 2011]; Devins, 2010). According to the CDC the definition of quality of life encompasses evaluations of both positive and negative features of life. QOL may include many domains and elements in life impacted by one's health including ability to function, social interaction, life satisfaction, and psychological well-being, (Eastwood, Doering, Roper, & Hays, 2008). QOL of life may also echo life events, life experiences, socioeconomic status, and your current stage of life (Sevinc & Akyol, 2010). HRQOL involves the individual's goals and ambitions which may be constrained by the course of the disease or treatment (Taylor, Gibson & Franck, 2008).

Researchers have included the patient's perceptions of their physical abilities and functions in definitions of HRQOL. HRQOL for chronically ill individuals usually refers to the individual's perception of their physical and emotional states of health including their evaluation of their own abilities for social and physical functioning in comparison to the ideal level of functioning (Megari, 2013). The manner in which a patient experiences an illness or treatment can become a feature of their QOL (Megari, 2013). HRQOL is accepted as a multidimensional construct with three domains; physical, psychological and social. The physical domain includes symptoms and the person's ability to perform daily living activities (Eastwood et al., 2008) well-being to extreme psychological stress or

overall mental well-being (Eastwood et al., 2008; Sprangers, 2002) and the social domain may include all aspects of social relationships (Eastwood et al., 2008; Sprangers, 2002).

Extensive research exists regarding quality of life and chronic disease and treatment. QOL was found reduced in cancer patients due to limited activities, type of surgery or treatment, and psychological factors (Avis, Crawford, & Manuel, 2005; Richardson, Wingo, Zack, Zahran & King, 2008;). Disease symptoms and severity of disease have been shown to affect QOL in a number of chronic diseases (Hrisanfow & Hägglund, 2012; Király & Gondos, 2012; Nagaraj, Taly, Grupta, Prasad, & Christopher, 2013; Raggi, Leonardi, Bussone, & D′ Amico, 2012; Robb, Cooke, Devins, Young, & Joffe, 1997). Research has indicated health-related quality of life is negatively affected by the chronic diseases such as heart disease in a study (n = 152) of atrial fibrillation patients finding that these patients showed substantially poorer quality of life compared to healthy patients in all the domains tested in the SF-36 (Dorian et al, 2000). Continuing, in MS patient's health related quality of life was found to be not only predicted by the physical indices and cognitive indicators but also by the patient's perception of the disease as well as the intrusiveness of the disease (Shawaryn et al., 2002).

The World Health Organization (1995) defines quality of life as the "individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectation, standards and concerns."(p. 1405). Utilizing this definition, the instrument the WHO recommends to measure QOL uses the four domains of social, environmental, physical and psychological health.

The Neuro-QOL Instrument

Some QOL disease specific measures utilized with MS patients include the Multiple Sclerosis Quality of Life questionnaire (MSQOL54), the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) and the Functional Assessment of Multiple Sclerosis questionnaire ([FAMS]; Baumstarck, Boyer, Boucckine, & Michel, 2013). There are no disease specific QOL measures for CIDP, MG, or MMN. It is important to use an instrument which is appropriate for all four diseases. The Quality of Life in Neurological Disorders (Neuro-QOL) instrument is tailored for patients with neurological disorders, and although it is not specific to each particular diagnosis it is purposely designed and created for patients with neurological disorders. It was the quality of life instrument utilized in the present study.

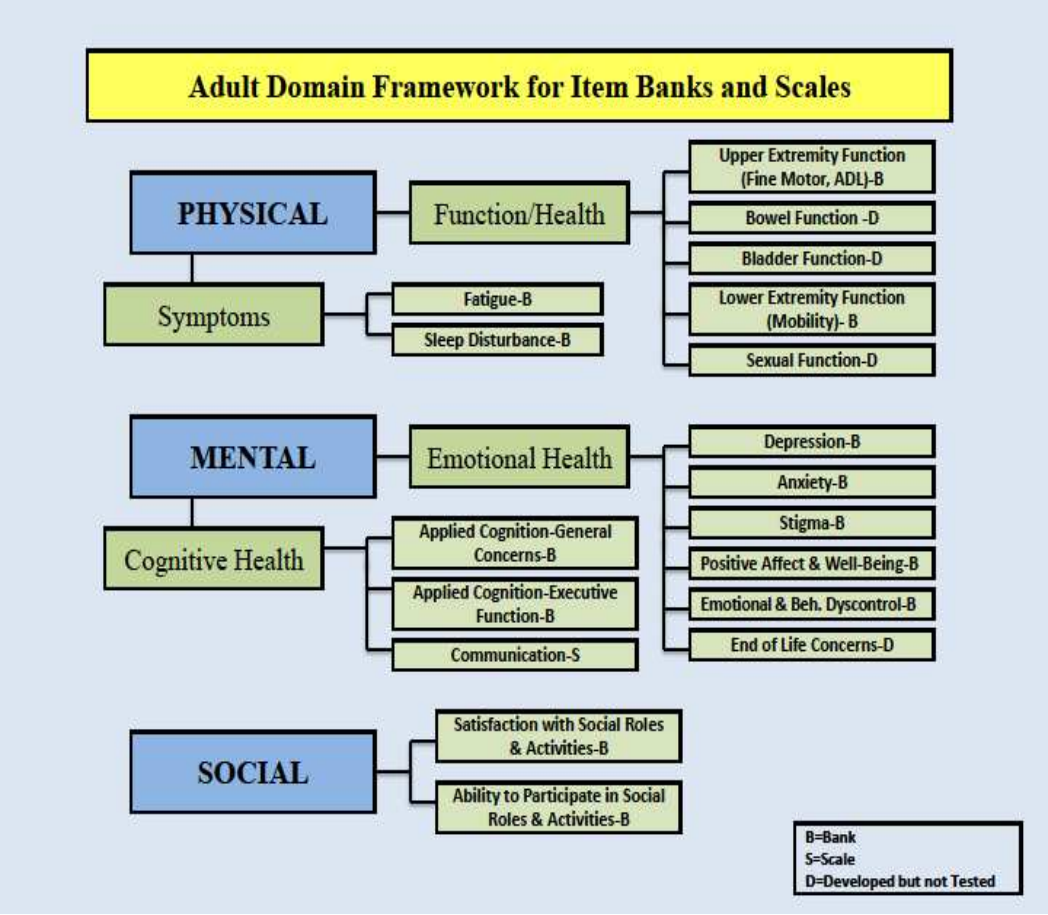

Figure 1. Neuro-QOL domain framework. Adapted from http://www.neuroqol.org. Copyright 2008-2013 David Cella and the PROMIS Health Organization on behalf of the National Institute for Neurological Disorders and Stroke (NINDS). Reprinted with permission.

The National Institute of Neurological Disorders and Stroke (NINDS) sponsored a 5 year health-related quality of life project to be developed which would be bilingual, psychometrically sound and clinically pertinent to major neurological diseases (Cella et al., 2011). The Neuro-QOL is brief, valid, reliable, utilizing item response theory. Consistency allows cross-disease comparison which makes it particularly applicable for the current study. Consistency was achieved through the development and testing of item

banks with determinate questions measuring shared concepts relevant to all the chosen neurological diseases (Cella et al., 2011). Experts compiled and identified domains of HRQL which are most often influenced by a neurological disease and/or treatment such as areas of function, symptoms and other important issues relating to neurological disorder when developing the instrument. Focus and caregiver groups were also conducted when developing questions for the instrument. Qualitative approaches were utilized in analyzing the data sources (Cella et al., 2011). The item banks incorporated physical health, social health, emotional health, emotional-behavioral dyscontrol, and cognitive health items. The Neuro-QOL developers engaged in a series of steps during the development process including: engaging patients and medical providers to identify potential items of importance and domains through interviews, focus groups and surveys; reviewing published literature; identifying gaps and writing new items; identifying domain specific items and organizing; revisions by integrating patient and stakeholder perspectives; and cultural review and translating to Spanish (Cella et al., 2011). This measurement instrument is appropriate for assessing disease burden in neurological health populations as well being utilized in research with studies utilizing predictors, mediators, and outcomes (Cella et al., 2011).

For the current study, I employed the short form measures (8–9 items in each item bank) of the Neuro-QOL. These short forms were calibrated from the larger item banks and were tested with three samples; a clinical panel *(n* = 553), the general population (*n* = 2,113) and a clinical outpatient population (*n* = 581). Correlations between the short and full length form 0.88 to 0.99 and internal consistency on the short forms was 0.85 to 0.97

(Cella et al., 2012). The brief measures were able to differentiate those individuals reporting health conditions and whether the conditions interfered with routine function (Cella et al., 2012). The Neuro-QOL is a standardized assessment which has shown validity and consistency in assessing patient reported outcomes regarding disease burden and treatment benefits (Cella, 2012). This is an appropriate instrument of measurement for examining the IVIG impact experience and QOL in the neurological populations selected for the current study.

Physical Domain of Neuro-QOL. The Neuro-QOL was developed with consideration to the physical problems experienced by neurological patients. The developers utilized expert groups, literature review and caregiver focus groups when selecting the QOL domains to be included in the instrument (Cella et al., 2011). The following literature is supportive in explaining the problems neurological autoimmune patients experience which have been addressed in the formation of the item banks for the Neuro-QOL.

Physical issues impact the lives of neurological autoimmune patients. Lower and upper extremity function controls mobility and is a main symptom of patients diagnosed with neurological autoimmune disease. For example, a study of 2,171 patients with MS, using a cross-sectional study design, reported that 43% identified walking and mobility problems (WMPs) as the aspect of their chronic disease which most negatively affected QOL (Pike et al., 2012). Another study (N = 166) using the United Kingdom Disability Scale (UNDS) had MS patients rate the most important bodily function. They found that lower limb function, which controls gait, was rated most important to these patients

(Heesen et al., 2008). Thus, mobility in neurological diseases is ranked as important and can cause patients to require more caregiver assistance and primary care intervention (Pike et al., 2012). Productivity through employment and work decreases with the presence of WMPs by either a reduction in hours or the ability to work at all (Pike et al., 2012), making the inability to support themselves physically and financially due to mobility problems one of the largest problems MS patients face.

Fatigue is another major concern for CIDP, MS, MMN, and MG patients and which may present as motor fatigue while walking and performing activities of daily living (Greim et al., 2007; Merkies & Faber, 2012). Fatigue was demonstrated to negatively impact QOL in neurological disease populations (Kobelt, Berg, Lindgren, Fredrikson, & Jönsson, 2006). The origin of fatigue in neurological diseases is not clear, but has been defined as problems in performing and sustaining mental and physical voluntary activities (Chaudhuri & Behan, 2004; de Vries, Hagemans, Bussmann, van der Ploeg, & van Dorn, 2010).

Significant correlations have been shown between disability and higher levels of fatigue. Pittion-Vouyovitch et al. (2006) found that greater levels of fatigue correlated with more disability, increased depression and lower levels of QOL among a sample of 237 MS outpatients (Pittion-Vouyovitch et al., 2006). Another case controlled cross-sectional study assessed 113 patients with autoimmune polyneuropathies using the fatigue severity scale (FSS scale) and found severe fatigue in 80% of patients, unrelated to sensory deficits, and duration of symptoms or general strength (Merkies et al., 1999). These patients concurred that fatigue was significantly disabling and it impaired their

QOL. Finally, Boukhris et al. (2005) studied 11 CIDP patients whose primary symptom was fatigue using the fatigue severity scale (FSS) along with clinical assessment examinations. Patients described fatigue to be the main problem interfering with activities of daily living and QOL.

Sleep disturbance is another symptom that can be a problem with various neurological diseases. Kaynak et al. (2006) performed a study with 27 MS outpatients and found that they experienced more wake time after sleep onset (WASO), more periodic leg movements (PLM), and more time in bed (TIB) compared to control patients, which led to lower sleep efficiency index (SEI) and sleep continuity index (SCI) scores compared to controls. This study supported an earlier study by Ferini-Strambi et al. (1994) in which 25 MS patients were compared to a non-MS control group using clinical assessments and brain magnetic resonance imaging. Ferini-Strambi et al. (1994) found MS patients experienced decreased sleep efficiency and awakened more during sleep. Lobentanz et al. (2004) showed marked reduced sleep efficiency in MS patients compared to healthy control group (Lobentanz et al., 2004). The study also found that greater neurological disability was associated with poorer subjective sleep quality. Adding to these studies, sleep apnea has been found in myasthenia gravis (Stepansky, Weber, & Zeitlofer, 1997) and excessive daytime sleepiness has been linked to many neurological diseases (Happe, 2003).

These studies provide supportive literature indicating the importance of including these particular domains: upper and lower extremity function, fatigue and sleep disturbance. The physical item banks of sexual function, and bowel and bladder function

were not included in the Neuro-QOL measurement since upper and lower mobility, fatigue and sleep disturbance are the most relevant of the physical domain for examining the IVIG treatment experience. The Neuro-QOL was developed so that researchers could choose the item banks which would be most useful for the purpose of an individual study. The Neuro-QOL was not developed as a disease-specific instrument but was created for a variety of neurological conditions so the researcher must determine which domains need to be assessed for any given neurological disease (Neuro-QOL, 2015).

Mental Domain of the Neuro-QOL. The mental domain involves a cognitive health component as well as an emotional health component. The cognitive component subscale measures the patient's ability to plan, keep appointments, control time, and accurately manage a checkbook and other important personal documents; the ability to think, plan, focus and remember new information; to carry on conversation, organize content of communication or make "to do" lists, speak clearly and understand family and friends (Neuro-QOL, 2015). The emotional component subscale measures anxiety, depression, stigma, affect, and emotional dyscontrol (Neuro-QOL, 2015).

Cognitive Component. Neurological diseases are often progressive and can impair cognition (Chiaravalloti & DeLuca, 2008). Cognitive problems can occur in various neurological disorders, but are most often studied in MS. Some of the areas impacted in MS include executive functioning and efficiency in processing. During a community-based study of 95 MS patients, Drew, Tippett, Starkey, and Isler (2008) reported that 17% of MS patients showed problems with at least five measures of

executive functions and the majority of participants showed problems in all three areas of cognition; general ability, memory, and executive function.

Paul, Cohen, Gilchrist, Aloia, and Goldstein (2000) performed a controlled study with 28 MG patients and 18 healthy subjects assessing cognitive performance. MG patients showed a diminished ability to generate word fluency in categories and letters, process information and verbal recall of words over five trials (Paul et al., 2000). However, there was no significant difference between the patient and control group on the percent of retention from the fifth trial recall to the long delay recall (Paul et al., 2000). Although this particular study concluded MG patients demonstrated significant problems with cognitive function in the areas of rapid processing of information, response fluency and visual and verbal learning, Paul et al. concluded these problems might not interfere with daily functioning.

Problems in complex attention, information processing speed and memory are often symptoms of a neurological disorder (Chiaravalloti, & DeLuca, 2008). These authors posited such problems may make daily life challenging as it becomes difficult to effectively manage a household, remain actively employed or participate in activities. The processing speed and efficiency deficits in MS may impact an individual's ability to carry on a small group discussion, speak clearly into a telephone or even make "to do" lists. The inability to remember information at a later point in time may hamper the person's ability to hold a conversation or communicate in a small group or at work.

Cognitive function is an item bank of the mental domain evaluated by the Neuro-QOL measurement tool which was used in this study. It examined patient perceived

difficulties in, calculating, planning as well as memory, attention and decision making (Neuro-QOL, 2015).

Emotional Component. A chronic neurological autoimmune disease may precipitate stress in the life of the patient which may negatively affect these aspects of QOL. As a result of the stress a patient may demonstrate psychological symptoms such as anxiety and depression. Depression has been found in high percentages in autoimmune diseases (Chen, Jiang, Ouyang, & Chen, 2009). Dantzer, O'Connor, Freund, Johnson, and Kelly (2008) reported that exacerbation in autoimmune diseases can lead to depression symptoms in susceptible individuals suggesting inflammation may play a critical role for the development of depression in the chronically ill neurological autoimmune patient. Feinstein and Feinstein (2001) assessed 100 MS patients for major depression using interview methods and self-report questionnaires. They found that 73% of the patients reported experiencing symptoms during the previous month. Symptoms reported included crying (40%), sadness (36%) and irritability (57%). Researchers concluded that although MS patients may not be formally diagnosed with major depression, they may have symptoms of emotional dyscontrol that impact QOL. In another study depression was independently related to lower quality of life after adjusting for fatigue and disability in a group of 60 MS patients (Janardhan & Bakshi, 2002).

Health-related stigma usually is distinguished by a social lack of acceptance of individuals who are distinguished by certain health problems (Weiss, Ramakrishna, & Somma, 2006). Stigma may impact emotional QOL. Jacoby, Snape, and Baker (2005) suggested there are three features of stigma in chronic illness: (a) the degree to which an

illness controls one's identity, (b) the extent to which others have problems understanding the symptoms of the disease; and (c) the seriousness of the social outcomes. In terms of this definition, these features can be observed in many of the neurological diseases. Individuals with neurological conditions may have trouble with ambulation, writing, and speech or may need help with activities of daily living. For example, considering the four neurological diseases in this study, other individuals or members of society in general may have difficulty understanding such symptoms as fatigue, slow gait or mobility challenges in CIDP, MS, MG, or MMN. A lack in understanding of symptoms may lead to the neurological immune patient being ostracized or excluded from social activities or even assume themselves incapable of participating in programs and activities due to the stigma. This lack of understanding can create stigma surrounding any of these chronic neurological diseases. Stigma may be distinguished as self-stigma (self-felt shame or being different) or enacted stigma (actual exclusion or discrimination) for individuals with chronic disease (Scambler, 1998). Patients with neuromuscular diseases experience intense feelings of stigma and report low qualities of life according to one cross-sectional study (van der Beek, Bos, Middel, & Wynia, 2013). In addition, this study revealed patients experienced shame and fear of stigma more than the realized stigma. Other studies reported stigma has influenced quality of life negatively in a variety of chronic diseases (Dancey et al., 2002; Rusch, Angermeyer, & Corrigan, 2005; Suurrmeijer, Reuvekamp & Aldenkamp, 2001).

