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Posttraumatic growth in Huntington disease: measuring the effects of genetic testing and disease on positive psychological change

Justin John Francis O'Rourke
University of Iowa

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POSTTRAUMATIC GROWTH IN HUNTINGTON DISEASE: MEASURING THE
EFFECTS OF GENETIC TESTING AND DISEASE ON POSITIVE
PSYCHOLOGICAL CHANGE

by

Justin John Francis O'Rourke

An Abstract

Of a thesis submitted in partial fulfillment of the requirements for the Doctor of
Philosophy degree in Psychological and Quantitative Foundations (Counseling
Psychology) in the Graduate College of The University of Iowa

July 2011

Thesis Supervisors: Professor Elizabeth M. Altmaier
Associate Professor Leigh J. Beglinger

ABSTRACT

Huntington disease (HD) is a genetically transmitted fatal neurodegenerative condition that currently has no cure. The symptoms of HD are manifested as cognitive declines, neuropsychiatric disturbances, and motor dysfunction. An autosomal dominant genetic defect is responsible for the onset of HD, which means that the children of an affected parent have a 50% chance of inheriting the disease. Predictive genetic testing for HD has been available since 1993, and a positive test result means that a person will develop HD with 100% certainty. People who have the HD-gene expansion, but have not yet manifested unequivocal motor signs, are said to be in the prodromal phase of HD. A number of studies have examined concerns about the utility of genetic testing and its negative psychological consequences for gene-expanded and non-expanded individuals (e.g., traumatization, suicidal ideation). Although research has understandably focused on the potential for distress, there has been some evidence suggesting that individuals may actually experience psychological growth related to a receiving a genetic test result (e.g., improved relationships, pursuing new opportunities). The aim of the present study was to understand the relationship between genetic testing, prodromal HD symptoms, and posttraumatic growth (PTG).

Participants were recruited through the multinational PREDICT-HD study (Jane Paulsen, PI) and they completed the Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1996) to assess permanent positive psychological change as a result of learning about their HD-gene status. The Symbol Digit Modalities Test (Smith, 1991), Unified Huntington's Disease Rating Scale Motor Exam (Huntington's Study Group, 1996), and

the SCI-90-R Depression subscale (Derogatis, 1994) were also completed. A total of 82 gene-expanded patients and 37 non-expanded patients took part in this study.

Results revealed that gene-expanded and non-expanded individuals reported experiencing PTG, particularly in their appreciation for life and ability to relate to others. Gene-expanded and non-expanded participants did not differ in the amount of growth they reported, which indicated that the outcome of genetic testing was not related to how much growth people experienced. Age and gender were associated with PTG, with younger participants and women reporting the most growth. The amount of time elapsed since genetic testing, estimated proximity to a diagnosis of HD, and the clinical characteristics of prodromal HD were not related to PTG. In conclusion, people experience positive psychological change as result of genetic testing for HD. The findings of this study have important implications for future research and for mental health professionals assisting people through the genetic counseling process.

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CERTIFICATE OF APPROVAL

PH. D. THESIS

This is to certify that the Ph. D. thesis of

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has been approved by the Examining Committee for the thesis requirement for the Doctor of Philosophy degree in Psychological and Quantitative Foundations (Counseling Psychology) at the July 2011 graduation.

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Jane Paulsen

William Liu

To my wife, Lori

We also glory in our sufferings, because we know that suffering produces perseverance; perseverance, character; and character, hope.

Romans 5:3-4, the Holy Bible

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ABSTRACT

Huntington disease (HD) is a genetically transmitted fatal neurodegenerative condition that currently has no cure. The symptoms of HD are manifested as cognitive declines, neuropsychiatric disturbances, and motor dysfunction. An autosomal dominant genetic defect is responsible for the onset of HD, which means that the children of an affected parent have a 50% chance of inheriting the disease. Predictive genetic testing for HD has been available since 1993, and a positive test result means that a person will develop HD with 100% certainty. People who have the HD-gene expansion, but have not yet manifested unequivocal motor signs, are said to be in the prodromal phase of HD. A number of studies have examined concerns about the utility of genetic testing and its negative psychological consequences for gene-expanded and non-expanded individuals (e.g., traumatization, suicidal ideation). Although research has understandably focused on the potential for distress, there has been some evidence suggesting that individuals may actually experience psychological growth related to a receiving a genetic test result (e.g., improved relationships, pursuing new opportunities). The aim of the present study was to understand the relationship between genetic testing, prodromal HD symptoms, and posttraumatic growth (PTG).

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CHAPTER I

INTRODUCTION

Introduction to Huntington Disease

Huntington disease (HD) is a genetically transmitted fatal neurodegenerative condition that is relatively rare, affecting 5-7 of every 100,000 persons (Walker, 2007). There are currently no treatments or cures for HD. An autosomal dominant genetic defect characterized by an abnormal trinucleotide repeat (i.e., CAG) in gene IT-15 on chromosome 4 is responsible for the onset of the disease (The Huntington's Disease Collaborative Research Group, 1993). The genetic nature of the mutation means that gene-expanded (i.e., HD “positive”) individuals have a 50% chance of passing on the disease to their children (Hayden, 1981). The symptoms of HD are manifested as cognitive declines, neuropsychiatric disturbances, and motor dysfunction. A diagnosis is made after the development of an extrapyramidal movement disorder that has chorea as its primary feature (Paulsen, 1999). After diagnosis, symptoms continue to progress until the disease ultimately takes the life of the affected individual. The progressive and devastating nature of the symptoms is traumatic for HD patients and family members.

Predictive genetic testing has been available to individuals with a family history of HD since 1993 (The Huntington's Disease Collaborative Research Group, 1993). The disease is fully penetrant for those who have an abnormal number of CAG repeats (≥ 41), which means that if they test positive for the gene-expansion they will inevitably manifest the symptoms of HD (Walker, 2007). An inverse relationship between CAG repeat length and age has been established that indicates those with greater CAG repeats will manifest the disease at an earlier age (Brinkman, Mezei, Theilmann, Almqvist, & Hayden, 1997; Langbehn, Brinkman, Falush, Paulsen, & Hayden, 2004). People who

have the gene-expansions but have not yet manifested motor symptoms are in the prodromal phase of HD. The accuracy of predictive testing and the sophistication with which it predicts disease onset has raised concerns about the psychological impact of test results on both gene-expanded and non-expanded individuals.

Psychologists, bioethicists, and geneticists have all raised concerns about the impact of genetic testing because of its traumatic nature (Evers-Kiebooms & Decruyenaere, 1998; Huggins et al., 1990; Kessler, Field, Worth, & Mosbarger, 1987). Legitimate apprehensions exist about inducing suicide, psychological distress, relational turmoil, and genetic discrimination by providing confirmation of the HD gene-expansion. Additionally, the practical benefit of testing was questioned because of the fact that HD lacks any cure. Given the psychological risks of testing, research has focused primarily on the potential for testing to catalyze severe distress (Almqvist, Brinkman, Wiggins, & Hayden, 2003; Broadstock, Michie, & Marteau, 2000; Codori, Slavney, Rosenblatt, & Brandt, 2004; Decruyenaere et al., 2003; Evers-Kiebooms & Decruyenaere, 1998). The findings of these studies have been variable with some reporting significant distress after testing (Bloch, Adam, Wiggins, Huggins, & Hayden, 1992; Codori et al., 2004; Huggins et al., 1992) and others suggesting that the effects of testing are benign (Almqvist, Bloch, Brinkman, Craufurd, & Hayden, 1999; Brandt et al., 1989; Decruyenaere et al., 2003). Regardless of inconsistent findings, the preponderance of research has focused on negative reactions to trauma with very little attention paid to the potential for psychological growth following a genetic test.

*Huntington Disease, Predictive Testing,
and Posttraumatic Growth*

Recently, researchers have started to empirically investigate the potential for psychological growth following highly stressful events. The idea of growth after trauma may be counterintuitive; however, spiritual traditions and philosophers have acknowledged the transformative effect of trauma for thousands of years (e.g., Christianity, Judaism, Hinduism; Tedeschi & Calhoun, 1995). Investigators have been attempting to operationalize adversarial growth over the last 3 decades, and have created a number of terms to capture the essence of this phenomenon. Terms that have been proposed include: *perceiving, construing, or finding benefits* (Affleck & Tennen, 1996; Antoni et al., 2001; McMillen, Zuravin, & Rideout, 1995; Tennen, Affleck, Urrows, Higgins, & Mendola, 1992), *thriving* (Abraído-Lanza, Guier, & Colón, 1998; O'Leary & Ickovics, 1995), *positive changes in outlook* (Joseph, Williams, & Yule, 1993), *adversarial growth* (Linley & Joseph, 2004), *stress-related growth* (Park, Cohen, & Murch, 1996), *positive psychological changes* (Yalom & Lieberman, 1991), and *flourishing* (Ryff & Singer, 1998). A number of theoretical models have also been proposed to explain the existence of positive change after trauma (for reviews see Joseph & Linley, 2006; O'Leary, Alday, & Ickovics, 1998; Zoellner & Maercker, 2006b). The wide range of terms and models is an artifact of the field's infancy and reflects a need for conceptual agreement.

Tedeschi and Calhoun (1995, 1996, 2004) coined the term *posttraumatic growth* (PTG) to describe positive psychological change after trauma, and it has become one of the most widely accepted terms in the literature. The phrase *posttraumatic growth* is

conceptually useful for two reasons. First, it acknowledges the potential for growth without minimizing the distressing nature of the events that prompt change. Second, the term differentiates psychological growth from personality traits such as resilience, hardiness, optimism, and a sense of coherence. These qualities may make an individual more capable of enduring trauma but they do not result in psychological transformation.

Numerous studies have explored PTG in response to a wide variety of traumas, including medical conditions. Illnesses that have been studied include rheumatic disease (Abraído-Lanza et al., 1998; Danoff-Burg & Revenson, 2005; Evers et al., 2001), heart attack (Affleck, Tennen, Croog, & Levine, 1987), multiple sclerosis (Evers et al., 2001; Mohr et al., 1999; Pakenham, 2005), lupus (Katz, Flasher, Cacciapaglia, & Nelson, 2001), HIV/AIDS (Milam, 2004; Siegel & Schrimshaw, 2000; Updegraff, Taylor, Kemeny, & Wyatt, 2002), respiratory disease (Sodergren, Hyland, Crawford, & Partridge, 2004), arthritis (Tennen et al., 1992), and cancer (Antoni et al., 2001; Cordova, Cunningham, Carlson, & Andrykowski, 2001a; Daiter, Larson, Weddington, & Ulmann, 1988; Sears, Stanton, & Danoff-Burg, 2003; Tallman, Altmaier, & Garcia, 2007; Thornton & Perez, 2006; Tomich & Helgeson, 2004). PTG research has covered a wide range of medical conditions; however, no studies have been conducted in a population suffering from neurodegenerative illness. The PTG literature has also been lacking in its examination of genetic diseases and the relationship between predictive genetic testing and psychological growth.

Predictive testing for HD provides a unique opportunity to examine the impact of neurodegenerative disease and genetic testing on PTG. Receiving a genetic test result can be a traumatic event because it forces many individuals to change their assumptions

about themselves and the world (Janoff-Bulman, 1992). Many people have had adverse reactions as they attempt to accommodate their test results into their assumptive world (Huggins et al., 1992). Depression is a frequent reaction in gene-carriers with up to 20% of tested individuals exhibiting depressive symptoms that require treatment (Codori et al., 2004). A number of other studies have also identified subclinical levels of affective distress, hopelessness, isolation, grief, and interpersonal difficulties following the receipt of a genetic test result (Codori et al., 2004; Hayden & Bombard, 2005; Tibben, 2007; Timman, Stijnen, & Tibben, 2004). Psychological distress following predictive testing indicates that people are processing the implications of their test results. When people adjust their assumptions and schemas to accommodate genetic testing results, then the potential for PTG is present.

There have been indications in the HD literature that those who receive a genetic test may experience PTG after receiving their results, even though no explicit examination of PTG exists in the HD literature. For example, Williams and colleagues (2010) found that people psychologically benefited from learning about their HD family history or their HD test result. In another study, Kessler et al. (1987) found that 76% of individuals at risk for HD said that they would strive harder to take advantage of their remaining life if they tested positive. Growth has also been observed in interpersonal relationships, a greater appreciation for life, and the pursuit of previously disregarded opportunities (Bloch et al., 1992; Codori & Brandt, 1994). Reports of PTG can be intermittently found throughout the HD literature, but attempts to understand the psychological benefits of testing have been limited at best.

Rationale for the Current Study

The aim of this study was to conduct the first quantitative analysis of PTG following a predictive genetic test in HD. HD is unlike any other disease that has been studied in the PTG literature for a number of reasons. HD is unique because of its genetic etiology, the availability of an accurate predictive test, its transmission between family members, and its affect on a wide range of functions (i.e., cognition, mental health, and motor functioning). Mental health professionals working with clients following a predictive genetic test would benefit from an examination of PTG because of the documented relationships that exist between PTG and mental health outcomes (Hart, Vella, & Mohr, 2008; Helgeson, Reynolds, & Tomich, 2006; Tallman et al., 2007).

Research Questions

The primary aim of this study is to determine the relationship between genetic testing and PTG. This aim is investigated by answering the following questions: 1) What is the frequency and magnitude of PTG in gene-expanded and non-expanded individuals as a result of learning their HD gene-status?, and 2) Do individuals who learn that they have the HD gene-expansion differ from non-expanded individuals in the PTG they experience?

A secondary aim of this study is to determine how demographic characteristics, time since testing, estimated proximity to diagnosis, and clinical characteristics of HD are related to PTG following a genetic test result. PTG studies in other health populations have examined the relationship between demographic variables and time on the experience of growth but have yielded mixed results. Therefore, this study will examine the relationship of age, gender, and time to PTG by addressing the following questions:

1) Are age and gender related to PTG?, 2) Is the amount of time that has elapsed since receiving a genetic test result related to PTG?, and 3) Is the estimated proximity to a diagnosis of HD related to PTG?

Additionally, to explore if the various clinical symptoms of HD are related to PTG, the following questions will be asked: 1) Are cognitive declines in prodromal HD related to PTG?, 2) Are prodromal motor signs related to PTG?, and 3) Are prodromal depressive symptoms related to PTG? It is hypothesized that increasing clinical symptoms reduce the level of PTG experienced by individuals.

CHAPTER II

LITERATURE REVIEW

This review of the literature examines research on posttraumatic growth (PTG) and Huntington's disease (HD). The aim of this chapter is to integrate the two bodies of research in a manner that provides a rationale for studying PTG as a result of predictive genetic testing for HD.

The review begins with an examination of the PTG literature. First, the conceptualization and definition of *trauma* is explained. Next, the concept of PTG is introduced followed by a discussion of the relevant theoretical models of PTG. Special attention is given to Tedeschi and Calhoun's (1995, 1996, 2004) functional-descriptive model of growth (FDM) and its supporting research. An overview of the salient predictors of PTG (e.g., demographic characteristics) is also incorporated into the FDM discussion. Components of PTG according to Tedeschi and Calhoun's model are then explained. The initial portion of this review ends with a brief overview of the traumas that have been examined in the research. The rationale for examining PTG in genetic and neurodegenerative illness is then explained.

In addition to a review of the PTG literature, the broader research on HD is also considered. An overview of the general characteristics of HD is provided and will include a discussion on differentiating prodromal HD from diagnosed HD. Research on the neuropathological, cognitive, psychiatric, and neurological aspects of disease in HD and prodromal HD populations are then examined. Predictive testing for HD, its psychological consequences, and implications for PTG are also discussed.

Posttraumatic Growth

Conceptualization of Trauma

Defining what qualifies as a *traumatic experience* has been debated over the last three decades since the inclusion of posttraumatic stress disorder (PTSD) in the Diagnostic and Statistical Manual of Mental Disorders-III (DSM-III; American Psychiatric Association, 1980; van der Kolk, Friedman, Keane, & Resick, 2007). Developing a definition has been particularly difficult because of the wide variety of potentially traumatic events. Negative events differ in their complexity, frequency, severity, manageability, and duration; and each of these dimensions exists on a continuum ranging from the trivial (hassles) to the catastrophic (severe trauma). Events are often deemed traumatic when they cross an arbitrary threshold that acts as a demarcation between ordinary stressors and traumatic stress (Weathers & Keane, 2007).

Creating an objective definition for trauma is further complicated by the varying degree of subjectivity in trauma victims themselves (Weathers & Keane, 2007). An interaction exists between the nature of the stressor and the fortitude of the victim. A highly stressful event may be experienced as a minor disruption to a resilient individual while a relatively banal inconvenience may be experienced as trauma by an individual with a low tolerance for ordinary stress or limited psychological resources (e.g., psychiatric disorder). The less resilient person may experience genuine trauma in spite of the apparent triviality of the event. Such variability in traumatic encounters moves the threshold between stress and trauma for each individual.

Changes in the diagnostic criteria for PTSD between versions of the DSM (American Psychiatric Association, 1980, 2000) illustrate the ever-changing definition of

trauma as mental health professionals attempt to understand the interaction among the characteristics of negative events and individual differences. Weathers and Keane (2007) note that recent versions of the DSM have significantly changed the conceptualization of trauma in two major ways. First, the diagnostic criteria for PTSD have become more considerate of subjective individual experiences over time. Second, the text of the DSM-IV-TR identifies a wider range of events that qualify as potentially traumatic, including being “diagnosed with a life threatening illness” (American Psychiatric Association, 2000).

The inclusion of additional traumatic events and individuals’ subjective experience into the DSM-IV-TR indicates a broader understanding of what constitutes trauma, both clinically and in the literature. Indeed, Breslau and Kessler (2001) found that new criteria in later versions of the DSM increased the prevalence rate of trauma by 22% over previous iterations. They also found the lifetime prevalence of exposure to traumatic experiences was 77.6% (73.3% for males and 81.6% for females). Increases in lifetime prevalence have led some researchers to become cautious about creating a definition of trauma that is too inclusive (e.g., McNally, 2004). The increased magnitude of reported trauma signifies that people are expanding their understanding of what constitutes a traumatic experience.

Given the expanding definition of trauma, establishing an operational definition for *trauma* may be difficult, but it is necessary for the proper study of highly stressful events. Clinicians and researchers must first acknowledge that an event does not need to produce clinical levels of distress in order to be considered traumatic. Janoff-Bulman’s (1992, 2006) widely accepted definition of trauma clearly illustrates this point and will be

used in this study. She defines trauma as an event that delivers “shocks to our inner world” (p. 83; Janoff-Bulman, 2006) and forces individuals to change long-held beliefs in order to accommodate the implications of the traumatic event. Events themselves are not traumatic, but the effects of those events on peoples’ schemas are. Janoff-Bulman’s definition of trauma focuses on the *meaning* of highly stressful events for people’s worldview instead of *comprehension* of the event’s facts (Janoff-Bulman & Frantz, 1997). Understanding the meaning of trauma comes about through the shattering of what Parkes (1988) calls the *assumptive world*. The assumptive world is the framework of belief through which everything in the universe is thought to be true. It guides our understanding of self, others, and the world’s laws of operation. Our earliest experiences provide an initial foundation for our assumptive world. Assumptions then undergo constant modification through our interactions with the environment and others. Janoff-Bulman adds that traumas modify one’s assumptive world because they create enough distress to challenge fundamental beliefs.

Even the most fundamental components of one’s assumptive world are disrupted in a traumatic experience (Janoff-Bulman, 2006). These fundamental assumptions include such notions as the world is meaningful, others are benevolent, and the self is worthy. Janoff-Bulman proposes that the degradation of these assumptions leads to a diminished sense of security, trust, and confidence. Optimism begins to wane and people accept the realities of the misfortunes they face. The acceptance of harmful events and negative beliefs begins to displace previously held assumptions, even if those assumptions were naïve (Janoff-Bulman, 1992). Tightly held notions of security and worthiness succumb to a keen awareness of personal deficits and limitations. People

begin to feel threatened, confused, aimless, and unable to control their surroundings. The world may even become unpredictable, unjust, cruel, and dangerous.

Having one's assumptive world challenged can be distressing, even to the point of causing high levels of impairment. In fact, the debilitating effects of traumatic reactions are the most widely discussed issues in the professional trauma literature (Friedman et al., 2007). The negative effects of trauma have dominated research for decades; however, over the last thirty years a body of work has been developing that focuses on the counterintuitive concept of growth following trauma (Helgeson et al., 2006; Linley & Joseph, 2004; Tedeschi & Calhoun, 1996, 2004). The next portion of this chapter considers how researchers have begun to label and operationalize positive psychological changes after traumatic events.

Conceptualization of Posttraumatic Growth

The idea that people can experience psychological growth after trauma has been a prominent part of human thought and spiritual traditions for thousands of years. Tedeschi and Calhoun (1995) begin their book, *Trauma and Transformation*, by recognizing the benefits of suffering identified by followers of Christianity, Islam, Judaism, Buddhism, and Hinduism. Some non-religious schools of thought, such as existential philosophy and psychology, have also made the transformative power of trauma an essential part of their theoretical approach (e.g., Frankl, 2006; May, 1980; Yalom & Lieberman, 1991). The public has begun to embrace the relationship between the psychological benefits of suffering as evidenced by best-selling books that discuss the subject (e.g., Herman, 1997; Viorst, 1986).

Studies examining growth after trauma began expanding as positive psychologists developed a new interest in promoting health while also reducing their focus on pathology (Joseph & Linley, 2008a; Seligman & Csikszentmihalyi, 2000). A burgeoning interest in growth after adversity may have prompted more studies, but researchers have struggled to coin terms that adequately reflect this phenomenon. A plethora of terms have been used throughout the literature in an attempt to capture all the facets of growth after adversity, some of which include: *perceiving, construing, or finding benefits* (Affleck & Tennen, 1996; Antoni et al., 2001; McMillen et al., 1995; Tennen et al., 1992), *thriving* (Abraído-Lanza et al., 1998; O'Leary & Ickovics, 1995), *positive changes in outlook* (Joseph et al., 1993), *adversarial growth* (Linley & Joseph, 2004), *stress-related growth* (Park et al., 1996), *positive psychological changes* (Yalom & Lieberman, 1991), *flourishing* (Ryff & Singer, 1998), and *positive by-products* (McMillen, Howard, Nower, & Chung, 2001). Positive growth researchers have only recently begun to settle on terms that comprehensively capture the relationship between growth and trauma. No universally accepted term currently exists, although some are more widely acknowledged than others.

One of the most accepted phrases used in the literature is *posttraumatic growth* (PTG; Linley & Joseph, 2004), which was originally coined by Tedeschi and Calhoun (1995, 1996). PTG is defined as “positive psychological change experienced as a result of the struggle with highly challenging life circumstances” (p. 1; Tedeschi & Calhoun, 2004). Tedeschi and Calhoun suggest that the term *posttraumatic growth* comprehensively describes positive change after trauma for a number of reasons. First, the term clearly distinguishes between the growth of those who have encountered major

life difficulties from those who have undergone nominally stressful events (Park et al.'s [Park et al., 1996; Park, Lechner, Calhoun, & Tedeschi, 2006] term *stress-related growth* is perhaps more useful to describe psychological changes following common stressors). Second, the term PTG also implies that people experience enduring changes in their psychological constitution as a result of their struggle with trauma (Tedeschi & Calhoun, 2004). Posttraumatic changes are robust and not simply “illusions” as some researchers have suggested (e.g., Taylor & Brown, 1988). Lastly, Tedeschi and Calhoun note that the term *posttraumatic growth* emphasizes both the distressing aspects of trauma and the potential for growth. Significant pain frequently coexists with those who are experiencing growth (Calhoun & Tedeschi, 2008). Other terms, like *thriving* (Abraído-Lanza et al., 1998; O'Leary & Ickovics, 1995), capture the potential for growth but implicitly minimize the anguish that often accompanies traumatic events (Tedeschi & Calhoun, 2004). PTG is also different from *recovery*, since recovery implies that people have returned to the status quo and are no longer suffering (Tedeschi & Calhoun, 2008). Growth can co-occur with suffering which implies that the person may not have necessarily recovered from the traumatic event. Because of its comprehensive nature and widespread acceptance in the literature, the term *posttraumatic growth* will primarily be used throughout this study to encapsulate the phenomenon of positive psychological change following adversity.

In their conceptualization of PTG, Tedeschi and Calhoun (2004) differentiate psychological growth from personality traits such as resilience, hardiness, optimism, and a sense of coherence. These qualities may make an individual more capable of enduring trauma but they do not result in psychological transformation. In fact, the ability to avoid

the exigent nature of trauma may actually decrease one's ability to grow from the experience (Tedeschi & Calhoun, 1995; Westphal & Bonanno, 2007). Struggling with the difficulties of trauma is a necessary antecedent to experiencing growth, therefore those who have minimal distress following trauma are theorized to have less potential growth because their schemas are not adequately challenged.

Models of Posttraumatic Growth

In their overview of the PTG literature, Park and Helgeson (2006) ask if PTG is best understood as a process or an outcome. Many different theoretical models have been developed to answer this question (Bhushan & Hussain, 2007; Joseph & Linley, 2006; Zoellner & Maercker, 2006b). The literature is mixed on whether PTG should be described as a positive adaptive illusion (Taylor, 1983), a coping process (Davis, Nolen-Hoeksema, & Larson, 1998; Park & Folkman, 1997), or an outcome in its own right (Joseph & Linley, 2005; Tedeschi & Calhoun, 2004).

Each type of model has different implications for the methods used to conduct research. Investigators who view PTG as a coping process or a positive illusion will examine how PTG affects other psychological and physical outcomes without considering growth to be an outcome itself. PTG becomes an independent variable and other health outcomes (e.g., depression, quality of life, treatment recovery) are dependent variables. In contrast to process models, outcome models identify PTG as the dependent variable and examine other aspects of health as independent variables related to PTG.

Outcome models are the most widely accepted in the literature because of their comprehensive nature (Park & Helgeson, 2006; Tedeschi & Calhoun, 2004). These models emphasize PTG as an end in itself, but they also acknowledge the process that

leads to its development. Because of their all-encompassing nature, the most cited outcome models are the focus of the current study. For a more comprehensive discussion the reader is referred to Zoellner and Maercker (2006b), Bhushan and Hussain (2007), Joseph and Linley (2006), and O’Leary et al. (1998). Outcome models that emphasize growth after experiences with common stressors are not reviewed (e.g., Park et al., 1996) since they address materially different events (i.e., not trauma). Only models that explicitly address psychological growth related to highly stressful events are considered. Furthermore, models that are not widely accepted or discussed in the literature are not included in this review in the interest of brevity.

A caveat must be offered prior to exploring the outcome models of PTG.

Outcome models are a dominant part of the broader PTG literature but they are not without weaknesses. The most striking limitation is that empirical support is difficult to establish for many of these models due to the vague nature of their predictors and underlying constructs (O’Leary et al., 1998; Zoellner & Maercker, 2006b). The reader will notice that empirical support is conspicuously absent for many of these models. Each model is largely based on the clinical experience of its creator and his or her reading of the literature. As a result, there is a high degree of theoretical consistency but little research has been conducted to unequivocally validate many of these conceptualizations.

Outcome Models of Growth

Schaefer and Moos’s model of life crises and personal growth. Schaefer and Moos (1992, 1998) developed one of the earliest conceptualizations of growth in the aftermath of trauma. Their model outlines a process where 1) personal and environmental systems influence 2) the experience of life crises in the aftermath of

trauma, which 3) affects cognitive reappraisals and coping responses, and thereby 4) results in positive outcomes. The model is dynamic since each component is able to modify other components through a feedback loop. Each component of the model is described below.

Personal factors include sociodemographic characteristics, personality traits (e.g., resilience, optimism), temperament, motivation, physical health, and prior life experiences. Environmental factors include social systems, social support, financial resources, community characteristics, and living situations. Event-specific factors are also considered part of the environmental system and include the severity, duration, and timing of the traumatic event, as well as how the event came about (i.e., random vs. human origin).

Cognitive reappraisal and coping are divided into two categories in Schaefer and Moos's model (Moos & Schaefer, 1993). *Approach coping* is a process of attempting to resolve crises, seek social support, reasonably analyze the situation, and identify potentially positive outcomes. In contrast, *avoidance coping* occurs when individuals ignore or minimize the crisis, become excessively emotional, and avoid the difficult process of recovery in favor of alternative rewards.

If personal and environmental factors are favorable, and approach-oriented coping is used, then Schaefer and Moos (1992, 1998) suggest that three positive outcomes (i.e., PTG) are possible. First, individuals may gain new social resources through stronger relationships with loved ones and broader social networks. Personal resources may also increase and result in greater assertiveness, maturity, insight, and altruism. Lastly,

increased resilience and coping skills may develop and result in greater affect regulation, help-seeking, and problem solving.

Aldwin's transformational coping. Although the term “coping” is in the model’s title, Aldwin (1994) focuses on PTG as an outcome of coping. She emphasizes that negative events are necessary precursors for any psychological development, especially PTG. The model identifies three different coping processes that produce unique outcomes: homeostatic coping, negative transformational coping, and positive transformational coping. Homeostatic coping results in the maintenance of baseline functioning. The individual does not psychologically mature or decline following trauma. Negative transformational coping inevitably results in lower levels of functioning and a reduced capacity for coping. Individuals employing this coping style tend to develop longstanding pathology. Positive transformational coping leads to growth, which is defined as the development of additional coping resources (Aldwin, Sutton, & Lachman, 1996). Positive and negative changes can occur in varying magnitudes. For example, an individual who has become more altruistic might become more generous with close friends (small change) or may suddenly quit current employment to pursue a new career aimed at helping other victims (major change).