Emotional QOL may be measured through positive aspects as well. Some people report positive outcomes from chronic disease. Positive outcomes such as increased sense

of purpose, formation of closer relationships and an increased appreciation for life have been reported across a variety of diseases (de Ridder, Geenen, Kuijer, & van Middendorp, 2008). Psychologically adjusting to a chronic illness is important to the person's well-being, and so positive affect and well-being are also measured as emotional components of the Neuro-QOL.

These studies support the importance of examining the emotional issues experienced by neurological patients for which the emotional domain of the Neuro-QOL instrument was established to assess. The emotional domain of the Neuro-QOL was selected from expert interviews, focus groups and literature review. This domain was included in the current study.

Social Domain of the Neuro-QOL. Neurological autoimmune disorders, through their symptoms and as a result of the treatment, may result in changes to the individual's participation in leisure activities as well as adjustments in their socialization processes with friends and family. For example, Vanner, Block, Christodoulou, Horowitz, and Krupp (2008) conducted a cross-sectional study with a convenience sample of 43 MS patients to explore the association between impairment related obstructions with MS patients and leisure activity. Their findings revealed higher leisure activity levels associated with lower MS impairment barriers. Understanding the patient's ability to participate in social activities and their satisfaction with their social roles is important in assessing the QOL of patients with neurological disease.

In sum, the research demonstrates how QOL is affected across a number of domains. However, the research is fairly limited to MS patients, and has not been

conducted using persons suffering from other autoimmune diseases. The Neuro-QOL with its focus on the physical, mental, and social dimensions of most relevance to persons with these types of diseases, offers an opportunity to examine these dimensions with greater psychometric accuracy.

IVIG and Quality of Life

There is considerable research on the use of IVIG in persons with autoimmune disorders, but most of these do not include assessments of QOL. In fact, only two studies were found which evaluated QOL in patients receiving IVIG, both with small sample sizes. Gerschlager and Brown (2002) examined the benefits of IVIG with stiff person syndrome (SPS) patients in a small sample of six patients. They used the SF-36, a common QOL instrument and a Visual Analogue Scale at the beginning of treatment and two weeks after completion of therapy. Results showed significantly improved SF-36 scores for energy and vitality, pain, social functioning and general mental health. Although the researchers concluded that IVIG improved patient's QOL, it should be noted that the sample was quite small. The second study by Padua et al. (2005) evaluated the outcome of IVIG in 25 patients with neurological disorders using the SF-36 Italian version and the Disability of Arm, Shoulder, and Hand questionnaire (DASH). Results showed an improvement in the patient's physical health related QOL demonstrated by less fatigue, improved upper body and limb function and a smaller degree of pain. Since the authors noted no changes in mental scores from baseline to follow-up evaluation, they concluded IVIG did not improve psychological conditions (Padua et al., 2005). However, in evaluating this research study several methodological problems were noted. The study

contained a small sample and measurement was 8 days from the original administration of IVIG and follow-up measurement. One might suspect that patients would require a longer period of time to note any psychological improvement from this type of treatment. Another consideration is that the study does not indicate the length of time these 25 patients had been experiencing the neurological autoimmune disease. This information might be relevant in the overall picture. More studies with larger sample sizes may give a clearer picture of the effects of IVIG on the psychological features accompanying many autoimmune disorders.

The Influence of Illness Intrusiveness on Quality of Life

Some studies have shown illness intrusiveness to be an important construct in understanding the psychological adjustment of patients who live with a chronic illness. Autoimmune disease patients often live with uncertainty with respect to prognosis, treatment, and the daily variations of mobility and ability. One interesting study showed higher levels of uncertainty and illness intrusiveness correlated with high levels of psychological distress (using the SCL-90-R) in a group of MS patients (Mullins et al., 2001). As the MS patients experienced intrusion into day-to-day living, QOL can become compromised because of the uncertainty of diagnosis and treatment, or the intrusiveness of the disease. Although the Mullins et al. (2001) study showed higher levels of distress was associated with high illness intrusiveness and uncertainty, illness intrusiveness did not serve to mediate or moderate in the study, but did show illness intrusiveness directly influenced the patient's psychological adjustment to the chronic disease of MS. However, the Mullins et al. (2001) study did not assess the personal control variable which, as

discussed earlier, is considered instrumental in the illness intrusiveness theoretical framework (Devins, 2010; Poochikian-Sarkissian et al., 2008a; Shawaryn et al., 2002; Snyder et al., 2013).

Summary

This chapter presented a synthesis of pertinent studies regarding the role of illness intrusiveness and chronic disease. Chronic neurological autoimmune disease impacts the patient's life in many ways. IVIG treatment, although preferable in many autoimmune diseases, can further interfere normal life, because the treatment itself is complicated, expensive, time-consuming, and carries with it serious side effects. Only two studies with small samples have measured psychological aspects of the IVIG treatment experience. The limited available research regarding the relationship of IVIG and QOL for neurological autoimmune patients makes the present study salient for several reasons. However, research from a variety of related areas suggests that illness intrusiveness will enhance the understanding of the patients' IVIG experience, and offer insights to treatment providers about how to minimize impact on QOL.

Considerable evidence supported the use of the illness intrusiveness model in a broad range of medical diseases (Poochikian-Sarkissian, 2008a). Although illness intrusiveness has been established as a beneficial model in different diseases, previous research has not evaluated illness intrusiveness and QOL in autoimmune patients receiving IVIG treatment. Inclusion of the individual difference construct of control may provide insight as to why some autoimmune patients receiving IVIG are able to adjust to disease and treatment factors while others have a more difficult time with the

intrusiveness of disease and treatment. Chapter 3 provides information regarding methodology for the current study.

Chapter 3: Research Method

Introduction

The purpose of this quantitative study was to determine if the illness intrusiveness model (Devins, 1983) mediated the relationship between IVIG treatment experience and QOL in neurological autoimmune patients with MS, MMN, MG, CIDP. I also examined the mediating effect of control on the relationship between illness intrusiveness and QOL. In Chapter 3, I present the research design, sampling method, procedures, instrumentation, data analysis, and ethical protection of autoimmune patients participating in the study.

Research Design and Rationale

A nonexperimental survey research design was chosen to explore the predictive strength of the independent variable (IVIG treatment experience) in explaining the variance in the outcome variable (QOL) and to test the mediating influence of two variables identified as mediators (illness intrusiveness and personal control). A nonexperimental design was most appropriate for this study as it allowed for examining the predictive relationship between independent variables and outcome variable although causal relationships may not be concluded from this design (Frankfort-Nachmias & Nachmias, 2008; Stangor, 2011). This design was consistent with the exploration of predictive and mediating relationships according to the II theoretical framework (Hayes, 2013; Kenny, 2014; Stangor, 2011).

An advantage of a cross-sectional correlational design is that it permitted me to examine behavior in a real-life setting. A disadvantage is that causation cannot be tested and internal validity might be decreased (Frankfort-Nachmias & Nachmias, 2008; Stangor, 2011). A self-administered survey, paper and pencil research approach was employed for obtaining data from a sample of patients with autoimmune disease. This approach was chosen because data could be obtained in a timely way (i.e., when the individual patient arrived at the IVIG infusion center or by completing the forms on their own) since IVIG treatment is administered on individual time schedules.

This type of design is appropriate when collecting data that are quantified into variables or scales using psychometrically sound questionnaires (Vogt, Garnder, & Haeffele, 2012). Relationships (direct and mediated) can be examined for strength and direction. An advantage of using a survey design is efficiency and a low cost (Vogt et al., 2012). Other considerations in choosing this design according to Vogt et al. (2012) are that data concerning the IVIG treatment experience can best be obtained from the patients with briefly answered and structured questions, and an adequate response rate can be expected. Although Stangor (2011) mentioned a concern might be with response rate when using questionnaires, most patients completed the questionnaire while they were receiving treatment which expedited the response rate. Another advantage was that information was relayed while the patient was receiving their infusion so that it was convenient for the patient. A disadvantage of survey research design is a question of who completed the survey (Vogt et al., 2012); however, this problem was addressed in the fact that surveys were given to patients as they began their usual IVIG treatment and when

they agreed to participate in the study. The following subsections were the variables that I examined in this study.

Demographics

The variables of interest included: gender (nominal), age (ordinal), disease diagnosis (one of the four autoimmune disease categories), length of time since first symptoms in months or years (ordinal), employment status (nominal), and length of time receiving IVIG treatment in months and years (ordinal). The demographics form is included as Appendix A. Data collected were aggregated in order to describe the characteristics of the sample.

Quality of Life

The Neuro-QOL was used to measure the dependent variable, QOL. It is a set of self-report measures that contains 13 tested item banks each with 8 to 9 items. The Neuro-QOL was designed for the researcher to choose which item banks are most applicable to the population studies. I used 10 of the item banks with a total of 81 items in the questionnaires.

IVIG Single-item Visual Analog Scale

The independent variable, IVIG treatment experience, was measured using a single-item VAS. Patients were able to mark their subjective responses on the VAS and it was simple and rapidly administered (Rossi & Pourtois, 2012). The single-item VAS is included in the demographics questionnaire in Appendix A.

Illness Intrusiveness

The IIRS consists of 13 items, summed into a single score. The 13 items helped patients rate the degree the IVIG treatment interrupted the QOL domains. This measure was used as a mediating variable.

Control

The MHLC consists of 18 items (Wallston, 2007). The sum of the values circled for each item is the score for each subscale. Form C is designed for individuals having medical conditions. Wallston (2007) suggests the word "condition" on the form be replaced with the medical diagnosis. This study used the term, *neurological autoimmune disease*. Control was used as a second mediating variable.

Statistical Analyses Plan

A variation of multiple regression was used to test the predictive and mediating relationships between the independent and dependent variables (Baron & Kenny, 1986; Kenny, 2014; MacKinnon, Fairchild & Fritz, 2007; Shrout & Bolger, 2002). This approach allowed me to examine direct and indirect effects of select variables predicting a single outcome. Mediation is a causal model (Hayes, 2013; Kenny, 2014). Hayes (2013) hypothesized that a causal chain occurs in mediation where one variable (X) affects a second variable (M) which affects the third variable (Y). The intervening variable, M, is the mediator which mediates the relationship between the predictor and the outcome (Hayes, 2013). The direct effect is the path between X and Y without traveling through M (Hayes, 2013). The indirect effect is the path from X to Y through M which is considered the amount of mediation or the effect showing X leads to Y through

M (Hayes, 2013; Kenny, 2014). Current research indicates that most scholars of mediation analysis no longer require evidence of an association between X and Y prior to testing for mediation or indirect effects (Cerin & MacKinnon, 2009; Hayes, 2009; Rucker, Preacher, Tormala, & Petty, 2011; Zhao et al., 2010). PROCESS was used in SPSS to estimate the coefficients of the model, analyze, and interpret the direct, indirect, and total effects (paths *a, b, ab, c, c′*), and the Bootstrap confidence intervals as well for several different types of effect sizes (Hayes, 2013).

Bootstrapping was used to test the intervening variable since research has shown bootstrapping is a robust and valid method of testing the effect of intervening variables (Hayes, 2009; Preacher & Hayes, 2008; Williams & MacKinnon, 2008) and may be advantageous over the Sobel test as it requires no assumption about the shape of the sampling population (Hayes, 2009). In addition, simulation research has indicated the Sobel approach has low power and produces less accurate confidence intervals compared to other methods (Hayes, 2013; MacKinnon, Lockwood, & Williams, 2004). In other words, the Sobel approach is less likely to recognize the impact of X on Y through M (Hayes, 2013). Bootstrapping constructs a representation of the sampling distribution through resampling with replacement that then is used to create the confidence interval (Hayes, 2013). Moreover, power is higher when it is employed to test a hypothesis and in mediation analysis is more recommended than other methods for inference regarding the indirect effect (Hayes, 2013).

The predictor variable in this study was IVIG treatment experience and the outcome variable was QOL as measured by the 10 Neuro-QOL scales. Proposed

mediators were illness intrusiveness and control. Use of PROCESS, which employs ordinary least squares (OLS), was chosen over structural equation modeling (SEM), as SEM requires a larger sample size than I could obtain and requires more assumptions. Additionally, in regression analysis there is a clear difference between the independent and dependent variable, whereas with SEM these distinctions are applied in relative terms (Gunzler, Chen, Wu, & Zhang, 2013). The mediation model is a causal system where a predictor influences the outcome through one intervening variable (Hayes, 2013). The research model below shows the hypotheses that illness intrusiveness mediates the relationship between the IVIG treatment experience and QOL and that control mediates illness intrusiveness and QOL.

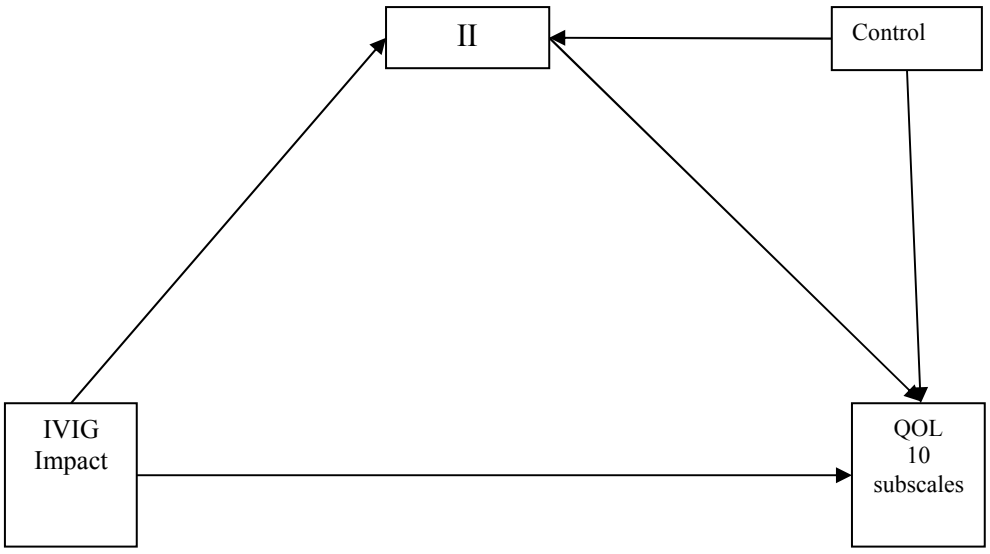

Figure 2. The research model. IVIG = intravenous immunoglobulin; II = illness intrusiveness; QOL = quality of life as measured with 10 scales; control = multidimensional health locus of control

Methodology

Population

The target population was neurological autoimmune disease patients, between the ages of 18 and 80 with diagnosis of MS, MMN, MG, or CIDP. Although these patients have different diagnoses they incur the same type of treatment, namely IVIG. The PNA assisted me in acquiring the required sample size according to the power analysis.

Sampling and Sampling Procedures

The sampling strategy was a convenience/nonrandom sample. While all potential participants meeting the criteria for inclusion in the study at PNA were contacted, it is always possible with convenience sampling that the sample is not representative of the entire population of MS, MMN, MG, and CIDP receiving IVIG as this is one of the disadvantages of this time sampling strategy (Trochim, 2006). External validity may have been threatened since it concerns the potential of generalizing the results of a study, which I was not be able to do only drawing participants from one infusion center (Trochim, 2006). The source for the accessible population for my study was invited to participate from one venue, PNA, located in Phoenix, AZ. PNA assisted in attaining the required sample size for this study. PNA is a neurology center with six experienced neurologists specializing in treatment and research involving many neurological diseases. For example, many of the neurologists are highly recognized in the treatment and research communities for their innovative practices such as the neuropathy clinic at Banner Good Samaritan Hospital in Phoenix, AZ. The infusion center within PNA gives infusions of IVIG to a variety of patients with neurological conditions. For the purposes

of this study only those with the diagnoses of MS, MMN, MG, and CIDP were invited to participate.

An a priori power analysis was calculated (Faul, Erdfelder, Buchner, & Lang, 2009) in order to estimate sample size. The original power analysis called for a sample size of 166 based on a Gpower of .09 for medium effect, .80 power, and .008 for probability based on Bonferonni with two predictors. However, given that only 79 surveys were returned to me, I performed a post hoc analysis with Gpower for each of the 9 QOL subscales which showed mediation during data analysis. I input the R^2 from the multiple linear regression, sample size of 79, two predictors, and probability .005 in Gpower then calculated the F^2 effect size followed by the estimation of power. Post hoc power analyses were reported with each mediation analysis. The effect sizes and the indirect effect are quantified in the analysis which follows. Kenny (2014) suggested two possible ways of determining medium effect size, either using the usual Cohen (1988) medium effect size of .3 or preferably squaring that to a medium effect of .09 since the indirect effect in a mediation is the product of the two different effects. Kappa-squared (k^2) were reported for effect size in the mediation analysis as it is also one of the effect sizes automatically calculated in PROCESS. The effect size, k^2, describes the size of the indirect effect in relation to the maximum possible of the indirect effect given the design and data (Preacher & Kelley, 2011). Kappa-squared is interpreted the same as Cohen's *d* (1988) with reference to small (.01), medium (.09), and large (.25) effect sizes. There are benefits to reporting k^2 as it is independent of sample size, is interpretable on a 0 to 1 metric and is agreeable to creation of confidence intervals (Preacher & Kelly, 2011).