The quality and magnitude of change in Aldwin’s model is dependent on a number of variable personality characteristics and resources (Aldwin & Sutton, 1998). Social support, determination, flexibility, intelligence, and motivation all contribute to positive transformational coping. Conversely, ineffective coping strategies, isolation, unavailable social resources, weak social networks, or a difficult disposition all increase the probability of negative change following a traumatic event.

O'Leary and Ickovis's theory of thriving. O'Leary and Ickovis (1995) developed a "value-added" theory of change after trauma. They suggest that individuals can go beyond *surviving* or *recovering* from trauma to *thrive*. Thriving is "defined as the effective mobilization of individual and social resources in response to risk or threat... [that] represents something more than a return to equilibrium (i.e., homeostasis) following a challenge" (p.122). Thriving can be manifested behaviorally, cognitively, or emotionally and can only result from an active engagement with adversity (O'Leary, 1998). Thriving after trauma is preferred since *recovery* indicates that pre-trauma levels of functioning are maintained and *survival* means that a decline in functioning has occurred. The likelihood that an individual will thrive is dependent on personal and environmental characteristics.

Joseph and Linley's Organismic Valuing Theory. Joseph and Linley (2005, 2006, 2008a, 2008b) have developed a social-cognitive model of growth called Organismic Valuing Theory (OVT). As the name implies, OVT is rooted in organismic valuing process theory, which asserts that people are growth-oriented and have the innate tendency to know the ideal path to their own personal well-being. OVT was developed to explain multiple aspects of the growth process including how PTG occurs, individual differences in growth, and the relationship between PTG and its known predictors (which are discussed in detail in the following section). One of the advantages of OVT is that it attempts to account for both negative and positive predictors of PTG.

OVT incorporates many central theoretical principles prevalent throughout the PTG literature (Joseph & Linley, 2005). One such principle is that people have a tendency towards integrating trauma-related information into their shattered worldview.

New information is either assimilated or accommodated by the victim (Joseph & Linley, 2008a). Assimilation occurs when trauma-related information is fit within the framework of pre-trauma assumptions. Accommodation is the process of changing pre-trauma assumptions about the world to incorporate new trauma-related information. The process of accommodation then leads to either positive or negative psychological changes.

According to OVT, cognitive outcomes can be manifested in many ways (Joseph & Linley, 2005, 2008a). Some traumatized individuals may not restructure their assumptive world following trauma; in which case they return to their pre-trauma baseline through assimilation. Some individuals may integrate negative changes into their assumptive world through maladaptive cognitive processing. Such negative accommodation often results in psychopathology. Ideally, people will engage in a process of positive accommodation that results in psychological growth. Joseph and Linley suggest that optimal growth occurs when individuals restructure their assumptive world to be more consistent with their true self. The highest form of growth is authenticity.

Summary of Outcome Models

All of the outcome models reviewed to this point have demonstrated remarkable theoretical consistency among themselves. As the reader may have noticed, O'Leary and Ickovics (1995) thriving, survival, and recovery mirror the three coping processes identified by Aldwin (2007; Zoellner & Maercker, 2006b). OVT also integrates the same three coping processes into a model that considers both the negative and positive results of trauma (Joseph & Linley, 2005). Each model restates the possibility of growth, stagnation, and decline following life crises. The outcome models have also evolved to

become more sophisticated in their attempts to include a wide array of variables that are pertinent to growth. Comprehensive models of PTG must account for the variables related to growth and their interaction with PTG.

Attempts have been made to improve on outcome models of PTG. For example, Tedeschi and Calhoun's (1995, 1996, 2004) *functional-descriptive model* retains many of the fundamental theoretical constructs present in literature while also correcting the weaknesses of other outcome models. Their model provides the most comprehensive framework for variables and processes related to PTG, as well as a detailed understanding of the components of PTG itself. The next portion of this chapter reviews the predictors of PTG within the framework of Tedeschi and Calhoun's model. The domains of PTG are also described.

Tedeschi and Calhoun's Functional-Descriptive

Model of Posttraumatic Growth

Tedeschi and Calhoun's (1995, 1996, 2004) functional-descriptive model (FDM; see Figure B1) is the most empirically supported model of PTG. Consequently, the model has become widely accepted in the PTG literature and has been described as the most comprehensive and established model to date (Joseph & Linley, 2006; Park & Helgeson, 2006).

FDM begins with the assumption that traumatic events do not result in growth, but that the ensuing emotional struggle provides the impetus for change (Calhoun & Tedeschi, 2008). In fact, the authors specifically caution against the suggestion that loss causes direct benefit (e.g., you will benefit from your child's death). Instead, they assert

that it is the struggle with trauma which has the potential to produce growth (e.g., you have benefited from your struggle with your child's death).

The first portion of the FDM acknowledges the importance of individual characteristics for predicting PTG. A number of demographic variables relevant to PTG have been identified in the literature. Helgeson and colleagues (2006) conducted a meta-analysis of 87 cross-sectional studies examining benefit finding after trauma and found that age, gender, education, and ethnicity all predicted PTG. Younger individuals were found to experience more growth than older adults, a finding that is consistent with much of the literature (Bellizzi, 2004; Polatinsky & Esprey, 2000; Stanton, Bower, & Low, 2006). Tedeschi and Calhoun (2004) suggest that younger people are more open to changing their schemas and thus experience greater PTG. Women were also found to experience more growth than men; however, this finding has been mixed in the literature with only limited studies producing similar results (Park et al., 1996; Tedeschi & Calhoun, 1996), and others suggesting gender has no relationship to PTG at all (Stanton et al., 2006). Ethnicity also predicts PTG since non-whites tend to report significantly more growth than their Caucasian counterparts. Helgeson and colleagues hypothesize that ethnic group differences exist because minorities generally have greater exposure to adversity as a result of their social status.

Certain personality characteristics are also related to PTG. Individuals who are open to change, optimistic, self-confident, and extroverted tend to experience more growth (Abraído-Lanza et al., 1998; Helgeson et al., 2006; Tedeschi & Calhoun, 1996; Tennen et al., 1992). Religiousness has also been associated with PTG, as those who engage in greater religious participation tend to exhibit greater PTG (Calhoun, Cann,

Tedeschi, & McMillan, 2000; Koenig, Pargament, & Nielsen, 1998; Park et al., 1996). Clearly, a variety of personal characteristics must be considered when examining PTG, and FDM allows researchers to incorporate all of them into a framework for understanding the process of growth.

FDM also considers the qualities of the critical events that prompt PTG (Tedeschi & Calhoun, 2004). Elapsed time since the trauma and perceived trauma severity are two variables frequently discussed in the literature. FDM suggests that PTG takes a significant amount of time to occur because the mechanisms necessary for processing highly stressful events are disrupted immediately following the event (Linley & Joseph, 2004; Tedeschi & Calhoun, 1995, 2004). Some researchers have even suggested that growth soon after a trauma is impossible, and that any immediate reports of PTG are actually denial or avoidant coping (Maercker & Zoellner, 2004; Zoellner & Maercker, 2006b).

Regardless of the theoretical relationship between time and PTG, empirical findings on the amount of time required for growth have been variable. A number of studies have supported the hypothesis that PTG increases with time (Cordova et al., 2001a; Park et al., 1996; Polatinsky & Esprey, 2000) while others have not (Fromm, Andrykowski, & Hunt, 1996; Helgeson et al., 2006; Milam et al., 2004; Widows, Jacobsen, Booth-Jones, & Fields, 2005). Frazier, Conlon, and Glaser, (2001) found that robust growth occurred in as little as 2 to 8 weeks for a sample of women who experienced a sexual assault, while Abraído-Lanza and colleagues (1998) found perceived growth 14 years post-trauma when they initially asked about PTG related to arthritis. A meta-analysis of the PTG literature (Helgeson et al., 2006) added more

uncertainty by finding a significant amount of variability in the time since trauma reported across 28 studies ($Q= 77.36, p<.001$). The tremendous discrepancies in the literature indicate that a verdict has not been reached on the relationship between time and PTG.

The relationship between perceived trauma severity and PTG is less equivocal than that of time. A number of studies have found a positive correlation between higher levels of perceived threat during the traumatic event and increased levels of growth (Armeli, Gunthert, & Cohen, 2001; Cordova et al., 2001a; McMillen, Smith, & Fisher, 1997); however, some authors caution that the relationship may not be linear (Linley & Joseph, 2004). Fontana and Rosenstock (1998) found a curvilinear relationship between severity and growth that suggested moderately severe traumas produced more benefits than low-grade or catastrophic events. The curvilinear relationship fits well with Tedeschi and Calhoun's model (1995, 2004) that claims trivial events do not provide enough distress to challenge schemas while extreme distress may override adaptive cognitive processing and rumination.

Rumination is another key component of FDM (Tedeschi & Calhoun, 1996, 2004). Significant distress inevitably produces emotional and cognitive turmoil. Rumination, a result of cognitive turmoil, is a common posttraumatic reaction. Rumination is defined as "several varieties of recurrent thinking, including making sense, problem solving, reminiscence, and anticipation" (Martin & Tesser, 1996). Two types of rumination are related to outcomes following trauma: self-punitive rumination and event-related rumination. Tedeschi and Calhoun focus primarily on event-related rumination as a catalyst for PTG rather than self-punitive rumination, which is often associated with

negative outcomes in the literature (Nolen-Hoeksema, Parker, & Larson, 1994; Stockton, Hunt, & Joseph, 2011; Treynor, Gonzalez, & Nolen-Hoeksema, 2003). Event-related rumination involves reminiscing, problem solving, and obsessing about the traumatic event as the person cognitively processes their experience. Tedeschi and Calhoun theorize that rumination is initially an automatic process that becomes more voluntary as the individual gains temporal distance from the trauma. Deliberative rumination is strengthened when victims are positively reinforced through early coping successes attributed to the ruminative process. Early successes encourage individuals to continue engaging in problem solving and recollection as they attempt to make coherent sense of trauma-related information (Stockton et al., 2011). The integration of traumatic events into one's schemas may be further enhanced by social support, especially when the relationships are satisfying (Park et al., 1996). Victims especially benefit from the perspectives of other traumatized individuals (Neimeyer, 2001).

Empirical support exists for FDM's understanding of rumination in PTG. Calhoun and colleagues (2000) examined the role of rumination immediately following participants' traumatic experiences as well as rumination long after the event (i.e., within 2 weeks of completing study procedures). Rumination was operationalized as automatic or deliberate attempts to understand and make sense out of traumatic events. The results indicated that cognitive processing after the event was significantly associated with posttraumatic growth ($\beta = .47$) but brooding long after the trauma was not, which is a finding that has gained backing from recent studies (e.g., Stockton et al., 2011). The importance of cognitive processing was further supported by Cordova, Cunningham, Carlson, and Andrykowski (2001b) who found that the appraisal and integration of

cancer patients' diagnoses into their schemas also resulted in significant benefits ($\beta = .24$). The results of these studies offer direct support for the predictions of FDM which purport that early trauma-related rumination is essential to later PTG.

There are clearly a number of factors that account for PTG within the framework of FDM. To this point, this chapter has focused on the predictors of growth without describing the characteristics of PTG itself. The next section describes the domains of PTG and their effect on an individual's assumptive world.

Domains of Posttraumatic Growth

Ultimately, PTG results in permanent adjustments to an individual's worldview (Janoff-Bulman, 2006; Tedeschi & Calhoun, 1996, 2004, 2008). Pre-trauma levels of functioning are unattainable after PTG has occurred because there have been substantial changes to one's fundamental assumptions. People who have experienced PTG rebuild their assumptive world by modifying the most fundamental aspects of their worldview (e.g., sense of safety or fairness). The changes people experience after trauma may be permanent but they are not uniform. Variability in PTG suggests that it may be comprised of qualitatively different domains.

The FDM acknowledges that PTG is a multidimensional construct. The multidimensionality of PTG has been empirically supported through the development of the Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1995, 1996). The items on the PTGI were chosen after a careful review of the literature that examined perceived benefits following trauma. A factor analysis of the items yielded five comprehensive domains, which Tedeschi and Calhoun believe are both descriptive and comprehensive. Recent empirical evidence has supported the multidimensionality of

PTG by suggesting that a 5 factor model is more robust than 3-factor or one-dimensional models of growth (Taku, Calhoun, Cann, & Tedeschi, 2008). The five factors of PTG include: 1) an increased sense of personal strength, 2) changes in the ability to relate to others, 3) greater appreciation for life, 4) changes in spirituality/religiosity, and 5) the realization of new opportunities in life.

Personal strength. An increased sense of personal strength often follows traumatic experiences (Tedeschi & Calhoun, 1995, 1996, 2004). In a study of mothers whose children were suffering from debilitating illnesses, Konrad (2006) found that mothers had more confidence in their resilience and coping abilities. One mother said, “I’d say there were some good and some positive and negative changes. Positive—I realize that I have more strength than I ever thought I had” (p. 107). Changes in personal strength often come from the belief that surviving trauma will increase the likelihood of withstanding future difficulties. Interestingly, those who report an increased sense of strength also develop a keen awareness of their own vulnerability (Tedeschi & Calhoun, 2004). People begin to acknowledge their lack of control over the environment while concurrently gaining confidence in their ability to survive negative events.

Relating to Others. Positive changes in the ability to relate to others have also been found in PTG (Collins, Taylor, & Skokan, 1990; Tedeschi & Calhoun, 1996, 2004). Many individuals experience the development of deeper and more meaningful relationships because they change their relational approach. For example, some deeper relationships stem from a willingness to accept help from previously ignored social support. Collins and colleagues (1990) found that trauma victims increased their interpersonal sensitivity through an expansion of compassion and empathy. Their sample

also had an intense desire to invest significant time and energy into building relationships. These findings also indicate that traumatized individuals may become more extroverted because they place less emphasis on social desirability and more emphasis on self-disclosure. Tedeschi and Calhoun (1996) suggest that increased self-disclosure contributes to PTG because it creates the opportunity for authentic relationships to develop with others.

Appreciation of life. Another domain of potential growth is an augmented appreciation for life itself. A greater desire to “live in the moment” and engage in previously neglected activities is common (Collins et al., 1990). People who experience PTG in this domain begin enjoying the smaller things in life, such as their natural surroundings or time with children. A greater appreciation for life is also frequently accompanied by a change in priorities (Tedeschi & Calhoun, 2004). Priorities alter as new values are assigned to experiences that were previously considered trivial. For example, some individuals may develop a lower tolerance for “busy work” or they gain an appreciation for time with loved ones. People who have developed a greater appreciation for life have a burgeoning desire to be more mindful. Life is viewed as a gift and not one moment is taken for granted.