Recruitment

Letters of explanation regarding the research study along with consent forms were distributed in sealed envelopes to the willing participants by the nursing director and the research coordinator for the infusion center. A meeting was held in May 2014 with the staff and me discussing the specifics of this distribution who were very interested as well as informed of ethical considerations. Inclusion criteria were specified as patients receiving IVIG treatment with one of the neurological autoimmune diseases MS, MMN, MG, or CIDP between the ages of 18 to 80 with the ability to read English. Exclusion criteria included any patients receiving IVIG who have a different medical diagnosis than those four being studied or are out of the age range 18 to 80. All patients meeting the inclusion criteria were invited to participate.

Demographic information collected included gender, age, marital status, diagnosis, length of time with the particular diagnosis, length of time receiving IVIG treatment, and employment. Since interruption in life activities can occur from the first IVIG treatment, it was not necessary to delineate a certain length of time a person had been receiving treatment in order to be eligible for the study. As patients came into the infusion center for their IVIG they were informed about the nature of the research study explaining that was being conducted by a Ph.D. candidate at Walden University. If they were interested in participating they were given a sealed envelope with a letter explaining the study and a consent form. If the patient chose to participate they were given the envelope with the consent form and the questionnaire, which they completed, sealed, and mailed back in the provided envelope or gave them back to the nursing director. They

were kept separately locked until mailed to me. Since people were invited as they came into the center it was possible it could have taken as long as 3 months to collect the data depending on the patient's length between infusions.

Participation

Consent forms were distributed to ensure appropriate ethical standards for patient privacy as well as patients understanding the study was of a volunteer nature. If a patient made the voluntary decision to participate in the study the IVIG Impact Questionnaire, Neuro-QOL questionnaire, the IIRS questionnaire, and the MHLC were administered as the patients come to the clinic for IVIG infusions. Participation was voluntary.

Data Collection

Since the total completion time for questionnaires was approximately 30 minutes, patients had ample time to complete them during their infusion. The director of nurses stated she did not believe that was a problem for any of the patients at the center. Patients had the privacy of their own infusion space to complete the questionnaires, and were provided a sealed envelope in which to place the completed response.

Instrumentation

IVIG Experience Visual Analog Scale. The single-item VAS measured the IVIG experience and was presented as a 10-cm horizontal line with each end anchor distinctly marked. Patients were asked to mark the point on the line representing how they feel about their overall IVIG treatment experience. The single-item VAS measure uses a horizontal scale from 1 to 10. The distance from one end of the line to the patient's

mark was measured and afforded a quantitative variable. This was used for quantitative analysis.

The single item VAS measure which I developed was presented as follows:

Think about your experience with IVIG treatment which includes symptom relief, side effects, financial cost, changes from usual activities, improved health, adjusting schedules or family events, and improved mobility and place a mark on the line where you think it best represents what your experience has been overall.

Anchors:

As bad as it can be . ……..As good as it can be

I used a single-item question in a VAS to measure the IVIG treatment experience which allowed the patient the opportunity to evaluate their total experience. Single-item VAS have demonstrated good reliability and validity in assessing QOL (de Boer et al., 2004). Medical experts were consulted and agreed this would be the best plan (C. Gooch, K. Clarke, & S. McBride, personal communications, December, 2013 through May 2014). The single-item question is included in the project questionnaire. Use of single-item questions for predictive purposes has been discussed in more detail in Chapter 2.

Illness Intrusiveness Rating Scale (IIRS). The IIRS measures illness intrusiveness in the following domains: health, active and passive recreation, diet, financial situation, work, relationship with partner, sex life, other social relations, family relations, self-improvement/self-expression, community and civic involvements, and religious expression. This was appropriate for the current study because the IVIG treatment experience was hypothesized to affect those potential domains in the patient's

life. The self-administered IIRS required respondents to rate the interference by the chronic disease on the central life domains.

The scale has 13 items and uses a 7-point Likert scale, ranging from 1 (not very much) to 7 (very much). The items ask individuals to rate the level of life interference attributed to their disease and/or treatment for health, diet, work, active recreation, passive recreation, financial situation, relationship with your spouse, sex life, family relations, other social relations, self-expression/self-improvement, religious expression, and community and civic involvement. If a patient does not believe an item to be relevant a score of "1" indicates disease and/or treatment do not significantly interfere with that life domain. Higher scores mean patients are experiencing a higher level of intrusiveness (Devins, 2010). One question was erroneously omitted from the IIRS; therefore, findings reflect answers to only 12 of the 13 questions.

The ratings are summed for responses to the 13 individual items in order to create a total score ranging from 13 to 91 (Devins, 2010). Internal consistency ranges from .80 to .90 for 36 different chronic disease groups with the exception of one group (prostate cancer) which was .78. Construct validity has been good across chronic diseases. Devins (2010) stated that evidence for strong validity with the IIRS is shown by contrasting groups actually showing different IIRS scores. An example would be end-stage renal disease patients (who need frequent treatments and special diets) showing higher IIRS scores compared to transplant patients (who require a less rigorous treatment schedule) demonstrating lower IIRS scores (Devins, 2010). Discriminant validity is reinforced by results showing negative correlation between total IIRS scores and personal control

measures (Devins, 2010). Question 13 (the final question) was inadvertently omitted from the IIRS questionnaire. This question asks the patient how much their treatment interferes with their civic involvement. Permission to use the IIRS was granted by G.M. Devins, author of the scale through personal communication.

Neuro-QOL. The Neuro-QOL instruments were developed as part of a NINDS research 6-year initiative (2004 to 2010) to develop psychometrically sound QOL measurements for neurological patients. The Neuro-QOL instrument is appropriate for individuals with common neurological disorders to determine health-related quality of life (Gershon et al., 2012; Nowinski, Victorson, Cacazos, Gershon, & Cella, 2010). The Neuro-QOL is a short self-assessment with 13 subscales (which the developers call item banks) that evaluate neurological patient issues, concerns, and symptoms and one stand-alone scale which measures communication (Gershon et al., 2012). Since the Neuro-QOL system contains measures assessing similar issues in the majority of neurological diseases cross-disease comparisons are possible (Norwinski et al., 2010). Item banks are based on the individual's responses concerning the past 7 days such as "In the past 7 days... I felt depressed or I felt hopeless." Responses consist of five possibilities: never, rarely, sometimes, often, and always.

As previously stated, the Neuro-QOL consists of one scale along with the 13 item banks. The one communication scale asks the individual to rate the difficulty they are having with writing, understanding communication, etc. The instrument demonstrated strong internal consistency (Chronbach α) ranging from 0.85 to 0.97 on the adult short forms (Cella et al., 2012) which was used in the current study. Scoring the short forms

consist of item responses being given a value (e.g., 1=Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always). The sum of the response values for each question will create the raw score (NINDS, 2015). As an example, there are eight questions in a particular item bank form with a potential of five responses for each question where the lowest and highest raw scores would be 8 and 40 (NINDS, 2015). Higher Neuro-QOL scores mean more of the concept being measured (NINDS, 2015)

The present study examined three areas of QOL health: physical, mental, and social. For physical health, functional health was assessed. For mental health, emotional and cognitive health was assessed. For social health, satisfaction with social roles and activities and the ability to participate in activities was assessed. Three item banks comprised functional health: upper extremity function, lower extremity function, and fatigue. Both upper and lower extremity function may be involved in neurological autoimmune diseases. Emotional health consisted of four item banks: depression, stigma, positive affect and well-being and emotional and behavioral dyscontrol. Cognitive health included applied cognition-general concerns, and applied cognition- executive. Finally, social health QOL incorporated satisfaction with social roles and activities, and ability to participate in social roles and activities (NINDS, 2015). The Neuro-QOL can be administered on-line or in paper format. Permission to use this instrument was granted by Northwestern University.

Scoring the Neuro-QOL, which is the instrument measuring the dependent or outcome variable, was achieved by computing one total score for the each of the Neuro-QOL subscales. These raw scores were computed by adding the total responses for each

subscale. For example, a subscale with eight questions and five possible responses would have a total raw score of 8-40. To accomplish this total score each of the 10 item banks were totaled in SPSS. The Neuro-QOL reports more of the concept being measured so subscales that are positive such as ability top in social activities would mean more of that ability and negatively worded subscales such as fatigue would reflect worse or less ability with a higher score (NINDS, 2015).

Multidimensional Health Locus of Control (MHLC). The MHLC originated by Wallston, Wallston, and Devellis (1978), assesses individuals' beliefs in their ability to personally control the health related factors in their disease and/or treatment. Form C of the MHLC was utilized for this study which was originally designed as a condition-specific scale which can be adapted with patients who have existing medical diseases (Wallston et al., 1994). This study substituted the words "neurological autoimmune disease" for the word "condition" as was intended at the time of development of Form C in order to specify the medical problem of the participant population. Form C contains 18 items. Two subscales, internal and chance contain six items each, and two independent subscales referred to as "doctors" and "other people" which contain three items in each (Wallston, 2007).

Form C from the MHLC was used in its entirety, 18 items. This form asked patients to consider their beliefs about their medical condition or disease, if they agreed or disagreed with the statement on the scale. The MHLC uses a 6-point Likert-type scale with answers ranging from (1) strongly disagree to (6) strongly agree (Wallston, 2007). An example of an item from the internal subscale of the MHLC form C states, "If my

condition worsens, it is my own behavior which determines how soon I will feel better again." An example representing the concept of control by chance states, "As to my condition, what will be will be." Sufficient internal consistency was demonstrated by the alpha reliabilities of $\alpha = .71$ to $\alpha = .87$ on the Form C subscales (Wallston et al., 1994). Discriminant and convergent validity were supported by significant correlations with corresponding items on subscales from Form B while conversely not correlating with non-corresponding items on Form B (Wallston et al., 1994). The subscales on Form C showed significant correlation with criteria which provided additional support for Form C validity (Wallston et al., 1994). Scoring Form C was accomplished by computing the sum of the values identified for each item (values 1 to 6), thus there was a potential score ranging from 18 to 108. Higher scores reflect more of the control being measured. The MHLC is a public domain instrument (Wallston, 2007).

Data Analysis Plan

The latest version of the Statistical Product and Service Solutions (SPSS) Package 21 was used for the statistical analysis. I used this statistical program to assist me in keeping track of my data as it came in to me which is an important first step in logging in data. The data was screened for accuracy and completeness, and stored in an SPSS file (Trochim, 2006). A codebook was generated which included variable names, description, format, instrument, method of collection variable location, respondent, and notes (Trochim, 2006).

Examination of each variable's distributional properties and extreme scores or outliers was examined to reduce threats to validity and problems with Type I and Type II

errors. Following the suggestions of Osborne (2010) in the case of extreme scores they were corrected, truncated, removed, reduced in importance, or data transformed. When extreme scores are removed inferential statistics and correlations show a lower rate of error (Osborne, & Overbay, 2004). The outlier labeling method was utilized to check for extreme scores. There were no outliers in the data.

The Neuro-QOL was analyzed in 10 separate scales for the dependent variable. It was imperative to score each Neuro-QOL subscale independently rather that computing one total score as each scale measures a different and independent physical, emotional or social domain and they are always scored independently. Bonferroni was used since the scales are being analyzed separately.

Mediation is a causal system (Hayes, 2013). It is proposed that one antecedent (X) influences an outcome (Y) by way of a single intervening variable (M). The pathways include the path leading from X to Y without passing through M which is referred to as the direct effect of X on Y and another pathway referred to as the indirect effect which is the path from X to Y through M. Earlier approaches recommended that mediation should only be undertaken when an association is demonstrated between X and Y (Baron & Kenny, 1986). It is no longer advocated by most scholars of mediation analysis in methodology literature (Hayes, 2013). In fact, many quantitative methodologists have agreed that the total effect of X on Y should not be required as a pre-condition prior to investigating indirect effects (Cerin & MacKinnon, 2009; Hayes, 2009; MacKinnon, 2008; Rucker et al., 2011; Shrout & Bolger, 2002; Zhao et al., 2010).

The research questions and hypotheses were as follows:

RQ1: Is the IVIG treatment experience (as measured by the VAS) a significant predictor of QOL in patients with autoimmune disorders who receive IVIG treatment as measured by 10 separate QOL scales?

$H_1$1: The IVIG treatment experience (as measured by the VAS) is a significant predictor of QOL as measured by 10 separate scales in patients with MS, MMN, MG, and CIDP who receive IVIG treatment.

$H_0$1: The IVIG treatment experience (as measured by the VAS) is not a significant predictor of QOL as measured by 10 separate scales in patients with MS, MMN, MG, and CIDP who receive IVIG treatment.

RQ2: Does illness intrusiveness mediate the relationship between the IVIG treatment experience and QOL (as measured by 10 separate scales of the Neuro-QOL) among individuals with autoimmune disease who received IVIG treatment?

$H_1$2: Illness intrusiveness mediates the relationship between the IVIG treatment experience and QOL (as measured by 10 separate scales of the Neuro-QOL) among individuals with MS, MMN, MG, and CIDP.

$H_0$2: Illness intrusiveness does not mediate the relationship between the IVIG treatment experience and QOL (as measured by 10 separate scales of the Neuro-QOL) among individuals with MS, MMN, MG, and CIDP).

RQ3: Does personal control mediate the relationship between Illness Intrusiveness and QOL as measured by 10 separate scales among individuals with autoimmune disease who receive IVIG treatment?

$H_1$3: Personal control does mediate the relationship between illness intrusiveness and QOL as measured by s 10 separate scales among individuals with MS, MMN, MG, and CIDP.

$H_0$3: Personal control does not mediate the relationship between illness intrusiveness and QOL as measured by 10 separate scales among individuals with MS, MMN, MG, and CIDP.

Demographic data were examined during the first phase of data analysis, and descriptive statistics are reported in Chapter 4. Then the predictor and outcome variables were examined, and descriptive statistics and exploratory analyses were conducted and reported. These exploratory analyses determined if the data met the assumptions for the regression and mediation analyses (Trochim, 2006; Kenny, 2014)

Mediation occurs when a predictor variable, relates to a dependent variable through a mediator and can be tested statistically. The direct path leads from predictor to the dependent variable without passing through the mediator and the indirect path travels from the predictor variable to the dependent variable through the mediator (Hayes, 2009, 2013; Kenny, 2014). Current research indicates verification of a simple association between the predictor variable and the dependent is not a prerequisite in mediation analysis (Cerin & MacKinnon, 2009; Hayes, 2013; Preacher & Kelly, 2011; Shrout & Bolger, 2002; Zhao et al., 2010). Therefore, Process Macro for SPSS (version 2.13) was used for the mediation analysis in this dissertation. PROCESS uses OLS regression for path analysis-based mediation analysis which estimates unstandardized model coefficients, *t* and *p* values, standard errors, confidence intervals as well as generating

direct and indirect effects and bias-corrected and percentile bootstrap confidence intervals and various effect sizes (Hayes, 2013). Model 4 in PROCESS was used which is designed for mediation models computing the indirect and direct effects.

Threats to Validity

The current study was a nonexperimental correlational, cross-sectional study, drawing participants from one IVIG clinic in the United States. The use of nonrandom sampling of treatment sites and study participants means the results of the study may not be generalizable to the population of patients receiving IVIG treatment. Further, selection bias might plausibly be a problem in the study as the participants will "opt-in" to create the convenience sample and are not randomly selected (Trochim, 2006). Bootstrapping methods was used to assess potential sample representativeness (Kenny, 2014).

Regarding internal validity, the nature of cross-sectional survey research design precludes the use of control or comparison groups, and the use of repeated measures. Therefore, internal validity is weak, as I had little control over who chooses to participate or the research conditions. Therefore, issues like maturation and history are not relevant (Willson & Putnam, 1982). To maximize internal validity, I selected measures with acceptable psychometric properties. Statistical conclusion validity was supported by exploring the data sufficiently to understand its distributional properties and employ appropriate statistical techniques using the conventional probability of .05 statistical significance level in order to avoid Type I error (Petrocelli, 2003).

Ethical Procedures

PNA of Phoenix, Arizona gave permission for access to the patients receiving IVIG for the purposes of this project. If patients agreed to participate in this research study they were given an envelope containing the self-reporting questionnaires previously mentioned in this chapter. Recruitment was voluntary as patients entered the infusion center to receive IVIG. If patients did not desire to participate they were not given the questionnaires. The patient could opt out of the study at any time. Patients at all times maintained control over their participation in the study. Questionnaires did not contain names or personal identification. Upon completion of the surveys they were remitted to me and remained under the sole care of me protected in a locked file box. Personal data was secured separately from research data and both will be password-protected.

Data from this research study will be disseminated in several ways. Dr. Gerald Devins has requested I consider sharing the raw IIRS item responses and relevant clinical data (e.g., medical and background information) with him for the purposes of accumulating norms and psychometric refinement of the instrument when he gave permission for the use of the IIRS in this quantitative study. The data results may also be shared with the medical staff of the PNA in Phoenix, AZ or potentially with IVIG nurses for educational purposes. Participants were notified of this in the Informed Consent Agreement. Permission to collect data was obtained from Walden University Internal Review Board ([IRB] approval # 01-13-15-0192064).

Summary

Chapter 3 explained the methodology for this quantitative nonexperimental research designed study. The purpose of the study was to examine the relationship between the IVIG experience and QOL in neurological autoimmune patients. The quantitative nonexperimental research study was based on the relevant constructs of the illness intrusiveness theory and personal control theory to assess the mediating influence of illness intrusiveness on the relationship between the IVIG experience and QOL as well as the possible mediating effects of personal control on the relationship between IVIG experience and QOL. Data was obtained through convenience sampling of neurological autoimmune patients receiving IVIG treatment at PNA in Phoenix, AZ. The following questionnaires were employed to collect data: IIRS to assess illness intrusiveness, Neuro-QOL to measure quality of life, MHLC-Form C to measure personal control, and a single-item VAS to measure the IVIG experience. Multiple regression was utilized to assess the mediation and predictive relationships. Precautions were used to assure privacy of all data. Chapter 4 presents the results and discussion of data collected.

Chapter 4: Results

Introduction

The purpose of the research was to examine the relationship between the IVIG treatment experience (predictor variable) and QOL (outcome variable) in neurological autoimmune patients. Responses from a project questionnaire were gathered from patients receiving IVIG treatment at PNA, an infusion center in Phoenix, AZ. Analysis was performed to ascertain the following: (a) whether the IVIG treatment experienced was a significant predictor of QOL in patients with autoimmune disease, (b) if illness intrusiveness mediated the relationship between the IVIG treatment experience and QOL, and (c) did personal control mediate the relationship between Illness Intrusiveness and QOL among individuals with autoimmune disease who receive IVIG treatment.

Data Collection

The data for this research study were collected using surveys distributed to interested patients at the PNA infusion center in Phoenix, AZ who were receiving IVIG treatment for neurological autoimmune disorders. Data collection began in January 2015 and ended in June 2015. Participants were offered the opportunity to participate in the study as they entered the IVIG infusion center, and if they chose to participate, could either fill out the questionnaires at the center and the nursing staff returned them to me by mail or the patient could return them on their own in the mail. A total of 79 patients responded by mailing their surveys back to me. The data collection site thought there would be access to more patients when the data collection process was originally begun.

Participants provided demographic information which included gender, age, employment status, diagnoses, length of time diagnosed, how often they receive IVIG treatment, length of time the administration of IVIG lasts, whether they receive premedication, and whether they experience side effects after IVIG treatment. Data were entered into SPSS 21. Total scores were calculated per SPSS computation directions.

Descriptive Statistics

The study included 25 male (31.6%) and 54 female (68.4%) participants who ranged in age from 18 to 80 with the largest percent (26.6%) being 60 to 70 and the second largest percent (25.3%) in the 50 to 60 age group. The IVIG patient group consisted of 37 (46.8%) employed or self-employed and 41 (51.9%) unemployed. All four diagnoses were represented with 30 MS, 25 CIDP, 13 MG, and 11 MMN patients. Patients had been diagnosed with a neurological autoimmune disease from 3 months (.25) to 44 years with a mean of 8.76 (SD = 7.97) years. The largest percentage of patients, 43% received IVIG every 4 to 5 weeks and 92.4% receive infusions over a 4 to 5 hour time period. Premedication prior to IVIG is given to 83.5% of the participants with 51.9% reporting side effects some of the time. This was not a random sample, so generalizability of the findings cannot be assumed. However, other infusion centers have populations similar to PNA, with a large percentage of their patients diagnosed with MS, MMN, MG, and CIDP (PNA, 2015). All four of these disease populations are underreported so it becomes difficult to speculate on an exact population number and comparison (Laughlin et al., 2009; Lawson & Arnold, 2014). This infusion center's medical staff indicated their population is similar to other IVIG infusion centers, so it is

reasonable to suggest that the current sample is likely typical of the population receiving IVIG at infusion centers. Table 1 displays demographics of the study participants.

Table 1

Descriptive Demographics of Study Participants

	Frequency	Percent
Gender		
Male	25	31.6
Female	54	68.4
Age		
18 - 30	3	3.8
31 - 40	13	16.5
41 - 50	13	16.5
51 - 60	20	25.3
61 - 70	21	26.6
71 - 80	9	11.4
Employment		
Not Employed	41	51.9
Employed or Self-Employed	37	46.8
Diagnosis		
MS	30	38.0
CIDP	25	31.6
MG	13	16.5
MMN	11	13.9
IVIG Frequency		
2 weeks	13	16.5
3 weeks	9	11.4
4 – 5 weeks	34	43.0
6 – 7 weeks	20	24.3
8 weeks or more	3	3.8

(table continues)

	Frequency	Percent
Length of IVIG		
1 hour	1	1.3
3 hours	5	6.3
4 hours	35	44.3
5 or more hours	38	48.1
Pre-medication		
No	13	16.5
Yes	66	83.5
Side Effects		
Never	18	22.8
Sometimes	41	51.9
Most of the time	9	11.4
Always	11	13.9

Examination of Distributional Properties

Outliers can differ from the main direction of the data and may influence the coefficients in regression (Field, 2013). The outlier labeling method was used in this study to determine if significant outliers were present. SPSS was used by taking the difference between the 25^{th} (lower quartile) and 75^{th} percentiles (upper quartile) multiplied by the standard factor 2.2 to define the presence of upper or lower outliers (Hoaglin & Iglewicz, 1987). Outliers for QOL total scores would have been 314.46 upper limit and 188.81 lower limit. There were no outliers in QOL total scores.

Missing data were sparse but were analyzed and the Little's Missing Completely at Random (MCAR) test was performed which was found to be nonsignificant at .879, which indicated missing values were missing completely at random. Missing data were

replaced using expectation maximization provided in the SPSS program. Expectation maximization is a missing value imputation strategy which estimates missing data from estimated parameters of observed data (Acock, 2005; Schlomer, Bauman, & Card, 2010). There was one VAS missing and 3 subscales missing, one quality of life lower extremity function (QOLLEF), one quality of life satisfaction with social roles and activities (QOLSSRA), and one quality of life depression (QOLDEPR). VAS and QOLLEF were from different participants and QOLSSRA and QOLDEPR were from the same participant. Nothing was changed after these analyses. I left these subscales missing in the analysis.

Examination of Multivariate Assumptions

Normality testing was performed by SPSS. Skewness and kurtosis were examined in order to evaluate if they would influence the analysis. Skewness reflects the symmetry of values with 0 being a normal distribution (George & Mallery, 2011). A skewness of +1 and -1 is acceptable. Kurtosis of +1 and -1 is viewed as excellent (George & Mallery, 2011). Results are presented in Table 2.

Table 2

Descriptive Statistics of Key Variables

Variable	*N*	Mean	*SD*	Skewness	Std. Error	Kurtosis	Std. Error
				Statistic		Statistic	
VAS	78	76.17	19.71	-.724	.272	-.071	.538
IIRS	79	41.41	16.07	.201	.271	-.892	.535
HCS	79	58.62	10.23	-.076	.271	.092	.535
SSRA	78	25.50	8.82	-.265	.272	-.819	.538
FATIG	79	26.99	7.17	-.244	.271	-.448	.535
DEPR	78	14.76	7.58	1.125	.272	.507	.538
PAWB	79	35.67	7.14	-.798	.271	.312	.535
STIG	79	14.49	6.23	1.03	.271	.498	.535
COG	79	30.03	7.59	-.472	.271	-.709	.535
SLP	79	20.30	6.99	.289	.271	-.983	.535
EBD	79	17.14	6.18	.741	.271	.221	.535
LEF	78	31.60	8.38	-.836	.272	-.446	.538
UEF	79	36.34	4.87	-1.18	.271	.211	.525

Note. VAS = Visual Analog Scale; IIRS = Illness Intrusiveness Rating Scale; HCS = Personal Control SSRA = Satisfaction with Social Roles and Activities; FATIG = Fatigue; DEPR = Depression; PAWB = Positive Affect and Well-Being; STIG = Stigma; COG = Cognition; SLP = Sleep; EBD = Emotional and Behavioral Dyscontrol; LEF = Lower Extremity Function; UEF = Upper Extremity Function.

The assumption of homoscedasticity was assessed by viewing a scatterplot between residuals and predicted values. The plot showed no suggestion of a pattern and the assumption was met. The assumption of linearity was met as the scatterplots were uniform around a linear fit line. Below the correlation matrix is presented for the independent variables and the dependent variables of QOL. Correlation of predictor variables and Neuro-QOL outcome scales are displayed in Table 3.

Table 3

Correlation of predictor variables and Neuro-QOL outcome scales

	VAS	IIRS	HCS
PAWB	.34**	-.47**	.13
SSRA	.32*	-.66**	.03
FATIG	-.29*	.61**	.04
DEPR	-.29*	.55**	-.07
COG	-.01	-.40**	.10
STIG	-.06	.50**	.06
SLP	-.10	.60**	.06
EBD	-.40	.43**	.03
LEF	.17	-.33**	.08
UEF	.16	-.09	.04

Note. VAS = Visual Analog Scale; IIRS = Illness Intrusiveness Rating Scale; HCS = Personal Control; PAWB = Positive Affect and Well-Being; SSRA = Satisfaction with Social Roles and Activities; FATIG = Fatigue; DEPR = Depression; COG = Cognition; STIG = Stigma; SLP = Sleep; EBD = Emotional Behavior and Dyscontrol; LEF = Lower Extremity Function; UEF = Upper Extremity Function.
*Correlation is significant at $p < .01$; ** Correlation is significant at $p < .005$

Multicollinearity can occur when there is a strong association between predictor variables (Field, 2013). I used SPSS to perform collinearity statistics for each of the predictors for Hypotheses 2 and 3. Each variable, VAS, IIRS, and MHLC took a turn as the dependent variable. None of the variables were found to have high correlations with the other variable. The variance inflation factor (VIF) was 1.05, 1.004, and 1.001 respectively. These values were below 3 which is considered to be a level of concern (Field, 2013; O'Brien, 2007). Tolerance values were .949, .996, and .999 respectively. These tolerance values do not fall below 0.2 which could indicate a multicollinearity problem (Field, 2013). Although SPSS produces multicollinearity statistics, the correlation matrix can also be scanned to see if any of the predictors are highly correlated. The scanning method may miss some more subtle signs of multicollinearity

according to Field (2013); however, the correlation matrix for the current study revealed no problems in collinearity either as the predictor variables were not highly correlated. There were some interesting correlations between some of the dependent variables (Neuro-QOL scales) which will be discussed in Chapter 5 as other noteworthy findings. Table 4 displays the correlations in the Neuro-QOL scales.

Table 4

Correlation of Neuro-QOL scales

	PAWB	SSRA	FATI	DEPR	COG	STIG	SLP	EBD	LEF	UEF
PAWB	1	.50***	-.45***	-.72***	.32**	-.41***	-.44***	-.36***	.26*	.35**
SSRA		1	.73***	-.64***	.34***	-.56***	-.56***	-.36***	.58***	.35***
FATI			1	.58***	-.52***	.44***	.68***	.37***	-.37***	-.28*
DEPR				1	-.42***	.66***	.59***	.43***	-.37***	.40***
COG					1	-.29**	-.50***	-.26*	.16	.16
STIG						1	.55***	.45***	-.47***	-.39***
SLP							1	.53***	-.42***	-.31**
EBD								1	-.04	-.09
LEF									1	.52***
UEF										1

Note. PAWB = Positive Affect and Well-Being; SSRA = Satisfaction with Social Roles and Activities; FATI = Fatigue; DEPR = Depression; Cog = Cognition; STIG = Stigma; SLP = Sleep; EBD = Emotional and Behavioral Dyscontrol; LEF = Lower Extremity Function; UEF = Upper Extremity Function.
*** Correlation at $p < .005$; ** Correlation at $p < .01$; * Correlation at $p < .05$

Results

Research Question 1

RQ1: Is the IVIG treatment experience (as measured by the VAS) a significant predictor of QOL as measured by the 10 Neuro-QOL scales in patients with autoimmune disorders who receive IVIG treatment?

Research Question 1 was answered by performing a Pearson's correlation analysis and regression with the test of path *c* in the mediational analysis. I conducted a correlational analysis to examine the associations between IVIG treatment experience (VAS) and the Neuro-QOL separate scales. Bonferroni correction was employed due to the testing of the 10 Neuro-QOL scales separately. Bonferroni may protect from Type I error at the risk of Type II error (Field, 2013). In this case Bonferroni meant the significance value would be $p < .005$. The predictor IVIG treatment experience as measured by the VAS showed a significant correlation (<.005) with the Neuro-QOL scale, positive affect and well-being. The results of the simple linear regression for the Neuro-QOL positive affect and well-being was significant ($R^2 = .12$). The other nine Neuro-QOL scales were not statistically significant at alpha .005. The Null Hypothesis 1 was rejected for the Neuro-QOL scale, positive affect and well-being. However, I failed to reject the null hypotheses for the other nine Neuro-QOL scales. Correlations for IVIG treatment experience and the Neuro-QOL scales are presented in Table 3.Although IVIG treatment experience (VAS) did not significantly predict QOL in the remaining nine QOL subscales, recent literature supports that mediation analysis does not require verification

of the simple association between X and Y to be able to test hypotheses regarding indirect effects, thus all ten QOL dependent variables were tested for indirect effects (Hayes, 2009, 2013; Rucker et al., 2011; Zhao et al., 2010).

Research Question 2

RQ2: Does illness intrusiveness mediate the relationship between the IVIG treatment experience and QOL (as measured by the 10 Neuro-QOL scales) among individuals with autoimmune disease who received IVIG treatment?

I performed a mediation analysis on all 10 of the Neuro-QOL subscales including those subscales that did not show a correlation between X and Y with Process Macro version 2.13. I used the robust test of bootstrap confidence intervals (a repeated sampling of the population) for estimating the indirect effect which makes no assumption about the distribution shape of *ab.* In fact, bootstrapping has been demonstrated to yield higher power when testing a hypothesis (Hayes, 2013).

Nine of the 10 QOL subscales revealed an indirect effect (Rucker et al., 2011) which are demonstrated in the tables of the statistical indices for each mediation and the path diagrams which follow. I rejected the null hypotheses in those nine QOL subscales. Unstandardized coefficients are reported as they are the preferred metric in causal modeling and results can be compared directly with studies performed utilizing the same measurement system (Hayes, 2013). VAS was the independent variable, IIRS was the mediator, and each of the Neuro- QOL variables were tested in a separate mediation analysis.

QOL Satisfaction with Social Roles and Activities

The first mediation analysis examined whether Illness Intrusiveness mediates the relationship between IVIG treatment experience and QOL in social roles and activities. The multiple regression was significant, $R^2 = .461$, $F(2, 74) = 31.68$, $p < .001$. The results indicate that 46% of the variance in satisfaction with social roles and activities was predicted by IVIG treatment experience and illness intrusiveness. The unstandardized coefficients for paths *a, b* and *c′* respectively were $b = -0.186$, $t(74) = -2.012$, $p = .048$; $b = -0.331$, $t(75) = -7.024$, $p < .001$; path $c' = 0.080$, $t(75), = 2.06$, $p = .0429$. The total effect, $b = 0.141$, $t(75) = 2.92$, $p = .004$ showed $R^2 = .10$ indicating IVIG treatment experience explained 10% of the variance in QOL but the larger portion of variance was illness intrusiveness.

A bias-corrected bootstrap confidence interval for the indirect effect ($ab = .061$) based on 10,000 bootstrap samples was entirely above zero [0.0085, 0.1271] indicating mediation. The null hypothesis was rejected for the QOL satisfaction with social roles and activities subscale. A post hoc test using Gpower with a probability error of .005 and sample size of 79 revealed a power of .99. The effect size $k^2 = .16$ with 95% CI [0.0227, 0.2888] was considered a medium effect (Preacher & Kelley, 2011). Figure 3 displays a statistical path diagram and Table 5 displays statistical indices of the result of the mediation of IVIG treatment experience (VAS) and QOL satisfaction with social roles and activities (QOLSSRA).

Table 5

Mediation Model Coefficients for IVIG Treatment Experience and QOL Satisfaction with Social Roles and Activities

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLSSRA)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.186	0.092	.047	*c′*	0.080	0.039	.0429
					b	-0.331	0.047	< .001
		R^2 = .051				R^2 = .461		
		$F(1, 75) = 4.049$, $p = .048$				$F(2, 74) = 31.684$, $p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLSSRA = Quality of Life Satisfaction with Social Roles and Activities.

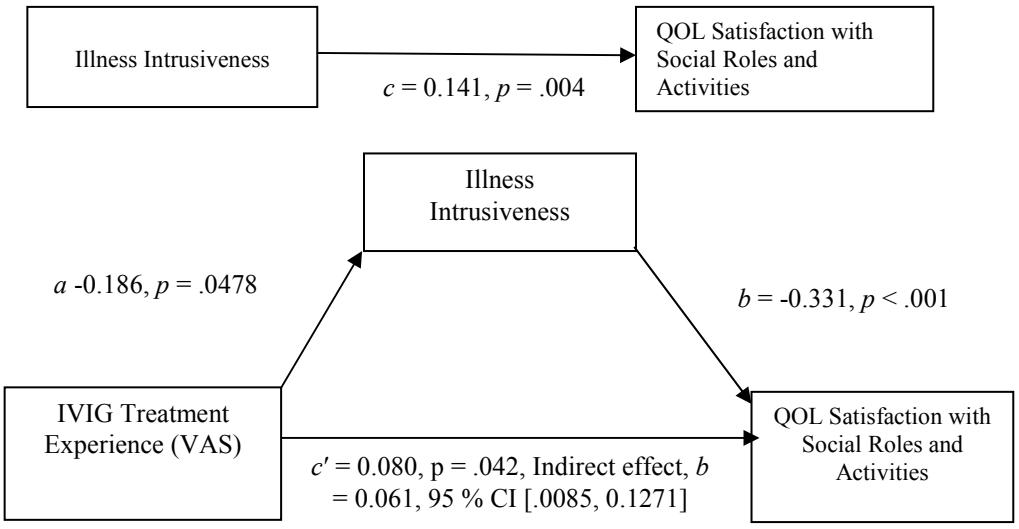

Figure 3. Model of IVIG treatment experience (VAS) and QOL satisfaction with social roles and activities mediated by illness intrusiveness.