Spirituality. Changes in spirituality are also a notable component of PTG. Konrad (2006) found that spiritual growth could be manifested in many ways. She identified three major spiritual changes in her sample which included finding new faith, strengthening existing faith beliefs, and reuniting with a former faith community. Siegel and Schrimshaw (2000) interviewed a person with AIDS who illustrates the type of religious growth that can occur with trauma:

When I found out I had HIV, that made [my religiosity] more intense, wanting to know how to get closer to my creator or make amends with my creator for the life that I've lived. And ah, my faith has grown tremendously. My life has changed differently. More different than it has been. And I'm more at peace with myself so I guess the mercy of Him has shined upon me. So the change—a great deal—whereas I pray when I wake up, pray when I go to bed, pray for meals. Pray thanks for this and thanks for that. Not a second thought. I wouldn't do it before. I do it now. (p. 1548)

In their review of studies investigating survivors of war, illness, and major disaster, Shaw et al. (2005) found that spirituality not only aided the coping process but was also an outcome in its own right.

Changes in spirituality are not necessarily limited to those who belong to a faith community or who have a religious background. Modifications to religious or spiritual behaviors can be experienced by non-religious individuals as well. By extension, changes in spirituality do not need to be directed towards a particular entity or deity (Sodergren, Hyland, Singh, & Sewell, 2002). Instead, existential questions may be engaged more thoroughly as a form of growth. Another interesting paradox observed in those who report posttraumatic spiritual changes is a new sense of uncertainty. A deeper faith seems to be concomitant with increased doubt. Perhaps, doubt serves as a stimulus for growth because it forces an affirmation of one's trust in a belief system.

New possibilities. Lastly people find that there are a number of new possibilities available to them after traumatic events (Tedeschi & Calhoun, 2004). A heightened perception of life's brevity and unpredictability promotes a greater awareness of opportunity. People who are experiencing PTG in this domain will often pursue lifelong dreams such as global travel or having children. Career changes or returning to school are some of the most common opportunities pursued by those who have experienced trauma.

Studies of PTG and a Gap in the Research

A number of events can lead to PTG. Qualifying traumatic events include natural disasters, human inflicted trauma, traumatization of loved ones, large scale disasters, and the diagnosis of life threatening illnesses. Natural disasters that have been examined in the literature include tornados (McMillen et al., 1997), earthquakes (Karanci & Acarturk, 2005), and floods (Dolinska, 2003). Some have reported PTG following trauma inflicted by other people. These reports include sexual assault (Frazier et al., 2001; Frazier, Tashiro, Berman, Steger, & Long, 2004), rape (Thompson, 2000), accidents/assault (Snape, 1997), child sexual abuse (McMillen et al., 1995), military combat (Fontana & Rosenheck, 1998; Schnurr, Rosenberg, & Friedman, 1993), and war refugees (Ai, Tice, Whitsett, Ishisaka, & Chim, 2007). PTG has also been examined in family members of individuals that have experienced a highly stressful event, such as those who have a child with Down syndrome (King, Scollon, Ramsey, & Williams, 2000), a child with leukemia (Best, Streisand, Catania, & Kazak, 2001), the death of a child (Polatinsky & Esprey, 2000), and bereavement (Davis et al., 1998). Large scale events such as plane crashes and mass shootings (McMillen et al., 1997), a ship sinking (Joseph et al., 1993), Oklahoma City bombing (Pargament, Smith, Koenig, & Perez, 1998), the bombing of Dresden (Maercker & Herrle, 2003), and the terrorists attacks on 9/11 (Ai, Cascio, Santangelo, & Evans-Campbell, 2005) have also prompted PTG.

Health conditions and the growth-related effects of diagnosis and treatment have also been examined. PTG prompted by a medical condition is a nearly ubiquitous finding in the literature. Illnesses that have been studied include rheumatic disease (Abraído-

Lanza et al., 1998; Danoff-Burg & Revenson, 2005; Evers et al., 2001), heart attack (Affleck et al., 1987), multiple sclerosis (Evers et al., 2001; Mohr et al., 1999; Pakenham, 2005), lupus (Katz et al., 2001), HIV/AIDS (Milam, 2004; Siegel & Schrimshaw, 2000; Updegraff et al., 2002), respiratory disease (Sodergren et al., 2004), and arthritis (Tennen et al., 1992).

Cancer has been the most widely studied medical condition in the PTG literature and has been shown to produce benefits regardless of diagnosis type (Stanton et al., 2006). Studies have been conducted with patients suffering from leukemia and lymphoma (Carboon, Anderson, Pollard, Szer, & Seymour, 2005; Daiter et al., 1988), breast cancer (Antoni et al., 2001; Cordova et al., 2001a; Sears et al., 2003; Tomich & Helgeson, 2004), prostate cancer (Thornton & Perez, 2006), and bone marrow transplants (Tallman et al., 2007).

Research in cancer populations illustrates how PTG can arise from a health condition. Reports of the frequency of PTG in cancer populations have been variable, and have reached as high as 83% (Sears et al., 2003). Cordova and colleagues (2007) conducted a study examining the nature of PTG in a population of breast cancer patients. More than 80% of the sample endorsed some level of growth related to a greater appreciation for life or interpersonal relationships. Growth also occurred in the domains of spirituality/religiosity and the desire to pursue new opportunities; however, to a lesser extent. These findings are consistent with what has been reported in other cancer studies within the PTG literature (e.g., Cordova et al., 2001a; Widows et al., 2005). Although cancer studies are relatively consistent in the prevalence of PTG, there have been inconsistent findings regarding predictors of growth. For instance, some studies have

found a positive relationship between time since cancer diagnosis and PTG (Cordova et al., 2001a) while others have not (Fromm et al., 1996). Level of education has also been shown to be inversely related, (Widows et al., 2005), not related (Sears et al., 2003), and positively related (Cordova et al., 2007) to PTG. Age is a more consistent predictor with younger age often being associated with greater PTG (Bower et al., 2005; Widows et al., 2005).

Research in PTG has covered a wide range of medical conditions; however, no study has been conducted in a population suffering from neurodegenerative illness. The PTG literature has also been lacking in its examination of genetic diseases and the relationship of predictive genetic testing to psychological growth. This study aims to expand the literature by examining PTG in Huntington disease (HD), a genetically transmitted neurodegenerative disease. The neurodegenerative and genetic aspects of the disease present a unique opportunity for examining the experience of PTG as a result of predictive genetic testing and neurodegenerative illness. The next section of this chapter will describe HD, prodromal HD, and predictive genetic testing for the disease.

Huntington Disease

Neurodegenerative Illness

Neurodegenerative illnesses are insidious neurological disorders characterized by unnatural neural apoptosis and nervous cell dysfunction (Hannay, Howieson, Loring, Fischer, & Lezak, 2004). There are currently no known medical cures for any neurodegenerative diseases and only limited treatments are available for symptom management. Parkinson disease, Alzheimer disease, frontotemporal dementia, and dementia with Lewy bodies are the most common neurodegenerative conditions. Each of

these illnesses is characterized by the pattern of neuronal death they initiate in the central nervous system and their subsequent neurobehavioral symptoms (e.g., subcortical vs. cortical dementias; Salmon & Filoteo, 2007). HD, a less prevalent subcortical neurodegenerative disease, will be the primary focus of this study.

Prevalence and Diagnosis of Huntington Disease

HD is a genetically transmitted neurodegenerative disease that affects 5-7 of every 100,000 Caucasians, but has varying prevalence in other ethnic groups (e.g., 0.5 per 100,000 in Japan; Takano et al., 1998; Walker, 2007). HD is characterized by a triad of motor, cognitive, and behavioral symptoms (Paulsen, 1999; Paulsen & Conybeare, 2005). The clinical diagnosis of HD occurs when an unequivocal extrapyramidal motor disorder has manifested in an individual with a known family history of HD or who has received a positive genetic test for HD. Once a diagnosis is made, the disease slowly progresses over an average of 15-20 years before death occurs. Individuals known to have the gene-expansion for HD but who do not yet demonstrate clinical motor dysfunction are said to be in the prodromal phase of HD. Although a diagnosis is only given with the onset of motor signs, many cognitive and psychological symptoms can develop years before the diagnosis of the disease (Paulsen et al., 2008). The presence of symptoms prior to diagnosis indicates that HD can have a pervasive impact on a person's life long before they fully manifest HD.

The next portion of this chapter discusses aspects of HD as they relate to both diagnosed and prodromal individuals. First, research explaining the genetic and neuropathological underpinnings of the disease is reviewed. Next, the motor, cognitive, and behavioral symptoms associated with HD are discussed. The review of each cluster

of symptoms begins with a discussion of how pathology is manifested in diagnosed HD, followed by a review of the symptoms that have been identified in prodromal HD. The final portion of this section will then examine the research concerning genetic testing for HD.

HD: Genetic etiology

HD is an autosomal dominant genetic disorder, which means that people with the gene-expansion for HD (i.e., gene “positive”) have a 50% chance of passing on the disease to their children (Hayden, 1981). The chromosome responsible for the development of HD was first identified by Gusella and colleagues (1983) in the early 1980’s. They conducted one of the first successful polymorphic DNA linkage analyses by comparing the pedigree of American and Venezuelan families affected by HD. Human chromosome 4 was identified as the source of the gene mutation responsible for the disease. A later study conducted by The Huntington’s Disease Collaborative Research Group (1993) identified the specific location of the gene that determines whether or not an individual will manifest symptoms of HD.

A trinucleotide repeat within gene IT-15 on the short arm of human chromosome 4 is responsible for the onset of HD (The Huntington’s Disease Collaborative Research Group, 1993). The trinucleotide sequence cytosine-adenine-guanine (CAG) repeats itself an abnormal number of times in individuals who develop HD. All people possess normal alleles at the offending site with CAG repeat lengths ranging from 10-34. People who inevitably manifest symptoms of HD have trinucleotide sequences that contain over 40 CAG repeats (Walker, 2007). There is some debate over the exact number of CAG repeats required for HD to become fully penetrant, but a trinucleotide repeat length ≥ 41

is a generally accepted clinical cutoff (McNeil et al., 1997; Rubinsztein et al., 1996). A positive genetic test result means that a person will develop HD with 100% certainty if they do not die of other causes first.

Repeat lengths of 36-40 are considered within the borderline range and result in incomplete penetrance (Walker, 2007). Individuals within the borderline range may not manifest HD but they are at an increased risk of passing on the genetic defect to their children. Interestingly, only males with an intermediate CAG expansion have been observed to transmit HD to their children (Goldberg et al., 1993).

An inverse relationship between CAG repeat length and age has also been identified in the literature (Brinkman et al., 1997; Langbehn et al., 2004). CAG repeat length accounts for the majority of variance observed in age of onset, with the magnitude of expansion explaining upwards of 60% to 73% of the variance (Andrew et al., 1993; Brinkman et al., 1997; Duyao et al., 1993). Langbehn and colleagues (2004) have developed a parametric survival model that is widely used to identify the age of onset for gene-expanded individuals using only their age and CAG repeat length. Despite its wide use, the Langbehn model has two major weaknesses. First, it produces large confidence intervals, especially for those far from diagnosis. Second, it was developed on retrospective reports of CAG repeat lengths provided by patients, which introduces error that affects its predictive accuracy.

To correct for the weaknesses of Langbehn and colleagues' (2004) formula, Zhang and colleagues (2011) created another method for estimating proximity to diagnosis: the CAG/Age Product (CAP). In contrast to the Langbehn formula, CAP had the advantage of being developed based on directly observed CAG repeat lengths and

age. The CAP was also simpler to calculate because it does not need to be fit to parametric survival models. CAP can be derived by simply multiplying participants' age and CAG repeat length. Regardless of the predictive value of the Langbehn model and CAP, they have only been used for research purposes and the information they yield has not been provided to patients.

HD: Neuropathology

Neurodegeneration in HD primarily occurs in the basal ganglia, specifically in the caudate nucleus and putamen, which are collectively referred to as the striatum (Gutekunst, Norflus, & Hersch, 2002; Vonsattel, Keller, & Pilar Amaya, 2008; Vonsattel et al., 1985). Vonsattel and Difiglia (1998) estimate that 95% of HD patients present with bilateral striatal atrophy, and 80% of those cases demonstrate severe volumetric loss. Other structural changes are observed in the frontal lobes (Vonsattel & Lianski, 2004), pyramidal neurons of the parietal angular gyrus (Macdonald, Halliday, Trent, & McCusker, 1997), nucleus accumbens (Vonsattel et al., 1985), area CA1 in the hippocampus (a notable 35% neuronal loss; Spargo, Everall, & Lantos, 1993), thalamus, cortical surface area, white matter (Beglinger et al., 2005; Rosas et al., 2003), cortical layers 5 and 6 (Hedreen, Peyser, Folstein, & Ross, 1991), globus pallidus (Rosas et al., 2003; Vonsattel & Lianski, 2004), amygdala, and brainstem (Rosas et al., 2003). Overall brain weight has been determined to decrease almost 20% over the course of the disease (Halliday et al., 1998).

At the cellular level, the medium spiny neurons that give a striated appearance to the caudate and putamen are particularly affected (Robitaille, Lopes-Cendes, Becher, Rouleau, & Clark, 1997; Vonsattel et al., 2008; Vonsattel et al., 1985). Medium spiny

neurons are GABAergic in nature, therefore abnormal apoptosis and astrocytosis in these cells result in a reduction of inhibitory synaptic activity (Wilson, 2004). Disruptions in neural projections from the striatum to the external globus pallidus soon follow (Gutekunst et al., 2002). Striatal compromise due to cellular changes are initially responsible for the triad of symptoms in HD (Penney & Young, 1983), which makes sense given the role of the basal ganglia in motor control and initiation, learning, and cognition (Lezak, Howieson, & Loring, 2004).

Neuropathological changes in HD have also been reported in prodromal HD (e.g., Aylward et al., 1996; Harris et al., 1996). Aylward and colleagues (2004) reported volumetric changes in the head of the caudate 11 years prior to estimated diagnosis and in the putamen 9 years before estimated diagnosis. They also found that the physiological changes in the caudate were able to predict the onset of disease with 100% accuracy for prodromal patients who were within 2 years of receiving a diagnosis. Decreases in white-matter volume and increases in cerebrospinal fluid have also been observed in addition to striatal changes (Ciarmiello et al., 2006). Functional imaging has revealed glucose hypometabolism in the cortex and basal ganglia (Ciarmiello et al., 2006; Feigin et al., 2007), reduced dopaminergic and D2 receptor binding (Feigin et al., 2007; Lawrence et al., 1998), and reduced activation in the basal ganglia (Paulsen et al., 2004).