QOL Depression

A multiple regression was performed to predict the variable Neuro-QOL Depression from IVIG treatment experience (VAS) and illness intrusiveness. The

regression was significant, $R^2 = .328$, $F(2,74) = 18.085$, $p < .001$. The R^2 value of .33 estimates that the model explains about 33% of the variance in QOL depression. Paths *a*, b, and *c′* respectively were $b = -0.1856$, $t\ (75) = 2.012$, $p = .048$; $b = 0.237$, $t\ (75) = 5.161$, $p < .001$, and $b = -0.070$, $t\ (75) = -1.840$, $p = .0698$. The total effect (path *c*) indicated VAS significantly predicts QOL depression even when illness intrusiveness is not in the model, $b = -0.1131$, $t\ (75) = -2.666$, $p = .009$.

A bias-corrected bootstrap confidence interval based on 10,000 samples for the indirect effect ($ab = -.044$) did not include zero [-.1031, -.0069] indicating mediation. I rejected the null hypothesis for Neuro- QOL depression. A post hoc test using Gpower was calculated indicating a power of .96 for the sample size of 79. The effect size $k^2 = .12$ with a 95% CI [0.0187, 0.2465] was medium. Statistical analyses in the form of a path diagram in Figure 4 and statistical indices displayed in Table 6 revealed there was significant mediation between illness intrusiveness and QOL depression.

Table 6

Mediation Model Coefficients for IVIG Treatment Experience and QOL Depression

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLDEPR)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.186	0.092	.047	*c′*	-0.0692	0.0376	.0698
					b	0.2366	0.0458	< .001
		$R^2 = .05$				$R^2 = .33$		
		$F(1, 75) = 4.049$, $p = .048$				$F(2, 74) = 18.0851$, $p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLDEPR = Quality of Life Depression.

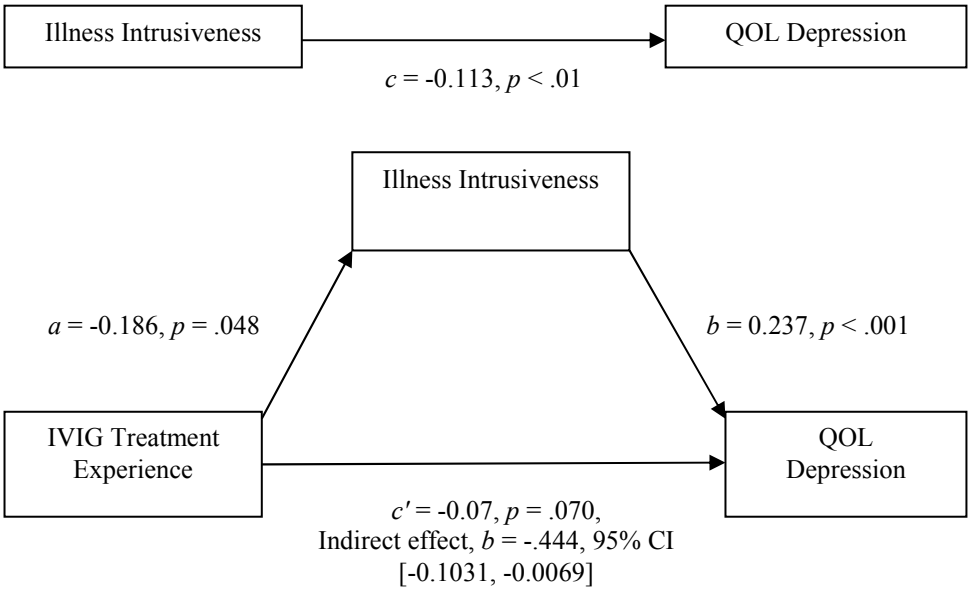

Figure 4. Model of IVIG treatment experience and QOL depression, mediated by illness intrusiveness with unstandardized coefficients.

QOL Fatigue

A mediation analysis was conducted predicting illness intrusiveness from IVIG treatment experience as well as QOL fatigue from both IVIG treatment experience and illness intrusiveness. The multiple regression was significant, $R^2 = .394$, $F(2,75) = 24.327$, $p < .001$ indicating 39% of the variance in QOL fatigue was accounted for by IVIG treatment experience and illness intrusiveness. Paths *a*, *b* respectively were $b = -0.184$, $t(76) = -2.01$, $p = .048$; $b = 0.252$, $t(76) = 6.16$, $p < .001$. The direct effect (path c′) was negative, $b = -0.060$, $t(76) = -1.79$, $p = .077$. The total effect (path *c*) was negative, $b = -0.106$, $t(76) = -2.68$, $p = .009$.

A bias-corrected bootstrap confidence interval for the negative indirect effect, $b = -0.046$ based on 10,000 samples did not include zero 95% CI [-0.096, -0.006] indicating

mediation. I rejected the null hypothesis for the Neuro-QOL Fatigue scale. A post hoc test using Gpower was performed indicating a power of .98 for the sample of 79. The effect size, $k^2 = .14$ with a 95% CI [0.0202, 0.2553] was medium. Figure 5 provides the statistical figure for the mediation analysis and statistical indices are displayed in Table 7.

Table 7

Mediation Model Coefficients for IVIG Treatment Experience and QOL Fatigue

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLFATIG)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-.184	.092	.047	*c′*	-.060	.033	.077
					b	.252	.041	< .001
		$R^2 = .05$				$R^2 = .394$		
		$F(1, 75) = 4.049$, $p = .048$				$F(2, 75) = 24.327$, $p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLFATIG = Quality of Life Fatigue.

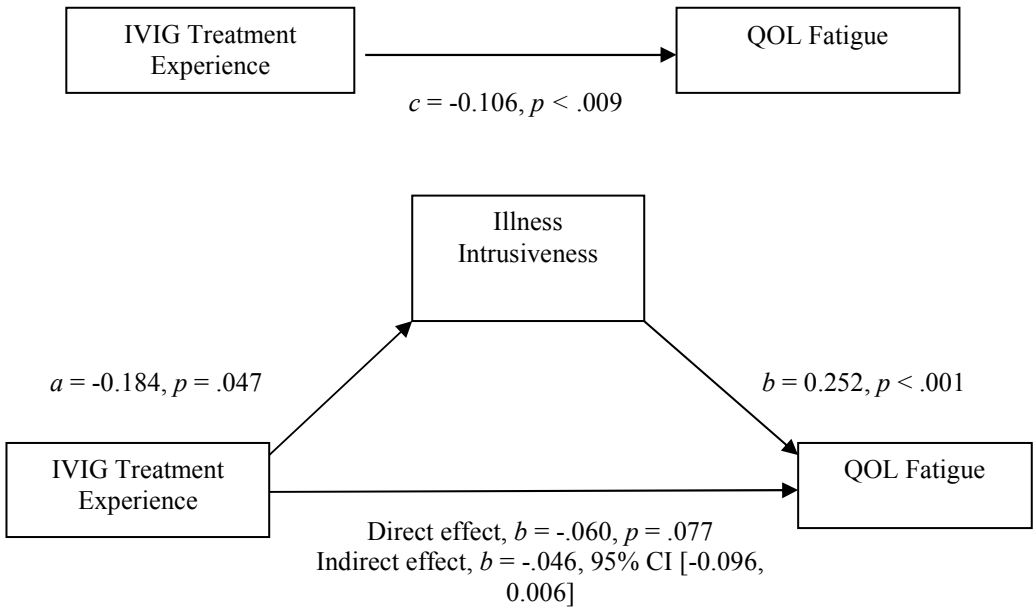

Figure 5. Model of IVIG treatment experience and QOL Fatigue mediated by illness intrusiveness with unstandardized coefficients.

QOL Positive Affect and Well-Being

A mediation analysis was performed to predict QOL positive affect and well-being from IVIG treatment experience and illness intrusiveness. The regression was significant, $R^2 = .273$, $F(2,75) = 14.06$, $p < .001$ indicating 27% of the variance in QOL positive affect and well-being was predicted by IVIG treatment experience and illness intrusiveness. Paths *a* and *b* respectively were $b = -0.184$, $t(76) = -2.012$, $p = .047$; $b = -0.180$, $t(76) = -4.029$, $p < .001$. The direct effect (path *c′*) was positive, $b = 0.089$, $t(76) = 2.452$, $p = .017$ and the total effect (path c) was positive and significant, $b = 0.122$, $t(76) = 3.15$, $p = .002$.

A bias-corrected bootstrap confidence interval for the indirect effect ($ab = .033$) based on 10,000 bootstrap samples was entirely above zero 95% CI [0.0062, 0.0787] indicating mediation. I rejected the null hypothesis for the Neuro- QOL positive affect and well-being. A post hoc test using Gpower with a probability error of .005 showed a power of .91 for the sample of 79. The effect size $k^2 = .10$ with 95% CI [0.0184, 0.1998] was medium. Mediation is illustrated by the path diagram in Figure 6. The statistical indices displayed in Table 6 indicated there was a significant indirect effect.

Table 8

Mediation Model Coefficients for IVIG Treatment Experience and QOL Positive Affect and Well-Being

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLPAWB)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	0.091	.048	*c′*	0.089	0.036	.017
					b	-0.180	0.045	< .001
		R^2 = .05				R^2 = .273		
		$F(1, 76) = 4.049$, $p = .048$				$F(2, 75) = 14.057$, $p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLPAWB = Quality of Life Positive Affect and Well-Being.

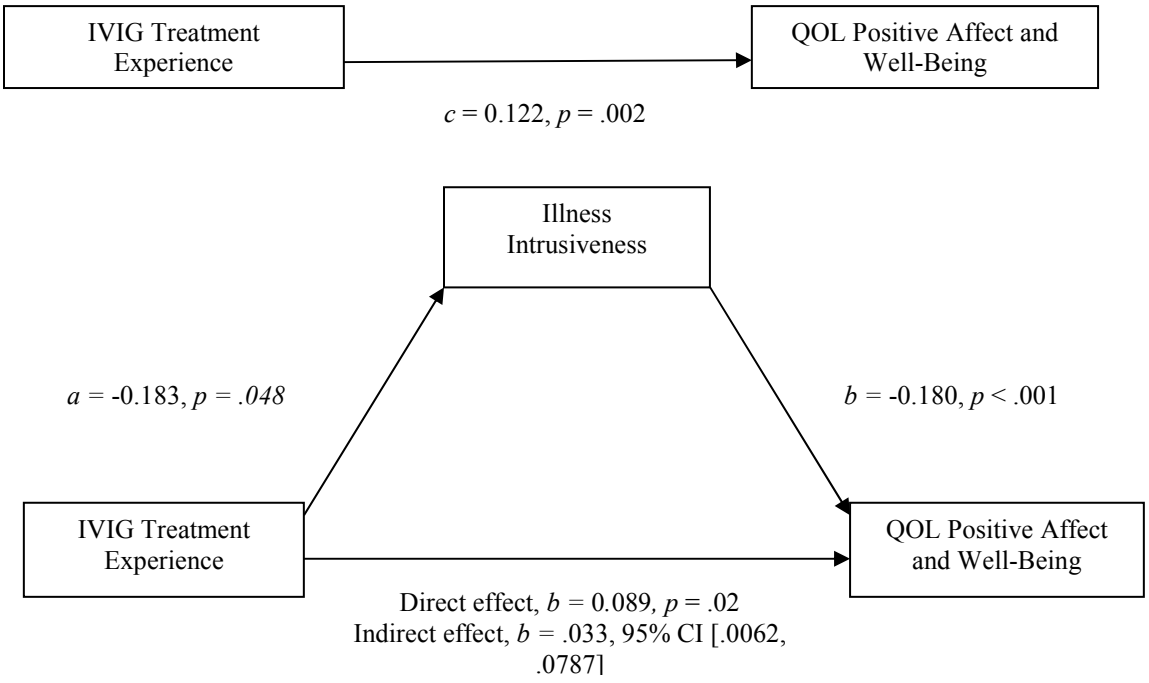

Figure 6. Model of the relationship between IVIG treatment experience and QOL positive affect and well-being mediated by illness intrusiveness.

QOL Sleep

A mediation analysis was conducted to predict QOL sleep from IVIG treatment experience and illness intrusiveness. The multiple regression was significant, $R^2 = .36$, $F(2, 75) = 20.634$, $p < .001$ indicating the model explained 36% of the variance in QOL Sleep. Paths *a* and *b* respectively were $b = -0.184$, $t(76) = -2.012$, $p = .048$; $b = 0.259$, $t(76) = 6.34$, $p < .001$. The direct effect was not significant, (c′), $b = 0.013$, $t(76) = .397$, $p = .692$. The total effect (path c) was not significant, $b = -0.034$, $t(76) = -0.857$, $p = .394$. A percentile bootstrap confidence interval for the indirect effect ($ab = -.048$) based on 10,000 bootstrap samples did not include zero 95% CI [-.1017 to -.0057] indicating mediation. I rejected the null hypothesis for the Neuro- QOL Sleep scale. I conducted a post hoc test using Gpower with a probability error of .005 which showed .97 power for the sample size of 79. The effect size, $k^2 = .16$ with 95% CI [0.0257, 0.3126] was medium. Statistical indices are displayed in Table 9 and a statistical diagram of the mediation model is displayed in figure 8.

Table 9

Mediation Model Coefficients for IVIG Treatment Experience and QOL Sleep

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLSLP)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	0.091	.048	*c′*	0.013	0.033	.692
					b	0.259	0.041	< .001
		$R^2 = .05$				$R^2 = .36$		
		$F(1, 76) = 4.049$, $p = .048$				$F(2, 75) = 20.6347$, $p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLSLP = Quality of Life Sleep.

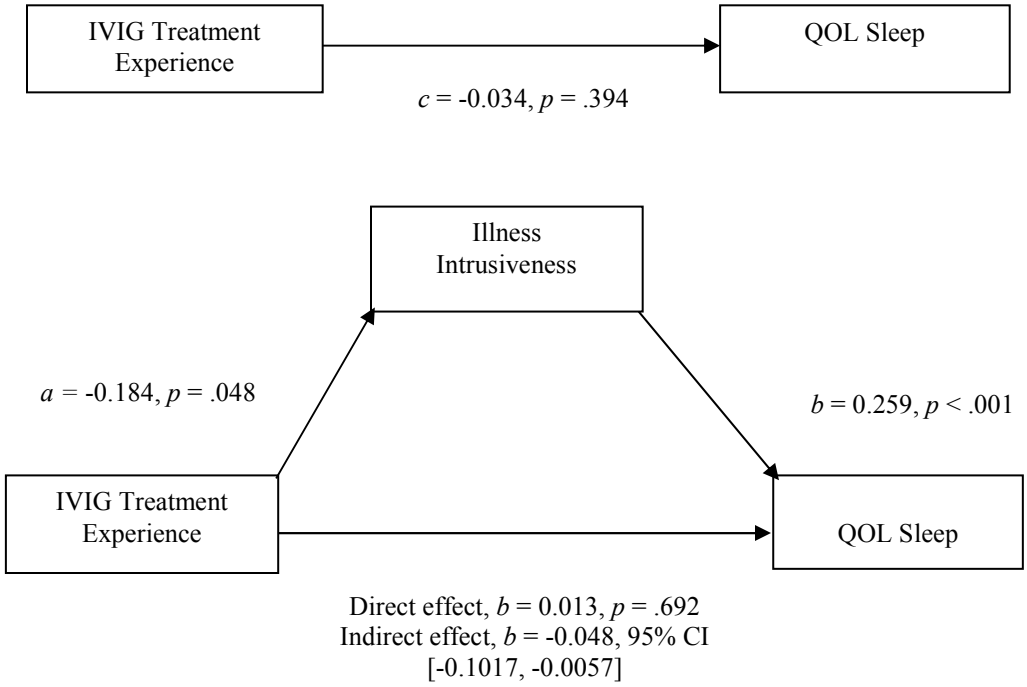

Figure 7. Model of the relationship between IVIG treatment experience and QOL sleep mediated by illness intrusiveness.

QOL Stigma

A mediation analysis was conducted to assess the relationship of IVIG treatment experience on QOL stigma through illness intrusiveness. The multiple regression was significant. R^2 =.249, $F(2, 75) = 12.472$, $p < .001$ indicating 25% of the variance in QOL stigma was explained by IVIG treatment experience and illness intrusiveness. Path *a* was negative, $b = -0.184$, $t(76) = -2.012$, $p = .048$ and path *b* was significant and positive , $b = 0.197$, $t(76) = 4.962$, $p < .001$. The direct effect was not significant (path *c′*), $b = .018$, $t(76) = .566$, $p = .573$. The total effect (path *c*) was not significant, $b = -0.018$, $t(76) = -.493$, $p = .623$. However, a bias-corrected bootstrap confidence interval of 10,000 samples for the indirect effect (*ab* = -.036) did not include zero 95% CI [-.0841 and -

.0052] indicating mediation. I rejected the null hypothesis for QOL stigma. A post hoc power analysis with Gpower with probability error set at .005 indicated a power of .88. The effect size of $k^2 = .13$ with 95% CI [0.0189, 0.2853] was medium. Statistical indices are provided in Table 10 and the statistical diagram of mediation is displayed in Figure 8.

Table 10

Mediation Model Coefficients for IVIG Treatment Experience and QOL Stigma

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLSTIG)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	.091	.048	*c′*	0.018	0.032	.573
					b	0.197	0.039	< .001
		$R^2 = .05$				$R^2 = .25$		
		$F(1, 76) = 4.049, p = .048$				$F(2, 75) = 12.4725, p < .001$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLSTIG = Quality of Life Stigma.

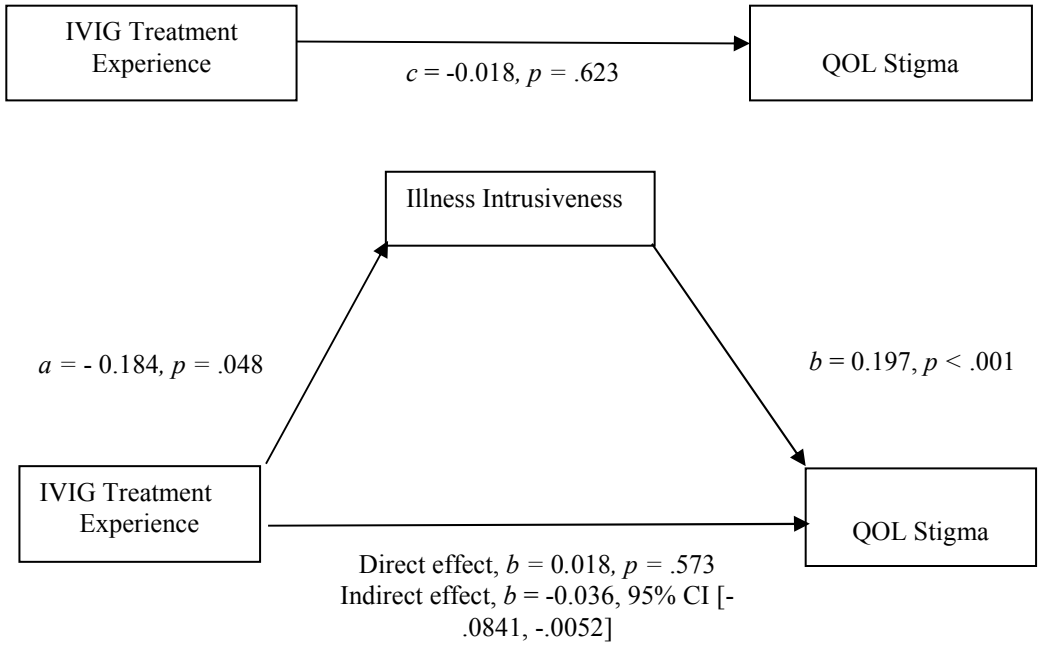

Figure 8. Relationship between IVIG treatment experience and QOL stigma mediated by illness intrusiveness.

QOL Cognition

A mediation analysis was performed to assess the relationship of IVIG treatment experience on Neuro-QOL cognition through illness intrusiveness. The multiple regression was significant, $R^2 = .164$, $F(2, 75) = 7.356$, $p = .0012$ indicating IVIG treatment experience and illness intrusiveness explained about 16% of the variance in QOL cognition. Paths *a* and *b* respectively were, $b = -0.184$, $t(76) = -2.012$, $p = .048$; $b = -0.196$, $t(76) = -3.834$, $p = .0003$. The direct effect (c') was not significant, $b = -0.041$, $t(76) = -0.9903$, $p = .33$. The total effect (path *c*) was not significant, $b = -0.005$, $t(76) = -.1211$, $p = .904$.

A percentile bootstrap confidence interval for the indirect effect ($ab = 0.036$) based on 10,000 bootstrap samples was entirely above zero 95% CI [0.0030, 0.0870] indicating mediation. I rejected the null hypothesis for the Neuro-QOL cognition scale. I performed a post hoc test with Gpower set at .005 probability error for Bonferroni correction which indicated a power of .62. The effect size $k^2 = .10$ with 95% CI [0.0123, 0.2259] was medium. The mediation unstandardized coefficients are displayed in Table 11 and the statistical indices in Figure 9.

Table 11

Mediation Model Coefficients for IVIG Treatment Experience and QOL Cognition

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLCOG)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	.091	.048	*c′*	-0.041	0.042	.325
					b	-0.196	0.051	.0003
		R^2 = .05				R^2 = .164		
		$F(1, 76) = 4.049$, $p = .048$				$F(2, 75) = 7.3567$, $p = .0012$		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLCOG = Quality of Life Cognition.

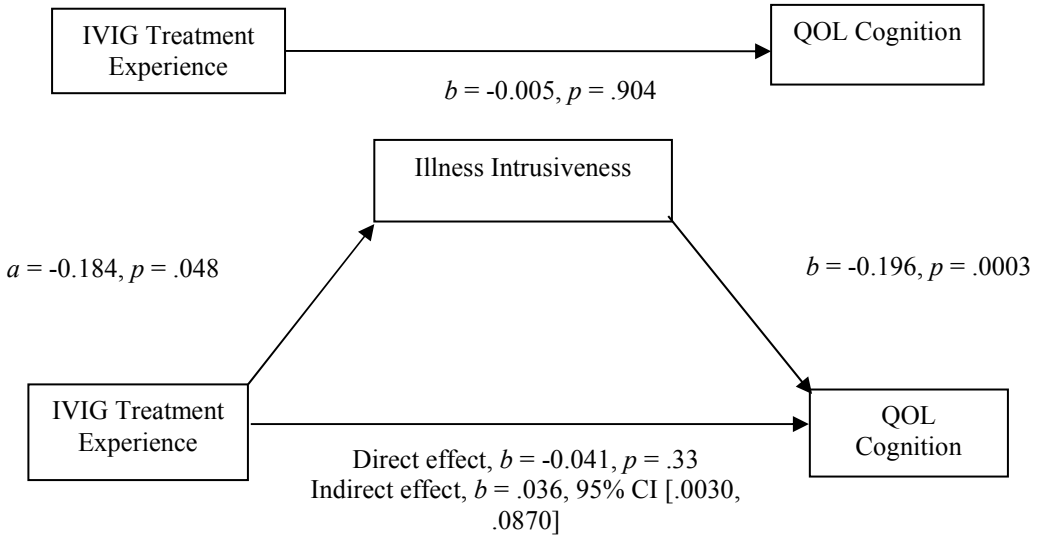

Figure 9. Model of the relationship between IVIG treatment experience and QOL cognition mediated by illness intrusiveness.

QOL Emotional and Behavioral Dyscontrol

A mediation analysis was conducted estimating illness intrusiveness influence on the relationship between IVIG treatment experience and QOL emotional and behavioral dyscontrol (QOLEBD). The multiple regression was significant, $R^2 = .197$, $F(2, 75) = 9.212$, $p = .0003$ indicating the model explained 20% of the variance in QOLEBD. Path

a was negative, *b* = -0.184, *t*(76) = -2.012, *p* = .048 and path *b* was positive and significant, *b* = 0.175, *t*(76) = 4.277, *p* = .0001. The direct effect was negative and not significant, (*c*′), *b* = 0.021, *t*(76) = .615, *p* = .540. The total effect was not significant (path *c*), *b* = -0.012, *t*(76) = -.3213, *p* = .749.

A bias-corrected bootstrap confidence interval for the indirect effect (*ab* = -0.032) based on 10,000 bootstrap samples did not include zero 95% CI [-0.0794, -0.0048] indicating mediation. I rejected the null hypothesis for Neuro-QOL emotional and behavioral dyscontrol. I performed a post hoc test with Gpower using .005 for alpha based on Bonferroni Correction which displayed a power of .77. The effect size k^2 = .11 with 95% CI [0.019, 0.239] was medium. Table 12 presents the mediation indices and Figure 10 provides the statistical diagram of mediation.

Table 12

Mediation Model Coefficients for IVIG Treatment Experience and QOL Emotional and Behavioral Dyscontrol

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLEBD)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	0.091	.048	*c′*	0.021	0.033	.5403
					b	0.175	0.041	.0001
		R^2 = .05				R^2 = .197		
		F(1, 76) = 4.049, *p* = .048				*F*(2, 75) = 9.2115, *p* = .0003		

Note. IVIG = Intravenous Immunoglobulin; VAS = Visual Analog Scale; QOLEBD = Quality of Life Emotional and Behavioral Dyscontrol.

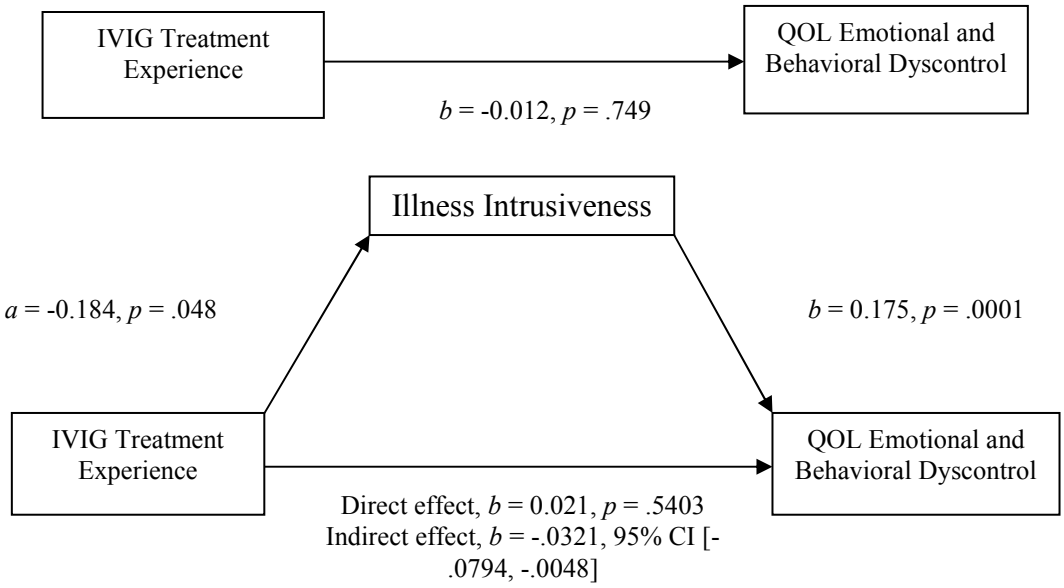

Figure 10. Model of the relationship between IVIG treatment experience and QOL emotional and behavioral dyscontrol mediated by illness intrusiveness.

QOL Lower Extremity Function

A mediation analysis was conducted by estimating illness intrusiveness influence from IVIG treatment experience as well as QOL lower extremity function (QOLLEF) from both IVIG treatment experience and illness intrusiveness. The model was not significant at the .005 level, $p < .005$, $R^2 = .11$, $F(2, 74) = 4.633$, $p = .01$. Path *a* and *b* respectively were not significant, $b = -0.176$, $t(75) = -1.902$, p = .061; $b = -0.153$, t(75) = -2.626, $p = .011$. The direct effect was not significant (c'), $b = 0.045$, $t(75) = .9414$, $p = .349$ and the total effect (path *c*) was not significant, $b = .072$, $t(75) = 1.483$, $p = .142$. However, a bias-corrected bootstrap confidence interval based on 10,000 bootstrap samples did not include zero 95% CI [0.0029, 0.0745] indicating a small indirect effect ($ab = .027$). This supports current literature that it is possible to find an indirect effect

when a sound inferential test is employed even if path *a* or path *b* are not statistically significant since the indirect effect is the product of *a* and *b* and should not be based on hypothesis tests of *a* and *b* (Hayes, 2013). I rejected the null hypothesis for the Neuro-QOL lower extremity function. Effect size of $k^2 = .06$ with 95% CI [0.0081, 0.1683] was small. Table 13 provides the statistical indices and Figure 11 presents the statistical diagram of mediation.

Table 13

Mediation Model Coefficients for IVIG Treatment Experience and QOL Lower Extremity Function

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLLEF)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.176	0.093	.061	*c′*	0.045	0.048	.350
					b	-0.153	0.058	.011
		$R^2 = .046$				$R^2 = .111$		
		$F(1, 75) = 3.62$ $p = .061$				$F(2, 74) = 4.634$, $p = .013$		

Note. IVIG = intravenous immunoglobulin; VAS = Visual Analog Scale; QOLLEF = quality of life lower extremity function.

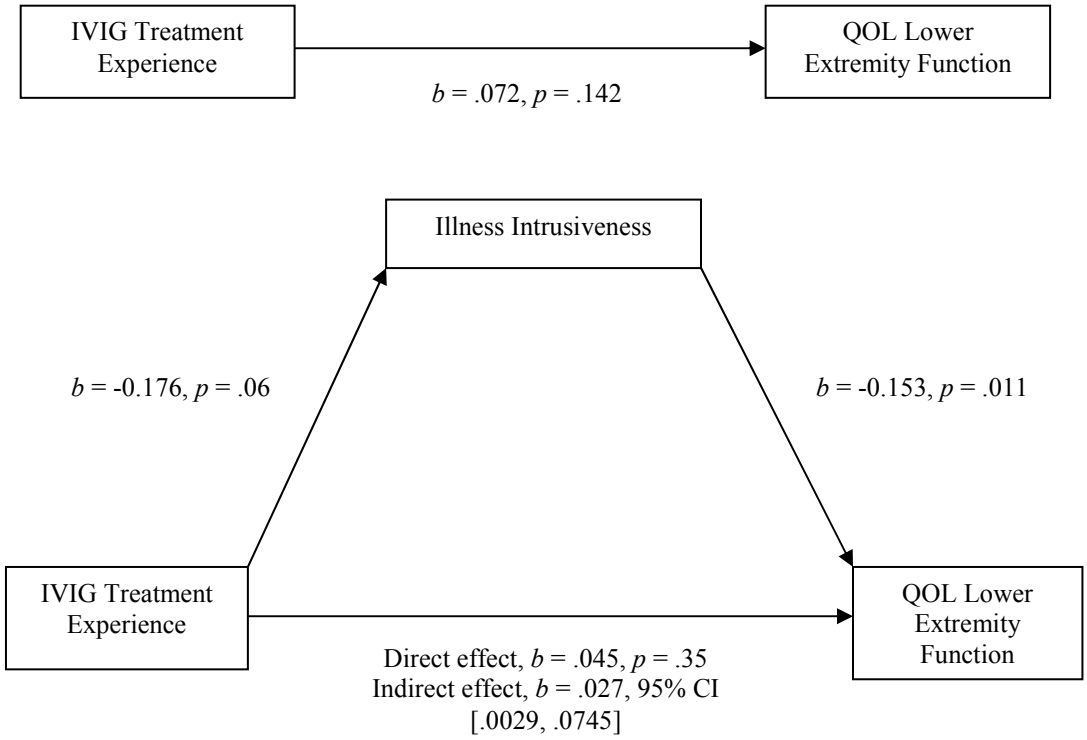

Figure 11. Model of relationship between IVIG treatment Experience and QOL lower extremity function mediated by illness intrusiveness.

QOL Upper Extremity Function

A mediation analysis was performed estimating illness intrusiveness influence mediated from IVIG treatment experience as well as QOL upper extremity function (QOLUEF) from both IVIG treatment experience and illness intrusiveness. There was no evidence that IVIG treatment experience influenced QOLUEF through illness intrusiveness. The model was not significant, $R^2 = .027$, $F(2, 75) = 1.056$, $p = .353$. Path *a* was negative $b = -.184$, t(76) = -2012, $p = .048$ and path *b* was not significant $b = -0.015$, $t(2, 75)$ -0.4269, $p = .671$. The direct path was not significant (c'), $b = 0.036$, $t(76) = 1.258$, $p = .212$ and the total effect was not significant , $b = 0.039$, $t(76) = 1.397$, $p = .167$. A 95% bias corrected confidence interval for the indirect effect ($b = .0028$) included zero

(-.0097, .0218). I failed to reject the hypothesis for QOLUEF Upper Extremity Function.

Figure 12 shows the relationship between IVIG treatment experience and QOLUEF not mediated by illness intrusiveness. Table 14 presents the statistical indices.

Table 14

Mediation Model Coefficients for IVIG Treatment Experience and QOL Upper Extremity Function

		Outcomes						
		M (Illness Intrusiveness)				Y (QOLUEF)		
Predictor	Path	*b*	*SE*	*p*	Path	*b*	*SE*	*p*
IVIG (VAS)	*a*	-0.184	0.091	.048	*c′*	0.036	0.029	.212
					b	-0.015	0.036	.671
		$R^2 = .05$				$R^2 = .027$		
		$F(1, 76) = 4.049$, $p = .048$				$F(2, 75) = 1.056$, $p = .353$		

Note. IVIG = intravenous immunoglobulin; VAS = Visual Analog Scale; QOLUEF = quality of life upper extremity function.