Structural and functional neuropathological changes in HD have consistently been correlated with the triad of symptoms gene-expanded participants eventually manifest. Relationships between neuropathology and cognition are widely established in the literature for both diagnosed and prodromal HD (Aron et al., 2003; Beglinger et al., 2005; Ciarmiello et al., 2006; Gomez-Anson et al., 2007; Hennenlotter et al., 2004b; Paulsen et

al., 2004; Tekin & Cummings, 2002). Similar findings exist for movement-related symptoms (Deckel, Weiner, Szigeti, Clark, & Vento, 2000; Douaud et al., 2006; Penney & Young, 1983, 1986). Correlations between the psychiatric symptoms of HD and neural compromise are less clear, although some efforts have been made to define their relationship (Mayberg et al., 1992; Paradiso et al., 2008). Nonetheless, the neural circuitry affected in HD has been correlated with many of the psychiatric symptoms that are observed (Calabrese, Colombo, Bonfanti, Scotti, & Scarone, 1993; Drevets, 2000; Duff, Paulsen, Beglinger, Langbehn, & Stout, 2007).

HD: Cognition

HD eventually results in a syndrome of cognitive declines that can be characterized as a subcortical dementia (Hannay et al., 2004). Other comparable dementias are observed in Parkinson disease and progressive supra-nuclear palsy, and they have a unique cognitive profile (Cummings, 1986; Hannay et al., 2004). Neuropsychological declines are observed in processing speed and attention, executive dysfunction, visuospatial disturbances, and memory dysfunction that affects retrieval more than learning. Notably absent are archetypal 'cortical' dysfunctions such as amnesia, agnosia, and aphasia. Individuals suffering from subcortical dementias also have increased rates of personality change, depression, and apathy. Cognitive declines in HD fit a prototypical subcortical dementia well (Morris, 1995; Paulsen et al., 1995).

Identifying cognitive declines in HD is a complex task. The neuropsychological literature has become more focused in recent years, but the results regarding specific cognitive deficits continue to vary. Zakzanis (1998) attempted to summarize the research by conducting a meta-analytic review of the literature on

cognition in HD. She aimed to identify and organize the cognitive impairments demonstrated on a variety of neurocognitive tasks. Her review included a total of 760 HD patients and 943 normal comparisons across 36 studies. Cognitive deficits were ranked according to the degree to which those impairments appeared to occur within HD. Delayed recall, memory acquisition, cognitive flexibility and abstraction, manual dexterity (fine motor movements), attention and concentration, and visual perception were identified as the most notable deficits in HD. Language skills were comparatively intact, although some declines were noticed on broad scales of dissimilar verbal abilities (i.e., WAIS-R Verbal IQ index). The most prevalent cognitive deficits identified by Zakzanis are discussed in more detail below.

Memory. One of the hallmark cognitive changes in HD is a retrieval-based episodic memory impairment. Butters, Wolfe, Martone, Granholm, and Cermak (1985) conducted one of the earliest studies of memory loss in their examination of HD patients compared to amnesic patients (e.g., alcoholic Korsakoff's patients). They found that HD patients had as much difficulty with the free-recall of verbal information as amnesic patients but that they differed in two important ways: 1) HD patients had a demonstrable learning curve across multiple trials, and 2) HD patients performed significantly better on recognition memory tasks with fewer false negative errors. These findings indicate that HD patients are able to learn declarative information despite their inability to recall that information without external prompts. Similar declines in free recall have been demonstrated elsewhere in the literature and are a robust finding in the HD research (Lang, Majer, Balan, & Reischies, 2000; Moss, Albert, Butters, & Payne, 1986; Paulsen & Conybeare, 2005; Zizak et al., 2005).

In contrast to retrieval deficits, retention and recognition memory are relatively preserved (e.g., Butters, Wolfe, Granholm, & Martone, 1986; Lundervold, Reinvang, & Lundervold, 1994; Paradiso et al., 2008) but research has been variable on this point (Lang et al., 2000). Montoya and colleagues (2006) attempted to clarify the research on memory in HD through a meta-analysis of 48 studies. The results indicated that deficits in both recall *and* recognition are notable in HD, even in the early stages of disease. However, their study also found that there was a significant discrepancy between the recall and recognition performances of HD patients that favored recognition abilities. In other words, although both retrieval-based and recognition-based memory are impaired in HD, there is evidence that retrieval-based memory declines much further than recognition.

Executive functioning. Declines in executive functioning and personality/emotional inhibition are also common in HD. Bachoud-Levi and colleagues (2001) conducted a longitudinal study of patients with HD using an extensive cognitive battery and found that tasks requiring rapid cognitive shifting and divided attention showed some of the earliest and most rapid impairments when compared to other domains of neuropsychological functioning. Deficits in cognitive efficiency have been prominent in a number of additional studies (Aron et al., 2003; Bamford, Caine, Kido, Cox, & Shoulson, 1995; Ho et al., 2003; Lawrence, Sahakian, Hodges, Rosser, Lange, K.W. & Robbins, T.W., 1996) and exist even after controlling for the effects of psychomotor speed on executive functioning tasks (Snowden, Craufurd, Griffiths, Thompson, & Neary, 2001). Poor anticipation of future events is also common and is due to slow and errant planning (Watkins et al., 2000). Surprisingly, deficiencies in planning

may or may not affect the ability to make advantageous decisions (Campbell, Stout, & Finn, 2004; Stout, Rodawalt, & Siemers, 2001; Watkins et al., 2000). Visual and verbal working memory deficits have also been identified (Lawrence et al., 1996). Of note, all of these declines in executive functioning have been correlated with atrophy in the caudate, putamen, and insular cortex (Peinemann et al., 2005).

Impairments in verbal processes that are mediated by executive functioning are also frequent in HD. Language impairments are typically characterized by a paucity of speech and limited verbal fluency. Aphasic syndromes that are common in cortical dementias (e.g., Alzheimers) are not typical in HD. To illustrate the differences in language impairment, Hodges, Salmon, and Butters (1990) examined language deficits in a prospective longitudinal study that matched HD patients to similarly demented Alzheimer disease patients. HD patients differed from Alzheimer and healthy groups by showing consistent decline on letter fluency tasks while performances on measures of semantic memory (e.g., Boston Naming Test, category fluency) remained impaired but stable. These results indicate that disruptions in cognitive organization and retrieval processes cause language deficits in HD, and not the decomposition of semantic knowledge itself. Additional findings have predominantly supported the presence of deficits in lexical retrieval (Bachoud-Levi et al., 2001; Ho et al., 2003; Snowden et al., 2001), although some studies have found no fluency deficits (e.g., Bamford et al., 1995) and one surprisingly found improvement over time (Kremer et al., 1999).

Attention and psychomotor speed. HD patients demonstrate marked declines on tests of simple attention that also have a speeded component. Both cross sectional and longitudinal studies have consistently demonstrated impairments on commonly used tests

of attention and speed, such as part A of the Trail Making Test and the Stroop Word and Color conditions (Bachoud-Levi et al., 2001; Ho et al., 2003). Snowden and colleagues (2001) longitudinally examined attention and psychomotor speed across a 3-year period and found that the simplest component of the Stroop (word condition) was the most sensitive to change over time, unlike the more attention-demanding interference condition, which only showed limited sensitivity. Similarly, tests of attention that lack a timed component (e.g. digit span) declined, but at a less rapid rate (Bachoud-Levi et al., 2001). In summary, apparent deficits in attention and concentration in HD are more likely due to slowed cognitive processing than a marked impairment in attention (Paulsen & Conybeare, 2005).

Visual impairment. Visual impairments in HD are common, but they appear to develop later in the disease. Research by Bamford and colleagues (1995) found visuoconstructional declines using tasks that require patients to reconstruct visual stimuli. Changes were found on constructional tasks that required varying degrees of fine motor skills (i.e., copying geometric figures vs. block design tasks), but visual declines were not the earliest declines when compared to other cognitive functions. Ho and colleagues (2003) found that pattern recognition was also impaired in HD patients. Again, people demonstrating visual impairments were further along in the disease process.

HD patients have also demonstrated impairments in the ability to accurately recognize emotions in others. Some researchers suggest that impairments in emotion recognition are limited to specific states, such as anger and disgust (de Gelder, Van den Stock, Balaguer Rde, & Bachoud-Levi, 2008; Kipps, Duggins, McCusker, & Calder, 2007; Sprengelmeyer et al., 1996; Sprengelmeyer et al., 1997). Snowden and colleagues

(2008) recently conducted a thorough study examining the ability of HD patients to recognize six different emotions (happiness, surprise, fear, sadness, disgust and anger) in test situations of varying difficulty. The findings indicated that HD participants were notably deficient in their ability to identify fear, disgust, and anger. These results were consistent on less demanding tasks and across modalities (i.e., visual and auditory). Snowden and colleagues concluded that declines in emotional recognition exist regardless of whether the emotions are being communicated by others' facial expressions or vocal intonation.

Cognitive declines in prodromal HD. Research has increasingly demonstrated that many of the cognitive symptoms present in HD actually precede motor abnormalities (Stout et al., 2011). Studies of cognitive symptoms in gene-expanded populations have been mixed. In their brief review of the literature, Lemièr, Decruyenaere, Evers-Kiebooms, Vandebussche, and Dom (2004) identified a number of factors that are likely contributing to the mixed findings in prodromal HD. These factors include: 1) differences in neuropsychological measures, 2) differences in genetic analysis (i.e., linkage analysis vs. molecular), 3) samples varying in size, age, and neuropsychological characteristics, 4) changes in clinical criteria for diagnosis of HD, and 5) an over reliance on cross-sectional research designs. Although these confounding factors have occasionally prompted mixed results, a preponderance of evidence supports the existence of cognitive symptoms in HD long before the development of motor signs.

Jason and colleagues (1988) conducted one of the earliest studies of cognition in a population of gene-expanded individuals. Since molecular confirmation for the HD gene was unavailable at the time of the study, at-risk participants were grouped based on

their probability of carrying the HD gene-expansion according to a genetic linkage analysis. Participants in the high probability group had a greater than 90% chance of carrying the HD gene. They found that cognitive symptoms appeared in some gene-expanded participants over a decade before their estimated onset of symptoms based on family history. Paulsen, Zaho, and colleagues (2001) followed up this research by conducting a prospective longitudinal study that found gene-expanded individuals who phenoconverted had significantly lower baseline cognitive scores when compared to their non-converting counterparts. The closer participants were to receiving their diagnosis, the poorer their cognitive functioning was.

Langbehn, Paulsen, and researchers in the Huntington Study Group (2007) added to the research by establishing the utility of cognitive symptoms for predicting the onset of manifest HD. A large cohort of healthy, at-risk individuals who had genetic testing but were not diagnosed, and who little or no motor abnormalities, were examined using psychiatric, motor, and neuropsychological measures to determine which domains provided the most meaningful predictor variables. They found that a discrepancy in verbal fluency and processing speed significantly predicted the onset of disease well beyond what could be accounted for by motor functioning. Their findings also suggested that measuring particular domains in prodromal HD is more useful than assessment of global cognitive functioning, which may be insensitive to prodromal changes in gene-expanded individuals.

Many of the cognitive deficits identified in prodromal HD individuals are similar to the deficits of those with manifest HD. New research examining impairments on time estimation and time discrimination tasks suggests that these functions are the earliest to

decline and they are the most sensitive to disease progression (Beste et al., 2007; Paulsen et al., 2008; Paulsen et al., 2004; Rowe et al., 2010). Impairments in processing speed and various executive functions are also prominent in the literature (Brandt, Shpritz, Codori, Margolis, & Rosenblatt, 2002; Foroud et al., 1995; Larsson, Almkvist, Luszcz, & Wahlin, 2008; Lemiere et al., 2004; Paulsen, Zhao et al., 2001; Snowden, Craufurd, Thompson, & Neary, 2002). With regard to processing speed, Verny and colleagues (2007) found significant differences in processing efficiency between gene-expanded and non-expanded individuals on three separate measures of psychomotor speed. Similar differences were found on an executively mediated measure of response inhibition and set-shifting (Trails B). The Symbol Digit Modalities Test (Smith, 1991), a measure of tracking and psychomotor speed, has consistently been found to be extremely sensitive to early cognitive changes in prodromal HD, and it correlates with estimated proximity to diagnosis (Brandt et al., 2002; Cadell & Sullivan, 2006; Campodonico et al., 1998; Foroud et al., 1995; Langbehn & Paulsen, 2007; Lemiere et al., 2004; Stout et al., 2010).

Impaired episodic memory has also been observed in prodromal gene-expanded patients and verbal memory loss can be one of the earliest signs of disease progression (Hahn-Barma et al., 1998; Jason et al., 1997; Lemiere et al., 2004; Robins Wahlin, Lundin, & Dear, 2007). Montoya et al.'s (2006) meta-analysis of memory studies in found that notable deficits in recall memory were found in prodromal HD individuals when compared to neurologically unremarkable individuals.

A number of other cognitive changes have been observed in prodromal HD, and many track with estimated time to diagnosis (Stout et al., 2010). Other declines are observed in semantic fluency (Larsson et al., 2008), visuospatial construction (Brandt et

al., 2002), attention (Lemiere et al., 2004; Verny et al., 2007), verbal memory (Campodonico et al., 1998; Hahn-Barma et al., 1998; Lemiere et al., 2004; Rosenberg, Sorensen, & Christensen, 1995; Verny et al., 2007), visual memory (Witjes-Ane et al., 2003), and emotional recognition (Hennenlotter et al., 2004a; Sprengelmeyer, Schroeder, Young, & Epplen, 2006).

HD: Psychiatric Symptoms and Depression

Psychiatric and behavioral symptoms are some of the most prominent features of HD. Affective disorders, irritability and aggression, apathy, abulia, suicide, obsessive-compulsive disorder, and psychosis have all been consistently reported in the literature (for comprehensive reviews see Craufurd, Thompson, & Snowden, 2001; Paulsen & Nehl, 2004; Rosenblatt & Leroi, 2000). Psychiatric symptoms in HD are considerably variable in their frequency and severity both within and between participants (Craufurd & Snowden, 2002; Thompson, Snowden, Craufurd, & Neary, 2002). Lifetime prevalence estimates for psychiatric disorders in HD have ranged from 33% to 76% (Cummings, 1995; Watt & Seller, 1993), with some estimates of psychiatric hospitalizations reaching as high as 65% (Jensen, Sorensen, Fenger, & Bolwig, 1993).

Depression has been identified as one of the earliest and most frequent psychological problems in HD. Paulsen, Ready, Hamilton, Mega, and Cummings (2001) found that dysphoria was the most common and disturbing symptom endorsed in a sample of HD patients (69.2%). Folstein, Abbott, Chase, Jensen, and Folstein (1983) found that 22% of HD patients met the full criteria for major depression. Despite the prevalence of depression in HD its etiology has remained difficult to establish.

The etiology of depression in HD individuals is likely multifaceted and can be attributed to both psychosocial and organic factors. Attributing depressive symptoms to the psychosocial difficulties that accompany HD is intuitive (Rosenblatt & Leroi, 2000). Speculation is not necessary to understand the detrimental effects of genetic discrimination, major disruptions in career and family life (including the possibility of transmitting the disease to children), and living with a very visible debilitating brain disease. Facing such seemingly insurmountable obstacles inevitably increases the likelihood of depression. Surprisingly, however, psychosocial difficulties do not account for the full range of depressive symptoms observed in HD patients. One study conducted by Mindham, Steele, Folstein, and Lucas (1985) compared HD patients with another patient group experiencing similar psychosocial pressures (i.e., Alzheimer patients), and they concluded that psychosocial factors were insufficient to describe depression in HD. HD patients were found to have twice the prevalence of depression compared to their Alzheimer disease counterparts even though both groups encountered similar stressors. These findings imply that depression in HD can also be attributed to the neuropathology of the disease. Some possible organic explanations include hypometabolism in the orbitofrontal cortex (Mayberg et al., 1992) or dysfunction in the medial caudate (Vonsattel et al., 1985).

Disentangling the psychosocial and organic factors that contribute to depression is a difficult task. Indeed, determining if depression in HD is neurological or reactive is as difficult as settling the nature vs. nurture debate. Regardless of depression's etiology, a few facts are clear from the research. First, depression is a prominent component of HD and it can be treated. Second, the organic and psychosocial components of depression

interact to perpetuate the severity of psychiatric disturbance in HD. Additionally, the prominent organic component of depression in HD only makes depression more difficult to cope with. The increased rate of depression exponentially increases the risk of suicide in the HD population. In an earlier study, Schoenfeld and colleagues (1984) found that suicide was the third most common cause of death in HD patients, and that the rate of suicide was three times higher than the general population's. They also found that the rate of suicide among suspected HD was four times higher than those who actually developed the disease.

Gene-expanded patients in the prodromal phase of disease face psychiatric disturbances similar to what has been found in diagnosed HD. Depression in prodromal HD occurs alongside other psychological disturbances including obsessive compulsive disorder, irritability, anxiety, and psychoticism (Berrios et al., 2002; Duff et al., 2007; Kirkwood et al., 2002b). Folstein et al. (1983) have suggested that depression develops an average of 5 years prior to diagnosis, with some patients showing symptoms as early as 20 years. Nonetheless, much of the research examining depression in prodromal HD has been variable; however, there have been methodological flaws among previous studies. Common flaws include retrospective methodology (Shiwach, 1994), a lack of a control group or ambiguity between groups (Baxter et al., 1992; Shiwach, 1994), the use of broad based measures of psychopathology (Kirkwood et al., 2002a), and inadequate power due to small sample sizes (Berrios et al., 2002). A recent study by Duff et al. (2007) corrected many of these flaws in an examination of a large cohort of prodromal HD participants. Approximately 681 individuals completed the Symptom Checklist 90-Revised (SCL-90-R; Derogatis, 1994) to determine the prevalence of psychiatric

symptoms in gene-expanded individuals prior to diagnosis. The findings show that depression is definitively present in prodromal HD, and that it begins far from disease onset. Psychiatric disturbances were also highly correlated with striatal volume, suggesting that there is a strong organic component perpetuating depression in prodromal HD.

HD: Motor Aspects

Motor symptoms in HD can be categorized as negative or positive according to their features (Mahant, McCusker, Byth, & Graham, 2003). Negative symptoms are characterized by a reduction of movement such as bradykinesia, apraxia, awkward gait, and slowed saccadic movements. Positive symptoms are characterized by an abundance of movement, and include chorea, dystonia, and motor impulsiveness. Both positive and negative symptoms co-occur in HD and have varying prevalence as the disease progresses (Penney et al., 1990; Thompson et al., 1988). Positive symptoms are common early in the disease process, especially chorea, oculomotor disturbances, and balance problems (Penney et al., 1990). Chorea worsens throughout the disease until it decreases during the final stages (Walker, 2007). The final stages of HD are dominated by negative symptoms; with the exception of dystonia which is also prominent (Penney et al., 1990).

The motor symptoms of HD are generally attributed to apoptosis in the striatum (Vonsattel et al., 2008). Striatal efferent pathways relay information from the neocortex to other nuclei in the basal ganglia, which then forward signals to the frontal cortex responsible for motor planning and execution (Graybiel, Aosaki, Flaherty, & Kimura, M., 1994; Paulsen, 1999). A decrease in striatal neurons initiates a sequence of disruptions in the frontostriatal motor circuit responsible for voluntary movement. Degeneration of the

caudate nucleus reduces the efficiency of inhibitory neural pathways between the external globus pallidus and subthalamic nucleus. An improperly functioning subthalamic nucleus then reduces the inhibitory effect of the internal globus pallidus on the thalamus itself. Unmediated thalamic activity then results in chorea (Vonsattel et al., 2008).

Limited research has been conducted on motor symptoms in prodromal HD. The most comprehensive study of prodromal motor symptoms was conducted by Biglan and colleagues (2009), and they found that gene-expanded participants exhibited enough motor signs to distinguish them from healthy comparisons. Total motor functioning, chorea, bradykinesia, and oculomotor dysfunction were the most sensitive to group differences, and they were correlated with estimated time to diagnosis and striatal degeneration. Significant differences in total motor functioning have also been observed between prodromal HD patients and normal comparisons before the onset of cognitive symptoms (Campodonico, Codori, & Brandt, 1996). Siemers and colleagues (1996) examined motor symptoms in a large cohort of genetically confirmed, gene-expanded participants (N=383), and also found that individuals exhibited motor slowing on tasks of auditory reaction time, movement time, and movement time with decision. Longitudinal declines have also been noted in optokinetic nystagmus and cerebellar motor functioning (i.e., rapid alternating movements; Kirkwood et al., 1999), as well as saccadic eye movement and fine motor control (Penney et al., 1990). Penney and colleagues also suggest that motor abnormalities may develop as far as 10 to 15 years prior to clinical diagnosis, which is consistent with Biglan and colleagues' findings.

HD: Genetics and Predictive Testing

As of 2009, approximately 1,400 clinical genetic tests exist with nearly 300 additional tests available in research settings (University of Washington, 2009). Huntington disease, hereditary breast and ovarian cancer, familial adenomatous polyposis (colon cancer), and spinocerebellar ataxia are some of the most frequently discussed genetically-linked disorders in the predictive testing literature (Broadstock et al., 2000; Timman, Stijnen et al., 2004). Since predictive testing for HD became available in 1994, HD populations have served as a prototype for genetic testing and genetic counseling in a wide array of other diseases. The unique genetic etiology of HD, advances in the prediction of disease onset, and the ability to identify gene-expanded patients decades before diagnosis has made HD the first adult onset genetic disease that has a *robust* predictive genetic test (Hayden & Bombard, 2005).

Psychological characteristics of those receiving a predictive test. The potentially disturbing effects of predictive testing in HD are likely reflected in the low uptake of at-risk individuals who actually pursue genetic testing. Studies conducted prior to the availability of predictive testing reported that upwards of 79% of at-risk individuals claimed they would voluntarily receive testing to determine their HD status. One-hundred percent of those surveyed said that predictive testing should be made available even in the absence of a cure or treatment for HD (Kessler et al., 1987). The actual number of at-risk individuals receiving a genetic test has been incongruent with the survey results obtained prior to the availability of linkage testing in 1983 and mutation testing in 1994. The worldwide uptake of predictive testing has ranged from 3% to 4% in Germany, Austria, Switzerland (Laccone et al., 1999) to 24% in the Netherlands (Maat-

Kievit et al., 2000). Clearly, the overwhelming amount of testing requests that were anticipated has not been realized.

A number of hypotheses have been offered to explain the unexpectedly low rate of predictive testing in HD. Many studies have found that the most commonly cited reason people do not undergo testing is doubtfulness in their ability to cope with the results (Codori et al., 1994; Craufurd, Dodge, Kerzin-Storarr, & Harris, 1989; Jacopini, D'Amico, Frontali, & Vivona, 1992; Simpson, Besson, Alexander, Allan, & Johnston, 1992). Codori and colleagues (1994) found that 75% of test decliners and 30% of those undecided chose not to proceed with testing because they were afraid that they would be unable to manage their emotional reaction to the test results. Some members of these groups also avoided testing because they did not believe the test result would make them any “happier” and they were concerned about the lack of a cure for HD. Less frequently cited concerns were fear of genetic discrimination and uncertainty about family members’ reactions. In contrast, 88% of those who chose to receive a genetic test reported that they were confident in their ability to effectively manage any subsequent distress. These individuals were also less concerned about a cure for HD and thought that the genetic test results would benefit them in some way. Research on persons considering genetic testing for HD collectively suggests that there is a strong self-selection bias among tested individuals. Volunteers undergoing testing tend to be socially extroverted and have higher ego strength, social support, and lower levels of affective disturbance (Decruyenaere et al., 1995).

Psychosocial responses to predictive testing. Research examining the emotional reaction to predictive genetic testing in HD has been variable. A rough distinction can be

drawn between the findings of quantitative and qualitative studies, although both methods have yielded mixed results. Quantitative research on the rate of psychiatric hospitalizations, suicide attempts, and completed suicides has found that these major maladaptive reactions to predictive testing are extremely rare worldwide (Almqvist et al., 1999; Almqvist et al., 2003). Other studies examining group differences on symptom scales suggest that a positive genetic test result does not prompt abnormally high levels of psychological distress (for a review see, Broadstock et al., 2000). Furthermore, these studies claim that test outcome does not directly impact emotional functioning. Instead, ego strength, parental status, motivation for undergoing testing, and baseline mood are purported to be more relevant to psychological health than the test outcome itself (Decruyenaere et al., 2003; Tibben, Timman, Bannink, & Duivenvoorden, 1997). These findings emphasize the primacy of individual characteristics in determining post-test reactions, regardless of whether the test outcome was positive or negative for HD. Perhaps the importance of individual characteristics helps explain why some non-expanded individuals experience psychological distress similar to that of gene-expanded patients (Huggins et al., 1992).

Many studies examining group differences on self-report measures of psychiatric symptoms have offered some insight into emotional responses following a predictive test, but the findings are problematic in a number of ways (Broadstock et al., 2000; Timman, Stijnen et al., 2004). First, the samples in these studies have a strong-self selection bias that favors individuals who possess greater psychological resources (Decruyenaere et al., 1995). The pre-test mental health status of study participants probably does not adequately represent the general HD population, and may consequently mask any adverse

affects of testing. These studies also do not thoroughly examine the prevalence of psychological symptoms within groups (Codori et al., 2004). Only statistically significant differences between gene-expanded and non-expanded groups were tested for, which means that the conclusions may be confounded by the overlapping experiences of both groups (e.g., at-risk status). Flaws in statistical methodology and limited sample sizes in many of these studies were also problematic (Timman, Stijnen et al., 2004). Reasonable arguments could be made that the studies lacked sufficient power to detect meaningful effects. Additionally, many longitudinal studies appeared to have a non-random, selective drop-out of participants with little or no drop-out analysis. In many cases the drop-out rate was greater than 50% (Tibben, 2007). The absence of attrition analysis is particularly disturbing since recent research has demonstrated that gene-carriers who drop out of studies lack a sense of well-being and are significantly more hopeless and avoidant (Timman, Roos, Maat-Kievit, & Tibben, 2004). Excluding drop-outs from the analyses is certain to reduce the differences between groups. Lastly, clinical intuition and anecdotal evidence are directly contradicted by the suggestion that test results concerning an incurable neurodegenerative disease are inconsequential. Implying that predictive testing is psychologically benign simply offends reason and negates the need for genetic counseling at all.

A number of researchers have improved the methodology of previous studies and resisted the temptation to rely on self-report scales alone (Bloch et al., 1992; Codori & Brandt, 1994; Codori et al., 2004; Hayden & Bombard, 2005; Huggins et al., 1992; Tibben, 2007; Timman, Stijnen et al., 2004; Williams et al., 2010). Many of these studies have found higher levels of distress as a result of test outcome. To illustrate, Codori and

colleagues (2004) modified some of their previous findings that suggested test results did not affect level of distress. They extended previous research in two important ways in their study of major depression following predictive testing: 1) they examined the one-year *prevalence* of a major depressive syndrome for the first 12 months following predictive testing, and 2) they used a mixed-method design by administering structured interviews alongside self-report measures. The results showed that the 1-year prevalence of major depression among gene-expanded patients was double that of non-expanded individuals who had a prevalence rate identical to the general population (3%); although, the difference was not statistically different. The findings ultimately indicated that approximately 20% of those who test positive for HD likely experience depressive symptoms within one year of testing that require professional treatment.

In addition to an increased risk of depression, those receiving a positive predictive test have been shown to experience high levels of subclinical affective distress immediately after the disclosure of test results (Hayden & Bombard, 2005; Timman, Roos et al., 2004). Hopelessness has been seen in gene-expanded individuals as they begin thinking about the implications of the disease on their futures (Codori & Brandt, 1994; Timman, Roos et al., 2004). Isolation from social support networks is also observed and perpetuates poor emotional adjustment, especially when individuals are alienated from family members or family members are not coping well with their loved one's HD status (Bloch et al., 1992). A sense of loss and grief can also be experienced with some people feeling as if part of them has died after learning they will develop HD (Bloch et al., 1992). Affective symptoms appear to improve approximately 1-2 years

after testing as people adapt to their gene status, but some increase 7-10 years later (e.g. hopelessness; Timman, Roos et al., 2004).

Intrusive thoughts and avoidance behaviors are also observed, especially within close temporal proximity to the receipt of test results (Bloch et al., 1992; Codori & Brandt, 1994; Timman, Roos et al., 2004). Gene-expanded individuals tend to think about HD more often and may begin to interpret normal age-related clumsiness or forgetfulness as symptoms of HD (Hayden & Bombard, 2005). The reactivation of traumatic experiences with regard to HD has also been observed. Genetic test results are known to stir up previously ignored experiences, feelings, fears, and memories related to HD (Tibben, 2007). Intrusive thoughts and avoidant behaviors may be frequent following testing but their severity declines approximately 3 years post-test and continues to decline after 7-10 years (Timman, Roos et al., 2004).

Those receiving a positive test result are not the only individuals to experience psychological distress. Many non-expanded individuals also feel some degree of emotional turmoil (Codori & Brandt, 1994; Hayden & Bombard, 2005; Huggins et al., 1992). Huggins and colleagues (1992) conducted one of the largest studies examining the psychological reactions of non-expanded patients following the receipt of their test results. Surprisingly, they found that 10% experienced notable difficulties in coping with their gene status. A follow-up case analysis showed that many distressed individuals had experienced depression and confusion about the future. Survival guilt and a loss of identity were also common. Some individuals had built their self-concept around the notion that they would develop HD and the negative test result shattered their

self schemas. Others were distressed because they had made major irreversible decisions based on the fact that they were going to manifest HD (e.g., became surgically sterile).