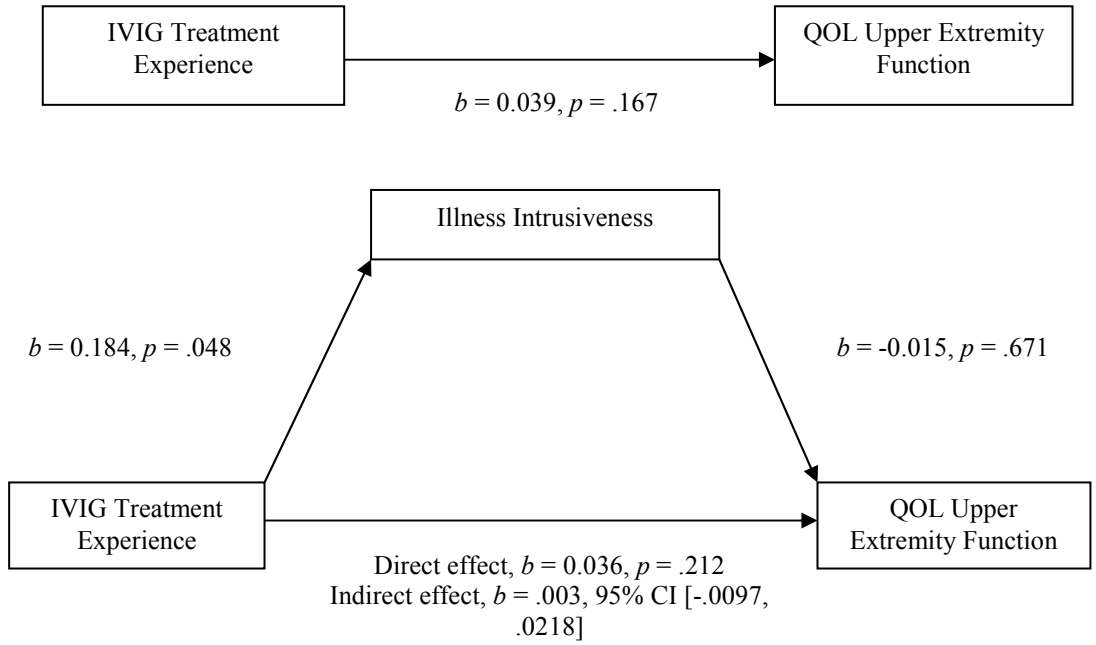

Figure 12. Model of the relationship between IVIG treatment experience and QOL upper extremity function not mediated by illness intrusiveness.

Research Question 3

RQ3: Does personal control mediate the relationship between illness intrusiveness, and QOL (as measured by the 10 Neuro-QOL scales) among individuals with autoimmune disease who receive IVIG treatment?

Mediation analysis was conducted to estimate if Personal Control (as measured by the MHLC – Form C) mediated the relationship between IVIG treatment experience (VAS) and QOL in neurological autoimmune patients. I performed mediation analysis using PROCESS Macro on all 10 of the Neuro-QOL subscales and employing the robust method of bootstrapping when conducting multiple regressions. According to the results with bias-corrected bootstrap of 10,000 samples there was no evidence of an indirect effect as all QOL variables effects included zero. In other words, there was no evidence that illness intrusiveness influenced QOL through personal control. Therefore, I failed to reject the null hypothesis that control influenced the relationship between illness intrusiveness and the Neuro-QOL variables. Table 13 displays the results of mediation analysis examining Hypotheses 3 estimating if personal control mediates the relationship between illness intrusiveness and QOL.

Table 15.

Indirect effect of Illness Intrusiveness (X) on QOL (Y) through Personal Control (M) with No Mediation

QOL	Effect	Boot SE	95% BC CI LL	95% BC CI UL
QOLSSRA	.0011	.0007	-.0068	.0237
QOLFATIG	.0003	.0043	-.0064	.0124
QOLDEPR	-.0015	.0070	-.0234	.0071
QOLPAWB	.0023	.0088	-.0093	.0320
QOLSLP	-.0008	.0052	-.0176	.0063
QOLCOG	.0019	.0092	-.0087	.0361
QOLEBD	.0002	.0052	-.0085	.0126
QOLSTIG	.0006	.0056	-.0060	.0191
QOLLEF	.0019	.0081	-.0070	.0290
QOLUEF	.0004	.0036	-.0043	.0119

Note: BC CI LL = bias-corrected confidence interval lower limit; BC CI UL = bias-corrected confidence interval upper limit; QOLSSRA = quality of life satisfaction with social roles and activities; QOLFATIG = quality of life fatigue; QOLDEPR = quality of life depression; QOLPAWB = quality of life positive affect and well-being; QOLSLP = quality of life sleep; QOLCOG = quality of life cognition; QOLEBD = quality of life emotional and behavioral dyscontrol; QOLSTIG = quality of life stigma; QOLLEF = quality of life lower extremity function; QOLUEF = quality of life upper extremity function.

Summary

The purpose of this chapter was to test three hypotheses regarding the relationship of IVIG treatment experience and QOL in neurological autoimmune patients. Specifically, the study investigated if IVIG treatment experience predicted QOL, if IVIG treatment experience influenced QOL through illness intrusiveness and if illness intrusiveness influenced QOL through personal control.

Research Question 1 revealed mixed results. One of the 10 Neuro-QOL subscales showed significant correlation; QOL positive affect and well-being. Therefore, the first

null hypothesis was rejected for that one QOL scale. However, the other nine subscales did not reveal correlation at the error probability of .005 so I failed to reject the first hypothesis for QOL satisfaction with social roles and activities, QOL depression, QOL fatigue, QOL sleep, QOL stigma, QOL cognition, QOL emotional and behavioral dyscontrol, QOL lower extremity function, and QOL upper extremity function. However, as was previously acknowledged since current literature regarding mediation no longer requires the simple association between X and Y in order to test for mediation (Hayes, 2013; Rucker et al., 2011) I proceeded with Research Question 2 for all ten of the Neuro-QOL variables.

Research Question 2 was answered by performing 10 mediation analysis estimating illness intrusiveness influence from IVIG treatment experience as well as QOL from both IVIG treatment experience and illness intrusiveness. A significant indirect effect was found for nine of the QOL subscales supported by the robust test of bias-corrected or percentage bootstrapping with 10,000 samples. Therefore, I was able to reject the null hypothesis for Research Question 2 in nine of the Neuro-QOL subscales. The only subscale that did not show an indirect effect or mediation was QOL upper extremity function. I failed to reject the null hypothesis for QOL upper extremity function for Research Question 2.

Research Question 3 was answered by a mediation analysis using PROCESS in order to determine if personal control influenced the relationship of illness intrusiveness on Neuro-QOL. All 10 QOL variables indicated no significant results, there was no indirect effect of illness intrusiveness on QOL through personal control. Therefore, I

failed to reject the null hypothesis for Research Question 3. The results of the study are discussed in more detail in Chapter 5.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

The purpose of this research was to examine the impact of IVIG treatment experience on the QOL of neurological autoimmune patients. It was hypothesized that IVIG treatment experience may intrude on the activities and lifestyle of patients through the construct illness intrusiveness which may affect QOL (Devins, 2010; Poochikian-Sarkissian et al, 2008a). The study specifically examined whether illness intrusiveness mediated the relationship between IVIG treatment experience and QOL.

Patients may vary as to how they react to the IVIG treatment experience or whether they consider the experience as intrusive which in turn may impact QOL. The illness intrusiveness theoretical framework also suggests that personal control may be limited by illness intrusiveness in that the individual is not able to control negative outcomes or influence positive ones (Devins, 2010). Considering this possibility, the study also tested whether personal control was a mediator between illness intrusiveness and Neuro-QOL. Although research has supported the effectiveness of IVIG treatment with autoimmune neurological disorders, there is no research relating to how the IVIG treatment experience may potentially influence illness intrusiveness, which in turn might affect QOL and only limited research regarding the relationship of IVIG and QOL with neurological autoimmune patients (Padua et al., 2005).

It is important for the medical treatment teams to understand how the experience of receiving this particular treatment might be affecting the patient's QOL so that

accommodations or treatment plans might be managed to support better patient care (Padua et al., 2005). Although medical staff may be aware of the fact that IVIG treatment may mean lengthy hours, strain on financial resources, complex treatment schedules, etc., they may not be knowledgeable as to how these ramifications from IVIG treatment affect the patient emotionally. The purpose of this study was to contribute to literature regarding IVIG treatment experience and to elucidate understanding of the consequences of the IVIG treatment experience on quality of life for CIDP, MS, MMN, and MG patients. This chapter contains interpretation of the findings of the data analysis in Chapter 4.

Interpretation of the Results

Prior to data analysis, I performed descriptive analysis. The data consisted of 79 returned questionnaires from neurological autoimmune patients receiving IVIG at PNA, an infusion center in Phoenix, AZ. The sample consisted of 25 (31.6%) males and 54 (68.4%) females. The sample included 30 MS patients, 25 CIDP patients, 13 MG patients, and 11 MMN patients.

Hypothesis 1: IVIG Treatment Experience as a Predictor of Quality of Life

IVIG treatment experience significantly predicted QOL in patients with MS, MMN, MG, and CIDP in the Neuro-QOL scale positive affect and well-being subscale. Research indicates people experiencing the four diseases represented in this study have a lower QOL in comparison to healthy individuals (Benito-León et al., 2003; Cocito et al., 2006; Mitchell et al., 2005). It was a surprise that the IVIG treatment experience was not significantly correlated with more of the Neuro-QOL subscales. Although there has been no research examining the relationship of IVIG treatment experience and QOL, the

correlation of IVIG treatment experience and outcome variables seemed expected when considering that QOL seems to be impacted by these chronic diseases and treatment according to research (Avis et al., 2005; Richardson et al., 2008; Shawaryn et al., 2002). It was interesting to note that three of the outcome variables dropped from significance once we incorporated the Bonferroni Correction.

There was positive significant correlation ($r = .339$; $p = .002$) between IVIG treatment experience and QOL positive affect and well-being. It is possible that the patients receiving treatment view their chronic disease differently due to treatment and have an improved appreciation for life such as was found in one study where patients viewed their life as becoming more meaningful as a result of their chronic illness (de Ridder et al., 2008). Perhaps some of the patients viewed the IVIG treatment as a means to physical improvement which also makes their overall well-being enhanced. Perception of their well-being influences how the patient perceives their own QOL (Megari, 2013). Positive affect and well-being is part of the psychological domain of QOL and the positive correlation between IVIG treatment experience and this QOL scale indicates that as the patient views the experience positively their perception of their own positive affect and well-being improves. It may be that neurological autoimmune patients suffering from a chronic disease perceive the IVIG experience not only improves their physical abilities and function but improves their attitude toward life.

Three other outcome variables were correlated with the IVIG experience although not at the significant level. This was unexpected as previous literature would suggest there might have been a higher correlation. For example, fatigue is a common thread in

chronic neurological disorders which can ultimately affect QOL. The negative correlation between IVIG treatment experience (VAS) and fatigue in this study (b = -.294; p < .009) supports previous research that showed fatigue has a negative impact on people with neurological disease (Kobelt et al., 2006) and was a main problem interfering with QOL and daily activities (Boukhris et al., 2005). In MG, fatigue is easily exacerbated (Kulaksizoglu, 2007), is the symptom most often reported in MS (Dayapoglu & Tan, 2011), can be a major issue in CIDP (Van den Bergh et al., 2010), and correlates with higher levels of disability (Pittion-Vouyovitch et al., 2006). Considering the different aspects of IVIG treatment including rearranging life schedules, lengthy administration hours, and possible side effects as well as potential for improved physical symptoms, it was reasonable to postulate that IVIG treatment might be viewed as a factor in overall QOL fatigue. Patients may become fatigued by the long range (often for life) administration of IVIG treatment (Jolles et al., 2005).

Similarly, depression has been an observable symptom in these chronic autoimmune diseases (Amato et al., 2001; Dayapoglu, 2011). The negative correlation although not significant between IVIG treatment experience and QOL depression supported similar research which found depression high in autoimmune disease (Chen et al., 2009) along with a study which found depression correlated to lower QOL (Janardhan & Bakshi, 2002). As IVIG patients viewed the totality of their experience with treatment as positive, both the depression and fatigue decreased. However, both of these variables did not meet the Bonferroni requirements (p < .005) as both had the same correlations (r = -.294; p = .009). Although the correlations did not reach significant level, the similar

results might indicate there may be a correlation between fatigue and depression in those patients receiving IVIG which will be addressed later under other noteworthy findings.

Additionally, although not significant (r = .320; p = .005), there was a positive correlation between IVIG treatment experience and QOL satisfaction with social roles and activities. Previous research showed fewer impairment issues from disease relates to more leisure activity and participation allowing the patient satisfaction in their social roles (Vanner et al., 2008). Actually, illness intrusiveness may be considered an impairment issue. If the IVIG treatment itself becomes intrusive due to complicated schedules, disrupted employment, or side effects, then patients may become dissatisfied with their social role or inability to participate in activities. Additionally, if the patient deems the whole IVIG experience as beneficial, they may view themselves more capable and be more apt to participate in activities within their community or family such as service clubs, family games, or even holiday gatherings. They may even be encouraged to venture forth and attempt to participate in a leisure activity such as swimming, bowling, or attending a concert. They may also feel more content and satisfied with the current state of their social roles. The other six QOL scales showed no correlation with IVIG treatment experience which was a surprise. I would have expected there to be a correlation between upper and lower extremity function as some patients experience more mobility after an infusion (PNA, 2015).

Hypothesis 2: Illness Intrusiveness as a Mediator

The second research question examined whether the illness intrusiveness construct mediates the IVIG treatment experience and QOL as measured by 10 subscales

of the Neuro-QOL. It is important to note that this is the first research study to examine the possibility of the relationship between IVIG treatment experience and QOL mediated by illness intrusiveness. As was previously noted, illness intrusiveness has been defined as the degree disruptions of disease or treatment interrupt patient interests and meaningful activities (Devins, 2010). How a patient reacts to potential intrusion of treatment may make a difference in aspects of their QOL. Since illness intrusiveness correlated with nine of the QOL of life variables, it was meaningful to look further and examine whether illness intrusiveness acted as a mediating variable between IVIG treatment experience and QOL. By asking Research Question 2, I examined if the predictor IVIG treatment experience indirectly influenced the dependent variables QOL through the mediator, illness intrusiveness.

IVIG treatment experience indirectly influenced QOL through illness intrusiveness in nine of the 10 Neuro-QOL subscales tested in the current study. That is, illness intrusiveness mediated the relationship between IVIG treatment experience and QOL fatigue, QOL depression, QOL satisfaction with social roles and activities, QOL positive affect and well-being, QOL cognition, QOL stigma, QOL sleep, QOL emotional and behavioral dyscontrol, and QOL lower extremity function supporting the illness intrusiveness theory which suggests the construct does not directly affect QOL but acts as a mediator between the treatment and the QOL due to the factors such as disrupted activities, side effects, and complex schedules (Devins, 2010). These findings are important as they provide a possible explanation that illness intrusiveness is a construct

influencing QOL in this population of patients. How a patient interprets or perceives the level of intrusiveness of IVIG treatment influences the outcome QOL

Illness intrusiveness significantly predicted nine of the 10 QOL subscales which was consistent with previous research which found illness intrusiveness correlated with many indicators of QOL (Devins, 2010). This pattern supported Devins's (1993) theory that disease treatment may affect illness intrusiveness which in turn affects QOL. Moreover, since an indirect effect was found in nine of the mediation analyses, the study supports previous research which concluded illness intrusiveness is a mediator in various chronic diseases (Dancey et al., 2002; Devins et al., 1990; Devins et al., 1997; Lebel, Beattie, Arès, & Bielajew, 2013; Poochikian-Sarkissian et al., 2008a).

Important for these particular patients is how they evaluate the IVIG experience as an intrusive factor in their QOL determines the very value of the life experience. This may well offer an explanation as to why some patients accept the complications which may occur with the process of IVIG and others may become highly affected. For example, Bloom et al. (1998), in examining 308 breast cancer patients, found that disease treatment and QOL was mediated by illness intrusiveness, and Dancey et al. (2002) found illness intrusiveness was a significant mediator between symptom severity and QOL in irritable bowel syndrome sufferers supporting Devins's (1994) theory that illness intrusiveness is a mediating construct. Another important similarity in the current study and previous research suggested by the results of mediation analysis is that increased illness intrusiveness correlates significantly with decreased QOL as well as indicating illness intrusiveness may be an important contributor to the psychosocial impact of

disease treatment supporting previous research studies (Dancey et al., 2002; Poochikian-Sarkissian et al., 2008a; Shawaryn et al., 2002).

Other research has demonstrated illness intrusiveness correlated with such QOL factors as fatigue and depression (Goudsmit et al., 2009). Additionally, in the Shawaryn et al. (2002) study, illness intrusiveness mediated disease severity and depression, upper extremity function, memory, and fatigue. Similarly, in the current study, illness intrusiveness mediated the relationship between IVIG treatment experience and QOL fatigue, QOL depression, and QOL cognition. The positive relationship showed more illness intrusiveness led to more fatigue and depression in this study. However, the negative relationship between illness intrusiveness and cognition would suggest cognition might be poorer when more illness intrusiveness was present. This finding supported the previous literature as well as the Illness Intrusiveness theory.