Hayden and Bombard (2005) suggest that any test result can cause adverse reactions if it contradicts expectations of the outcome, even if it is a beneficial outcome. Genetic testing results for HD are a major life event for those who are at-risk, and the implications of the results need to be accommodated into one's perceptions of the world, others, and themselves. Adjustment problems occur when people are forced to make changes to their future intentions, expectations, and assumptions (Tibben, 2007). The fact that both gene-expanded and non-expanded people can experience emotional distress indicates that schemas are challenged in both groups. When people are forced to adjust their assumptions and schemas to accommodate genetic testing results, then the potential for PTG is present. The following portion of this chapter will examine the potential for PTG following a genetic test for HD.

*Huntington Disease, Predictive Testing,
and Posttraumatic Growth*

Many studies have uncovered the possibility of growth related to predictive genetic testing. Kessler et al. (1987) found that 76% of individuals at risk for HD said that they would "strive even harder to finish their life's work" if they received a positive genetic test result for HD. Nearly 70% of the same sample said that they would also become depressed if they received a positive genetic test result. These findings indicate that although individuals may experience distress after genetic testing, they also anticipated personal growth. The anticipated growth of individuals in Kessler et al.'s

study is especially meaningful since the majority of the people interviewed did not expect to be told that they had the HD-gene expansion.

Bloch and colleagues (1992) further illustrate the potential for PTG by presenting the case of a 27-year-old woman who underwent a predictive genetic linkage analysis, which was less accurate than the current methods of molecular confirmation. She received results that suggested she was at an increased risk for HD (96% chance of developing the disease). When receiving the news she was disappointed and tearful, but stated, "I am glad I know so that I can make the best of what I have now" (p. 500). She was uncertain about informing family members of her gene status; however, after much distress she decided to inform her father. Her brother and sister eventually learned about her gene status by recognizing her voice during an anonymous call to a radio station. The woman's relationships with her father and sister both became much closer because of her genetic test result. She also became closer to one of her friends and they eventually developed a romantic relationship. In contrast, the woman and her brother have avoided each other since the genetic testing. Two years after receiving a positive genetic test she said that she now believes time is precious and that she needs to take advantage of every moment.

This woman's experience closely reflects two areas of growth that Tedeschi and Calhoun have identified after traumatic events (Tedeschi & Calhoun, 1996, 2004). First, she experienced significant growth and in her ability to relate to others. Although some of her relationships were damaged (i.e., her brother) a number of others improved. She also developed a new appreciation for life, which seemed to occur after a significant

amount of time elapsed. Her desire to “make the most of everything [she has]” (p. 501) indicates that testing prompted her to reorder the priorities within her assumptive world.

Other studies have documented PTG in a variety of domains for people who have undergone genetic testing for HD. Williams and colleagues (2010) examined genetic stigma and discrimination in people at-risk for HD, and found that 74 of the 433 people in their study reported benefits from learning about their HD family history or gene-status. Participants reported the greatest benefits in life knowledge, certainty about the future, relationships with others, and life meaning. One can easily see that these reported benefits parallel the domains of PTG identified by Tedeschi and Calhoun (1996), even though they are not explicitly labeled as PTG. In another study, Bloch and colleagues (1992) described a woman who had a particularly adverse reaction to her test results. In spite of her psychological distress, she reported that she had taken her life in a new direction by deciding to have children although she was previously opposed to the idea. Cordori and Brandt (1994) found that participants experienced growth by developing a stronger appreciation for life and interpersonal relationships. Participants said, “Knowing that the risk is high gives you a chance to assess priorities and re-prioritize some of them. Instead of presuming something could be done in the future. . .some things can be [done] sooner... It heightens your awareness and teaches you to appreciate things around you” (p. 178). A number of people expressed desires to take advantage of the time they had left before the onset of disease, and some developed a newfound gratitude for the life they had already been given. Some participants also pursued new possibilities, such as going on international trips. One of the most notable findings of Cordori, Hanson, and Brandt’s (1994) study was the number of participants who described deepening

relationships with their spouses or partners. One person said, “My husband and I are closer; [we] try to do things together” (p. 181).

Rationale for the current study:

A case for the examination of PTG after genetic testing

The potential for PTG clearly exists following predictive testing but it has not been adequately researched. A quantitative analysis of PTG would be the first of its kind and would significantly contribute to the HD literature. There is nothing in the HD literature that has examined PTG using a widely accepted measure of growth.

In addition to benefiting the HD literature, a study of PTG after genetic testing would contribute to the broader literature on growth after trauma. No other disease in the PTG literature is similar to HD. HD is unique because it: 1) has a highly accurate predictive genetic test so people know they are going to develop an untreatable disease long before they are diagnosed, 2) HD’s genetic nature makes it a disease of families, 3) genetic counseling is offered to patients, and 4) it affects a broad range of functions (i.e., cognition, mental health, and motor functioning). The unique characteristics of HD provide rich opportunities for researchers to understand how the aspects of disease contribute to PTG.

The fact that gene-carriers are able to know that they will develop an incurable disease long before they manifest symptoms provides the opportunity to study PTG before a disease is even diagnosed. Predictive testing long before diagnosis also provides researchers with a window of opportunity to distinctly examine the relationship between PTG and the amount of time that has elapsed after receiving a genetic test result. Codori and Brandt (1994) found that many participants required weeks or years to adjust to their

test result. Even participants who anticipated being gene-expanded their entire life still needed “time to fully comprehend and accept the greater certainty afforded by genetic testing” (p.177). If genetic testing and disease onset were too close to each other, then researchers would not know if they were assessing PTG as a result of the genetic test or PTG as a result of disease onset.

The autosomal dominant nature of HD makes it a disease of families. Because HD is transmitted between family members, there may be unique interpersonal dynamics that exist. A strengthening of one’s ability to relate to others is one of the primary domains of PTG, and one could reasonably assume that the transmission of HD between family members would necessarily have an effect on any potential changes in interpersonal relationships. Many of the other diseases studied in the PTG literature do not have such a strong genetic component, therefore HD offers a unique opportunity to study the relationship between genetic disease and relational abilities.

Genetic counseling is particularly relevant to HD when compared to most other diseases that have been studied in the PTG literature, perhaps with the exception of some forms of breast cancer. Genetic counselors and their clients would benefit greatly from an examination of PTG because of the documented relationships that exist between PTG and mental health. PTG has been associated with a reduction in depression and an increased sense of well-being (Helgeson et al., 2006; Tallman et al., 2007). Increased optimism and positive affect have also been related to PTG (Hart et al., 2008). Gaining a better understanding of PTG following a genetic test would allow genetic counseling to facilitate PTG in the hopes of having better psychological outcomes.

The broad effects of HD on cognitive, psychiatric, and motor functioning also allow PTG researchers to observe how each of these aspects of disease contribute to growth. Researchers would be able to track the symptoms of disease, and their various effects, since it is possible to know with certainty that participants will eventually develop HD. Additionally, the fact that HD presents with a unique triad of symptoms allows researchers to examine how cognitive, psychiatric, and neurological symptoms may be related to the experience of PTG.

Because of the potential benefits that a study of PTG may offer HD gene-expanded and non-expanded individuals, the present study aims to be the first quantitative examination of PTG following predictive genetic testing for HD.

CHAPTER III

METHODS

Participants

Both gene-expanded and non-expanded participants in this study were obtained from the ongoing PREDICT-HD research project, a multi-site longitudinal examination of the neurobiological predictors of Huntington's disease (Jane Paulsen, PI). What follows is an explanation of inclusion/exclusion criteria and recruitment procedures for PREDICT-HD, and then a discussion about additional inclusion/exclusion criteria relevant for to the current study.

PREDICT-HD recruitment. A total of 32 sites are affiliated with PREDICT-HD in North America, Europe, and Australia. The University of Iowa is the primary coordinating center for the study and is responsible for study administration and recruitment protocols. The United States Department of Health and Human Services National Institutes of Health (NIH) and the Cure Huntington's Disease Initiative (CHDI), Inc., currently provide funding for the PREDICT-HD project.

At the time of this study, 1,197 participants were enrolled in the PREDICT-HD study. Individuals were recruited for PREDICT-HD through an active HD registry that contained the contact information for participants interested in research. Additionally, participants were recruited at events such as Huntingtons Disease Society of America's National Conference and the Annual Meeting of the Huntington Study Group. Word of mouth and the website for the University of Iowa's Huntingtons Disease Center of Excellence (<http://www.uihealthcare.com/depts/huntingtonsdisease/>) were also used for recruitment. After expressing interest in participation, individuals were deemed eligible

for the study if they met the inclusion/exclusion criteria (described below) and they completed the informed consent procedures approved by the institutional review board at their respective study sites.

Individuals met a number of criteria to participate in PREDICT-HD. All participants underwent genetic testing for the HD gene because they had a parent with the disease. Independent genetic testing was voluntarily completed prior to study enrollment; however, test results were confirmed through polymerase chain reaction (PCR) analyses conducted on blood samples participants' provided to their respective research sites. All blood samples were analyzed by lab personnel at Massachusetts General Hospital. Following PCR analyses, participants were classified into a gene-expanded group or non-expanded control group based on their genetic test results. The gene-expanded group (i.e., HD "positive") had a CAG repeat length greater than or equal to 36 and the non-expanded group had a CAG repeat length less than 36. Commitments to complete annual evaluations for five years and to retain a support person to travel to all visits were also required to enhance retention. Individuals completed study activities during a regular clinical research evaluation. Participants agreed to complete an extensive battery of tests that included cognitive, motor, psychiatric, and functional measures examining prodromal changes in HD. The battery of tests took approximately 4 hours to complete and included the Stroop Test, Symbol Digit Modalities Test (SDMT), Controlled Oral Word Association (COWA), Frontal Systems Behavioral Scale (FRSBE), Symptom Checklist 90-Revised (SCL-90-R), Substance Use Form (SUF), The Columbia Suicide Severity Rating Scale, select portions of the Unified Huntington's Disease Rating Scale (UHDRS '99), HD Behavioral scale, Structured Interview for Behavior in HD, the

Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1996), surveys for symptoms of irritability and apathy, and assessments about occupational and social functioning. Other inclusion criteria for participation in PREDICT-HD were agreements to undergo neuroimaging, provide urine and blood samples, and to secure a companion that would complete surveys about the participant.

Several exclusion criteria were established for participation in PREDICT-HD. Individuals younger than the age of 18 were excluded (as a result juvenile HD was not examined). People displaying any evidence of unstable ongoing medical disease, mental illness, or substance abuse were not enrolled. A history of any of the following was not present: severe learning disability, mental retardation, seizures, traumatic brain injury, or other diseases of the central nervous system. Anyone who received psychopharmacological treatment with phenothiazine-derivative antiemetic medications greater than 3 times per month or anti-psychotic medications (typical or atypical) were excluded. Additionally, those with a Pacemaker or metallic implants were not permitted to participate in the study.

Current study participants. All participants in the current study were recruited from research universities and clinics in the United States, Australia, and Canada that were a part of the PREDICT-HD study. Participants who displayed motor signs that could reasonably be diagnosed as HD were also not included. As such, participants scored a 0-3 on a diagnostic confidence level rating scale (DCL) that ranged from 0 to 4, which indicated that the person did not exhibit a level of motor symptoms warranting a clinical diagnosis of HD (the scale is described in more detail below). Participants were no further than 8 years from receiving their genetic test results. Eight years was

established as a reasonable cutoff because it allowed for an appropriate number of participants to power the statistical analyses while also minimizing the confounding effects that other life events may have had on PTG after individuals underwent their genetic testing. An 8 year cutoff was also supported by previous longitudinal research in the health psychology literature, which suggested that individuals can experience PTG as long as 10 years after the traumatic event (e.g., Hawley & Joseph, 2008; Pollard & Kennedy, 2007; Powell, Ekin-Wood, & Collin, 2007). Furthermore, research indicated that traumatized individuals can still discern which aspects of PTG could be directly attributed to a particular traumatic event years after the event occurred (Curbow, Somerfield, Baker, Wingard, & Legro, 1993).

Study Procedure

All participants in the current study completed the standard PREDICT-HD protocol, which is described here. First, the informed consent process will be discussed followed by a description of the data management procedures.

Both gene-expanded and non-expanded participants completed the same consent process. All individuals were informed about the procedures, obligations, risks, and benefits associated with participating in PREDICT-HD, which included completing the measures used in this study. Participants that expressed continuing interest were asked about inclusion/exclusion criteria and informed of their eligibility. Ineligible participants were informed of their exclusion from the study, and eligible participants continued study procedures with a trained research assistant. The research assistants explained the informed consent document in detail and obtained a signature (see Appendix C). Participants had the opportunity to ask questions and raise concerns before signing the

consent. All participants received a copy of the consent form for their records. No participants continued study procedures without a completed informed consent form.

Trained research assistants administered all cognitive, behavioral, and functional measures in the previously described test battery after participants signed the informed consent document. Certified motor raters conducted all motor assessments.

Demographic information and medical history were also collected, including genetic test results, genetic test date, gene status, and CAG repeat length. All study information and testing materials were labeled with previously assigned subject numbers that were used to deidentify the data and protect confidentiality.

Data management. Paper and electronic copies of data were kept in accordance with the standard operating procedures of the PREDICT-HD study. Hard copies of surveys and assessments were labeled with identification codes that did not directly link participants with data. All paper copies were kept in locked file cabinets in locked offices. Only authorized research team members were allowed access to the data. All other information was kept in binders in locked offices, locked file cabinets, or password protected computer files.

All electronic records were maintained by full-time system administrators at the University of Iowa. All computers were password protected and continuously ran virus-protection software. Network traffic was heavily encrypted and security software ran continuously to reduce the potential of malicious attacks. The primary server was located in a secure room that was only accessible to authorized administrators and personnel. Server data was backed up to tape every 24 hours and was mirrored by a second offsite server more than 50 kilometers away, which was similarly secured. Study

data were fully auditable so all changes could be monitored. A permission-based security system limited access to the study database according to assigned levels of permission. System administrators took extensive measures to ensure that data were protected and that the confidentiality of electronic records was maintained.

Measures

All measures used in the current study were obtained from the larger PREDICT-HD battery. Archival demographic and medical data from previous PREDICT-HD visits were also used. Of note, all individuals in PREDICT-HD provided permission to utilize archival data when completing the informed consent process. The following section only describes the measures specifically used in this study.