In order to understand the impact of IVIG treatment experience on QOL it is necessary to depict the degree that a patient perceives the treatment as helpful or on the other hand disruptive. Although this study resulted in nine quantified indirect effects of IVIG treatment experience on QOL through illness intrusiveness, some of them seem to reflect a larger effect size perhaps indicating more effect on QOL. Looking closer at the individual Neuro-QOL subscales there are some interesting observations. For example, 46% or almost half of the variance in the QOL satisfaction with social roles and activities variable was explained by both IVIG treatment experience and illness intrusiveness. However, only a small portion ($R^2 = .05$) of the total variance is accounted for by the IVIG treatment experience. The larger portion of the total variance is carried by illness

intrusiveness. This would support the concept that fatigue, complex schedules, side effects, and other factors involved in the construct of illness intrusiveness and how it relates to IVIG treatment experience may decrease the patient's ability or desire to participate in various social activities. The relationship is negative meaning that as illness intrusiveness increases QOL satisfaction with social roles and activities decreases. In essence, one might speculate that if the intrusiveness of the IVIG treatment experience could be diminished a patient might enjoy improved social relationships or activities.

The mediation model explained 33% of the variance in QOL depression and 39% of the variance in fatigue. Although that variance allows for other possible unidentified mediators or factors in the dependent variables QOL depression and QOL fatigue the variance explained in this study was considerable. However, once again, illness intrusiveness explains most of the variance in these mediation models as the IVIG treatment experience only accounts for about 5% of the total variance. Previously, fatigue has been found to negatively affect QOL in neurological disorders (Kobelt et al., 2006). It is clear from the results of the positive effect of illness intrusiveness on depression and fatigue that as the patient considered the treatment experience to be more disruptive or intrusive depression and fatigue increased. Similar results were found in earlier research when more fatigue was expressed by MS patients when higher levels of illness intrusiveness were present (Shawaryn et al, 2002). Fatigue is a common feature in these four autoimmune diseases but the pathogenesis is unclear (Merkies & Faber, 2012) and it sometimes prevents individuals from social and family activities. The implication that QOL can be either positively or negatively affected by IVIG treatment and illness

intrusiveness is clear from the results in the current study. The study implies illness intrusiveness may add to the impact of QOL variables in the neurological autoimmune patient. It may be possible for example that a patient might have side effects of IVIG treatment, or work interruptions created due to the IVIG schedule which might then cause more fatigue or depression. As mentioned previously, IVIG is an expensive therapy which may or may not be covered by insurance. This complication alone may be a factor in increased depression or fatigue experienced by the patient. How a patient interprets each intrusion may influence their QOL.

Looking closer at the mediation analysis of IVIG treatment experience on QOL positive affect and well-being once again the total variance of 27% was mostly accounted for by illness intrusiveness. There was a negative relationship which was in the expected direction in that when illness intrusiveness increased a patient's positive affect and feelings of well-being decreased. Interestingly, the mediation analyses between IVIG treatment experience and QOL sleep showed a variance of 35% with most again being accounted for by illness intrusiveness. The negative relationship meant that as IIRS increased the sleep scores decreased which meant more sleep disturbance and interrupted sleep patterns. Again, this would be in the expected direction and supported previous research which showed poorer sleep quality with neurological disability patients (Happe, 2003; Lobentanz et al., 2004; Stepansky et al., 1997)

The fact that QOL lower extremity function showed mediation and QOL upper extremity function did not show mediation was interesting but could reflect that lower extremity mobility is more affected by the disruptive factors of treatment. It may simply

be that patients view their ability to walk and move as the most important factor in extremity function. There is another interesting point regarding the mediation with QOL lower extremity function. Although the direct effect and the total effect were not significant a bias-corrected confidence interval signified a small indirect effect supporting current literature which posited an indirect effect may be present even when paths *a* and *b* are not significant (Hayes, 2013). It would be reasonable to conclude IVIG treatment experience does influence QOL lower extremity function through illness intrusiveness to some degree.

It is interesting to note that eight of the mediations in this study showed a medium effect size with only QOL lower extremity function showing a small effect size. This is important to consider as this is the first study investigating the illness intrusiveness theory with neurological autoimmune patients receiving IVIG treatment. It is also the first study investigating illness intrusiveness and MMN, MG, and CIDP. However, considering the indirect effect sizes (k^2) were medium there is also room to consider other potential mediating variables which might influence that relationship. One of those potential mediators which might be tested would be coping.

Hypothesis 3: Personal control as a mediator (Null not rejected)

There was no significant indirect effect of personal control on the relationship between illness intrusiveness and Neuro-QOL in each mediation analyses with the 10 QOL variables. There was also no correlation between illness intrusiveness and personal control. This was a surprise as one would expect personal control to be associated with QOL since previous research shows low levels of personal control were associated with

high levels of illness intrusiveness (Poochikian-Sarkissian et al., 2008a). On the other hand, one other study examining the relationship of diabetic complications and depressive symptomology mediated by illness intrusiveness found that a better fitting model excluded personal control (Talbot et al., 1999). The illness intrusiveness theory implies illness intrusiveness negatively influences psychological well-being by reducing personal control and the individual's ability to achieve positive outcomes (Devins, 2010). The results of this study did not support personal control mediating the relationship between IVIG treatment experience and QOL. This could be that patients surveyed do not view themselves as having a lack of control over their IVIG treatment experience. It may also imply patients do not consider personal control has any influence on the relationship between how intrusive they consider IVIG treatment is to their QOL.

Other Noteworthy Findings

In addition to the one QOL subscales that correlated with IVIG treatment experience as measured by VAS there were some other interesting correlations between some of the other Neuro-QOL subscales that are worth noting. These additional findings may be important in helping medical staff understand some of the psychological factors which may be prevalent in IVIG patients and assisting them in determining treatment direction. For example, the moderate negative correlation between QOL depression and QOL positive affect and well-being supports previous research which found reduced positive affect is distinct to depression (Forbes & Dahl, 2005). Another importance of such a correlation in this study is that depression has been viewed for some time as a predictor of increased health risks (Cohen & Pressman, 2006). Higher levels of positive

affect may increase social interaction which may in turn help the patient experience needed social support during the IVIG treatment experience. It is also possible that positive affect may result in fewer disease symptoms being reported by the patient (Cohen et al., 2003). Thus, such a correlation could be of significance to medical staff so they will be aware of potential vulnerability to risks for some patients. Similarly, the moderate negative correlation between QOL depression and QOL satisfaction with social roles and activities supported previous research which found an inverse relationship between social activity and depression (Holtfreter, Reisig, & Turanovic, 2015).

The moderate positive correlation between QOL fatigue and QOL depression supported previous research which found that more fatigue correlated with increased depression (Pittion-Vouyovitch et al., 2006). The negative moderate correlation between QOL fatigue and QOL cognition reinforced findings that attention, memory, and cognition may be affected by neurological disease but may also mean consideration might be warranted to consider the effect fatigue might have on aspects of cognition. Fatigue was found to be a significant predictor of self-reported cognitive concerns among MS patients in a recent study using the same measurement Neuro-QOL subscale as in this study (Beier, Amtmann, & Ehde, 2015). The challenges of fatigue and cognition may indeed make daily life more difficult. Moreover, the negative correlation between QOL depression and QOL cognition supported research that found depression and fatigue influence subjective complaints about cognition in MS patients (Kinsinger, Lattie, & Mohr, 2010) along with another study that found depression was associated with subjective cognitive impairment (Julian, Merluzzi, & Mohr, 2007). The Kinsinger et al.

(2010) study administered a 16 week telephone treatment program for depression and found post treatment results indicate subjective cognition complaints may be decreased through treatment. Likewise, the current research may provide IVIG nurses information regarding the importance of the relationship between depression and cognitive complaints which may encourage them in identifying patients with these symptoms.

Mobility and physical functioning are very important to neurological patients as sometimes problems are experienced in these realms. The moderate positive correlation between QOL lower extremity function and QOL satisfaction with social roles and activities supported previous research which found lower limb function was rated most important affecting QOL negatively in patients with chronic neurological disease (Heesen et al. 2008; Pike et al., 2012). Problems with sleep quality have also been linked with neurological disability in MS patients and MG patients (Lobentanz et al., 2004; Stepansky et al., 1997). The correlations in the current research study support those findings as QOL sleep showed significant strong correlation with QOL fatigue meaning that as the patient experienced more fatigue quality of sleep decreased. QOL fatigue displayed moderate negative correlation with QOL satisfaction with social roles and activities. Similarly, other research reported fatigue as a major problem interfering with patients participating in family and professional activities (Boukhris et al., 2005).

Inflammation is a characteristic of most autoimmune diseases which research suggests can lead to depression in those patients who are susceptible (Dantzer et al., 2008). In the current study, QOL depression was moderately positively correlated with QOL sleep and QOL stigma. This positive relationship supported previous research

which suggests individuals with neuromuscular diseases experience strong feelings of stigma (van der Beek et al., 2013).

The results also supported research by Feinstein and Feinstein (2001) who found that QOL may be impacted by symptoms of emotional dyscontrol. The variable QOL emotional and behavioral dyscontrol showed significant correlation with seven of the 10 QOL variables in the current study. While it is true only one of the correlations in the current study showed significance between IVIG treatment experience and QOL, it is important to recognize that other QOL correlations were apparent which support previous research. Finally, it is important to mention illness intrusiveness (the mediator in the current study) significantly correlated with all QOL subscales with the exception of QOL upper extremity function supporting previous research which found illness intrusiveness correlated with QOL in a number of conditions (Devins et al., 2013; Mucsi et al., 2004; Shawaryn et al., 2002; Snyder et al., 2013). However, Illness intrusiveness also did not correlate with personal control (HCS).

Limitations

The current study was composed of returned surveys from 79 neurological autoimmune patients receiving IVIG treatment. One limitation would be that all patients came from the same IVIG infusion center so while generalizing the results to similar infusion centers may be possible making a national population generalization of these diseases may not possible. However, all four diagnoses in the study were representative of autoimmune diseases receiving IVIG, and the staff of this facility indicated that it is

fairly typical of most treatment centers of this kind. Another limitation is that patients could not be randomly selected but volunteered to participate in the study.

Question #13 of the IIRS was inadvertently omitted from the survey given to participants. The question asked how much the patient's illness interfered with their civic involvement. Therefore, the IIRS instrument did not match perfectly the original instrument and could potentially be a threat to the validity of findings. Questions similar to this one are part of the QOL satisfaction with social roles and activities. This Neuro-QOL subscale had eight questions for the patient to evaluate their ability and satisfaction with social roles and life in the community. Exclusion of a question of similar content in the IIRS could have potentially impacted the correlation coefficient between the IIRS and the satisfaction with social roles and activities subscale of the Neuro-QOL.

Implications

A premise of mediation analysis is that relevant underlying aspects of behavior might be identified so that interventions might be developed based on those variables identified (MacKinnon & Fairchild, 2009). IVIG is the common treatment for the four neurological diseases in the current study but that treatment comes with possible psychological, social, or emotional elements. Since indirect effects were found in this study results may be helpful in identifying in what areas IVIG patients deem IVIG treatment experience interferes with their lifestyle. This information could potentially assist medical staff or infusion centers in evaluating patient risks, needs, and help them create new effective services. For example, a patient might view the complicated scheduling of IVIG therapy as interfering (illness intrusiveness) with his ability to hold a

full time employment position and therefore may experience depression or lost sleep over the dilemma. If the medical staff involved in his/her treatment is aware of the situation there might be a plan devised to rearrange a schedule which would help to bring positive results for the patient and eventually reduce depression or increase the patient's ability to sleep. Moreover, it is possible that IVIG treatment is affecting other areas of the patient's life such as family relationships, freedom to travel, or the pursuit of goals and the results of this study may help the treatment team be more aware of the influence of IVIG treatment on a patient's QOL so they might ascertain what areas of the patient's life are being affected by the treatment and provide a plan or counseling in this regard.

Some patients may be able to deal and cope with the additional challenges of a long term treatment which may need to be completed in a hospital or infusion center and others may have more trouble adjusting to ongoing treatment. Identifying the areas where some patients are most challenged in the IVIG treatment process may make designing individual care plans more effective. One of the goals of this study was to provide IVIG nurses, patients, and treatment teams a richer understanding of the psychological factors in the IVIG treatment experience and in what areas those factors are influencing overall QOL. The findings of this study could potentially provide some answers for IVIG patients and staff since this was the first research study involving IVIG treatment experience and illness intrusiveness with this population.

Implications for Social Change

It is possible the results of the current study could be useful for positive social change as policy makers now will have some documentation and literature as to the effect

IVIG treatment experience has on the lives of patients. Certainly, the study can be shared with such pharmaceutical companies as Biofusion, which provides IVIG to many nurses across the country who then provide at home IVIG treatment. Understanding some of the psychological or emotional responses which might occur as a result of the IVIG treatment experience could assist infusion nurses in accommodating or modifying situations which might add to patient stress. It may also be helpful in guiding nurses or members of the treatment team as to appropriate counseling needed by the patient. When human and social conditions are improved, positive social change occurs in society (Walden University, 2013, p. 13).

This study impacts positive social change by potentially improving human and social conditions in three major ways: (a) the research study clarifies illness intrusiveness mediates the relationship of IVIG treatment experience on QOL, thus contributing to the understanding of the effects of this therapy on QOL in MMN, MG, MS, and CIDP patients; (b) the results of this study will be distributed to the staff at PNA, thereby adding to the medical staff's knowledge base in order to assist them in improving their patient's human and social condition; and (c) results will be made available to any interested nurses or stakeholders as they may find the information useful as they plan interventions for their IVIG patients treatment experience.

Recommendations

The current study was the first to examine the IVIG treatment experience and QOL. It was also the first study to investigate if illness intrusiveness was a mediator of the IVIG treatment experience and QOL. My first recommendation would be that the

study be replicated with another infusion center or in a hospital setting with IVIG patients. Perhaps a different geographical area might be an interesting perspective and provide further research support. While it appeared obvious from the study that IVIG treatment experience has an effect on the physical, psychological, and social aspects of QOL further research in a different facility might add to the current conclusions. Another idea might be to explore whether patients view lower extremity function as more important than upper extremity function since mediation occurred in lower extremity function but not in upper extremity function.

Although the majority of the effect sizes of mediation were medium there would appear to be other potential mediators of the IVIG treatment experience and QOL. One possible mediator of the IVIG treatment experience and QOL might be coping ability as this may in turn affect the levels of the patient's perceived intrusiveness of the treatment experience (i.e., complex schedules, side effects, etc.). In addition, it would seem interesting and worthy to explore coping as a possible mediator of illness intrusiveness and QOL since personal control was not a mediator in this patient population. It is reasonable to surmise coping ability is often required for IVIG patients to adjust to the many life changes which occur with long term medical treatment. This study used a single question visual analogue scale to measure the IVIG treatment experience. A different researcher may want to create a different scale with more questions. Finally, it might we worthy to explore individual emotions and psychological responses of IVIG patients through a qualitative approach interviewing patients who have been receiving this therapy for different period of times.

Conclusion

I began this research study for several reasons. Since being diagnosed with the neurological autoimmune disease, CIDP, 15 years ago, I was motivated to understand how IVIG treatment affects the QOL in patients with similar diagnoses receiving this treatment. It was clear to me as I received IVIG in many settings (infusion center, hospital, and at home) that my reaction to the treatment was not necessarily the same as many other patients. While completely aware of the ramifications which can occur from treatment such as scheduling problems, family disruptions, side effects, financial challenges, etc. I was also observing some patients seemed to deal with the challenges better than others. Thus, the desire arose to examine the relationship of IVIG treatment experience on QOL.

Three main hypotheses were examined in this study: (a) whether IVIG treatment experience predicted QOL in neurological autoimmune patients, (b) if the IVIG treatment experience indirectly affected QOL through illness intrusiveness, and (c) if personal control mediated the relationship between illness intrusiveness and QOL. According to the results, illness intrusiveness does mediate IVIG treatment experience and QOL in nine of the outcome variables demonstrating that illness intrusiveness is an important contributor to this relationship. The results of this study provide new and important information regarding the IVIG treatment experience and QOL. It is hoped the results will help nurses and medical personnel to understand the psychological effect of treatment on patient's QOL so that new or improved treatment plans may be developed which may serve to decrease some of the negative effects of the IVIG experience on

QOL. It is also hoped that this study will encourage future research into the effects of IVIG treatment experience on neurological autoimmune patients.

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Appendix A: Project Questionnaire

I. Please indicate your gender by placing an x on the line:
Male _____ Female _____

2. Age, please circle the appropriate group for your age:

21-30 30-40 40-50 50-60 60-70 70-80

3. Employment Status: Please circle one.

Employed or Self-employed Unemployed

4.. Please circle your medical diagnosis:

Multiple Sclerosis (MS)
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Myasthenia Gravis (MG)

Multifocal Motor Neuropathy (MMN)

5. How long have you had this diagnosis (months and years) _____

6. How often do you receive IVIG treatment?

a. Every 8 weeks or a longer time between treatments

b. Every 6-7 weeks.

c. Every 4-5 weeks

d. Every 3 weeks

e. Every 2 weeks or more often

7. How long does the administration of your IVIG infusion last?

a. 1 hour

b. 2 hours

c. 3 hours

d. 4 hours

e. 5 or more hours

8. I receive pre-medication before receiving IVIG treatment. Please circle your answer.

Yes No

9. After IVIG treatment I experience side effects other than fatigue

a. Never

b. Sometimes

c. Most of the time

d. Always

10. Think about your experience with IVIG treatment which includes symptom relief, side effects, financial cost, changes from usual activities, improved health, adjusting schedules or family events, improved mobility and place a mark on the line where you think it best represents what your experience has been overall.
Anchors:
As bad as it can be .....As good as it can be