Demographic and Medical Questionnaire

Participants completed a Demographic and Medical Questionnaire that consisted of several items about personal information and medical history. Participants provided information about date of birth, gender, ethnicity, race, years of education, occupation, marital status, and handedness. Medical questions included items about serious illnesses, allergies, psychiatric history, alcohol, substance abuse, and head injuries (including loss of consciousness). There were additional questions related specifically to HD. Information was gathered about genetic testing, including the date of testing, test result, and CAG repeat length. Information gathered from the Demographic and Medical Questionnaire was used to establish 6 variables relevant to the current study: participant age, gender, time since testing, and expected years to diagnosis (YTD), probability of HD diagnosis within 5 years (Prob5yr), and the CAG/Age Product (CAP). The YTD and Prob5yr variables were based on the parametric survival model derived by Langbehn and

colleagues (2004), which uses CAG repeat length and age to predict when HD symptoms will be clinically diagnosed in gene-expanded individuals. The YTD variable was expressed as the estimated number of years until a gene-expanded participant was predicted to fully manifest HD. The Prob5yr variable was expressed as the percent chance that an individual will develop HD within 5 years of their most recent study visit. Both YTD and Prob5yr are useful for predicting the onset of HD, and they are widely used in the research; however, they have an inherent weakness because the underlying Langbehn model was developed based on retrospectively obtained self-reported GAG data from gene-expanded individuals. To correct for the weakness of the Langbehn model, Zhang and colleagues (2011) developed the CAG/Age Product (CAP) variable, which is based on directly observed CAG repeat lengths and age. CAP is obtained by simply multiplying participants' age by a scaling of the CAG repeat length. The larger the CAP value, the closer an individual is to diagnosis.

UHDRS Motor Scale

The motor component of the Unified Huntington's Disease Rating Scale (UHDRS) consisted of 15 items that measured a range of HD-related neurological symptoms (Huntington's Study Group, 1996). Items were rated for right-sided and left-sided functioning when applicable. A factor analysis by Marder and colleagues (2000) yielded five dimensions for the UHDRS Motor Scale: 1) oculomotor, 2) bradykinesia/fine motor, 3) rigidity, 4) dystonia, and 5) chorea. Trained motor examiners rated each item in each dimension on a 5-point likert scale (0 to 4), with higher scores indicating greater impairment (e.g., Ocular Pursuit is rated as: 0= complete, 1=jerky movement, 2= interrupted pursuits/full range, 3= incomplete range, 4= cannot pursue). The range of the

scale's total score was 0 to 124. The current study used the total motor score as a predictor variable, since that was the accepted practice when examining the motor signs of HD.

Reliability and validity studies have been performed on the UHDRS Motor Scale. The Huntington Study Group (1996) utilized a sample of 489 participants with manifest HD to establish internal consistency, interrater reliability, and longitudinal rates of change. Internal consistency was assessed with Cronbach's alpha and was high ($\alpha = 0.95$). Two of three experienced motor raters examined 24 participants (16 each) to determine interrater reliability. The raters were blinded from each other's ratings throughout the study. Intraclass correlations were used to examine the results, and ranged from 0.94 for the total motor score to 0.62 for the dystonia score. Longitudinal rates of change were assessed with 180 participants who were: 1) reevaluated within at least 4 months of their previous visit, and 2) evaluated by the same clinician. A least square line was fitted to the data to produce an average rate of decline over a 6 month period. Participants were found to have a mean change score of 3.2 (SD = 8.4) with a range of -21.6 to 33.5.

In addition to the 15-item UHDRS motor scale, motor raters for this study provided an overall diagnostic confidence level (DCL) that used the following scale: 0=no motor abnormalities; 1=non-specific motor abnormalities (less than 50% confidence that the participant has manifest HD); 2=motor abnormalities that may be signs of HD (50–89% confidence); 3=motor abnormalities that are probable signs of HD (90–98% confidence); or 4=motor abnormalities that are definite signs of HD (>99% confidence). As mentioned above, participants were excluded from this study if they obtained a

DCL=4. There were two reasons for grouping participants as “4 versus not 4” according to the DCL rating they were given. The first was because the DCL demonstrated optimal interrater agreement when clinicians were asked to determine whether or not a person had HD (DCL=4) or did not (DCL=0-3; Hogarth et al., 2005). Interrater reliability estimates using the DCL to differentiate between diagnosed and non-diagnosed participants were relatively high ($\kappa = 0.67$). Reliability dropped noticeably when clinicians were asked to rate the severity of motor symptoms in non-diagnosed individuals with DCL <4 ($\kappa = 0.32$) or to identify those who were “0 versus non-0” ($\kappa = 0.42$) at the bottom end of the scale. In addition to reliability estimates, the second reason for including all prodromal individuals was to maximize variability in prodromal clinical symptoms for exploring the relationship between prodromal motor symptoms and PTG.

Symbol Digit Modalities Test

The Symbol Digit Modalities Test (SDMT) was used as a neuropsychological measure of visual scanning, divided attention, processing speed, and tracking (Smith, 1991; Strauss, Sherman, & Spreen, 2006). Participants were allowed 90 seconds to complete the symbol-number transcription task. A coding key at the top of the page illustrated nine pairings of numbers and symbols. Participants used the coding key to copy numbers under their respective symbols on the stimulus sheet as quickly as possible. Raw score was used to determine performance with possible scores ranging from 0 to 110. High scores indicated better functioning.

Test-retest reliability for the SDMT has been well documented. Smith (1991) reported a reliability coefficient of $r = .80$ ($r = .76$ for oral administration) in a study of 80 healthy adults who were given the test twice over an average of 29 days. A practice

effect resulting in a 4 point increase was also noted. Uchiyama et al. (1994) examined the SDMT in a large sample of men ($N > 1000$) over a six month period and found a significant test-retest coefficient ($r = .79$). No practice effects were noted in Smith's sample over a two year period.

Concurrent validity has been established between the SDMT and other measures of attention. Morgan and Wheelock (1995) examined the relationship between the WAIS-R Digit Symbol subtest and the SDMT in 100 people being seen for neuropsychological evaluation. They found a strong correlation between the two measures ($r = 0.85$). They also found the SDMT was more difficult because participants consistently scored lower on the SDMT than on the Digit Symbol subtest. Strauss and colleagues (2006) summarized the research establishing the validity of the SDMT with a number of other measures of visual tracking and processing speed such as the Stroop test, Trail Making Test, and Line Cancellation. Royan, Tombaugh, Rees, and Francis (2004) also noted moderate to high correlations with the Adjusted-Paced Serial Addition Test ($r = -.36$ to $-.54$).

The SDMT has been proven to be a sensitive measure of cognitive changes in prodromal HD. Langbehn and Paulsen (2007) found that the SDMT (examined in conjunction with the COWA) predicted HD diagnosis beyond what was accounted for by motor scores. Paulsen and colleagues (2001) conducted a prospective longitudinal evaluation of the motor, cognitive, psychiatric, and functional aspects of HD in a population of at-risk individuals ($N=260$), some of whom converted to diagnosis ($N=70$). The results showed a substantial difference in baseline SDMT performance between phenoconverters and non-converters with an effect size of 0.75. Change scores on the

SDMT over a two year interval yielded a large effect size of 1.4 between the two groups. These findings were later substantiated by Lemiere and colleagues (2004) and Stout and colleagues (2010). The SDMT has also been correlated with caudate atrophy in HD ($r = .65$; Starkstein et al., 1988).

Symptom Checklist-90-R: Depression Subscale

The Symptom Checklist-90-R (SCL-90-R; Derogatis, 1994) is a measure of general psychopathology. The depression subscale is one of the nine original psychometrically validated subscales of the SCL-90-R, and was used in this study to assess depressive symptoms. The scale consisted of 13 items, and examples include “crying easily” and “feeling lonely.” Participants were asked to rate the discomfort that they experienced from depressive symptoms during the last week. Ratings were made on a 5-point scale from 0 (not at all) to 4 (extremely). The depression subscale yielded a total score that was simply the average rating of all 13 items. The total score ranged from 0 to 4. High mean scores indicated greater depression. Norms were available for normal adults, normal adolescents, psychiatric inpatients, and psychiatric outpatients.

The psychometric properties of the depression subscale have been well established (Derogatis, 1994). Internal consistency reliability was determined to be very high ($\alpha = 0.90$) during the development of the SCL-90-R. Test-retest reliability over a 1-week period was adequate ($r=.82$). Convergent validity was demonstrated by the SCL-90-R Depression scale’s high correlations with other measures of depression, including: the CES-D Depression Scale, the Weissman and Beck Dysfunctional Attitudes Scale, the Zuckerman and Lubin Multiple Affect Adjective Check List, Beck Depression Inventory,

the Dempsey D-30 Depression Scale, the Raskin Depression Screen, and the Hamilton Depression Rating Scale (Payne, n.d.).

Posttraumatic Growth Inventory

The Posttraumatic Growth Inventory (PTGI; Tedeschi & Calhoun, 1996) was developed to assess positive psychosocial outcomes following traumatic experiences (See Appendix D). The scale consisted of 21 items that provided a total growth score. The PTGI also produced scores on five subscales: 1) relating to others, 2) new possibilities, 3) personal strength, 4) spiritual change, and 5) appreciation of life.

Participants in this study responded to items using a 6-point Likert scale (0 to 5), with a total score ranging from 0 to 105. Higher scores indicated greater posttraumatic growth. Examples of items included: “I have a better understanding of spiritual matters,” “I have a greater feeling of self-reliance,” and “I changed my priorities about what is important in life.” Instructions for the scale stated: *Please indicate for each of the statements below the degree to which this change occurred in your life as a result of being informed of your HD genetic status.*

Psychometric characteristics of the PTGI were established in a population of undergraduate students (N=604) who experienced a range of traumatic experiences (Tedeschi & Calhoun, 1996). Tedeschi and Calhoun reported high internal consistency for the total scale ($\alpha = 0.90$) and moderate to high internal consistency across subscales [α ranged from .67 (appreciation for life) to 0.85 (relating to others, spiritual change)]. Test-retest reliability was adequate ($r = 0.71$) in a subsample of participants ($n=28$) tested over a 2-month time period. Test-retest reliability for the subscales ranged from $r = 0.37$ to $r =$

0.74. Intercorrelations among scales ranged from $r = 0.27$ to $r = 0.52$ and the range of correlations for each scale with the total PTGI score ranged from $r = 0.62$ to $r = 0.83$.

Tedeschi and Calhoun (1996) established discriminant validity for the PTGI by examining correlations with optimism, religious participation, social desirability, and personality characteristics. Optimism, religiosity, and all of the Big Five personality characteristics, except neuroticism, were positively correlated with the PTGI. There was not a significant relationship between the PTGI and social desirability. Construct validity was assessed by examining the relationship between trauma severity and PTGI scores in a sample of undergraduate students ($N=117$). Individuals who perceived traumas to be stressful reported more growth than those who perceived the event as less traumatic.

The factor structure of the PTGI has also been well validated. The five PTG domains were originally established through a principal components analysis and varimax rotation of the PTGI items from the sample of 604 participants that experienced traumatic events (Tedeschi & Calhoun, 1996). In a follow-up study, Taku, Cann, Calhoun, and Tedeschi (2008) conducted a confirmatory factor analysis examining how well various factor models fit the underlying structure of the PTGI. The 5-factor model was most robust, followed by 3-factor and one-dimensional models, suggesting that Tedeschi and Calhoun's original 5-factor model was the most accurate way to characterize PTG.

Post-hoc Power Analysis

A post hoc power analysis was conducted because the sample size and statistical analyses were improved over what was originally proposed for this study. *An a priori* analysis determined that a sample of 74 gene-expanded and 37 non-expanded participants

provided adequate power for the study's primary analysis. Fortunately, eight additional gene-expanded participants were able to participate in the study, which resulted in a gene-expanded sample approximately 10% larger than the expected sample size of 74. The increased sample size required a post-hoc power analysis to determine how much power was gained from the greater number of participants.

Post-hoc testing was also necessary because the *a priori* power analysis initially proposed for this study was conducted under the assumption that a 2-to-1 matched sampling scheme—two gene-expanded participants matched to one non-expanded participant on age and gender—was going to be used to control for the relationship between demographic variables and PTGI scores. The 2-to-1 matched sampling has since been replaced with an ANCOVA and MANCOVA because of their ability to reduce within-group error variance and eliminate confounds.

The parameters used in the post hoc power analysis were the same as those of the *a priori* analysis: $\alpha = .05$ and Cohen's $f = .30$ (medium effect size). The number of covariates used in the ANCOVA and MANCOVA was added as an additional parameter to calculate power for these tests. Similar to the *a priori* analysis, post hoc testing was aimed at an ANCOVA for two groups, since the analyses of primary importance in this study was the comparison of gene-expanded and non-expanded individuals' PTG. Given an $N = 119$, $\alpha = .05$, $f = .30$, and three potential covariates (i.e., age, gender, education), the achieved power was $1 - \beta = .90$. In terms of correlational analysis, an $\alpha = .05$, a medium effect of $\rho = .30$, and a sample of 82 gene-expanded participants resulted in a power level of $1 - \beta = .88$. The larger sample size and the use of ANCOVA and

MANCOVA yielded gains in power to examine differences in posttraumatic growth between non-expanded and gene-expanded individuals.

CHAPTER IV

RESULTS

This chapter presents and summarizes the results of the statistical analyses used to answer each of the proposed research questions. First, the sample is characterized and preliminary analyses are presented, including an examination of score distributions and outliers, as well as procedural checks on the relationship between demographic variables and the dependent variables of interest (i.e., Posttraumatic Growth Inventory scores). Next, the results of an ANCOVA and MANCOVA comparing gene-expanded and non-expanded participants on Posttraumatic Growth Inventory (PTGI) scores are reported. Findings are then presented for regression analyses examining gender, age, time since testing, and estimated time to diagnosis variables (i.e., YTD, Porb5yr, CAP), and their relationship with the PTGI total score and subscales. Lastly, results from three exploratory regression analyses examining the relationship between clinical measures of motor functioning, depression, and cognition with PTGI total score are reported.

Participants

In total, 1,197 participants were enrolled in the PREDICT-HD study between September 2001 and August 2010, and 395 completed the PTGI between February 2009 and August 2010. Fifty-eight had incomplete test data, and an additional 86 had incomplete demographic information about age, education, or gender. An additional 25 did not have enough information to determine their estimated proximity to HD diagnosis and 4 did not have information about the date they received genetic testing. Of the remaining participants, 103 had genetic testing more than 8 years ago, and were subsequently excluded from the study. The final sample consisted of 119 participants, of

which 82 had the HD gene-expansion and 37 did not. For the small exploratory analysis of clinical variables, a total of 81 participants had complete Symptom Checklist-90 Revised (SCL-90-R) scores, 76 had complete Unified Huntington Disease Rating Scale Motor scores, and 67 had complete Symbol Digit Modalities Test scores.

Sample Characteristics

More females (69.7%) than males (30.3%) participated in the current study. Mean age was 44.0 years old ($SD = 13.1$) for the entire sample. The sample was predominantly Caucasian (99.2%) with one participant endorsing more than one racial background (0.8%). Mean years of education was 14.3 ($SD = 2.3$), with a range of 10 to 20 years. Most participants were recruited from the United States, followed by Australia and Canada. None of the Canadian participants had the HD gene-expansion. The mean number of years between completing the measures utilized in this study and receiving an HD-gene test was 5.19 years ($SD = 1.8$). The overall range for years since genetic testing was 1.10 to 8.00 years. Approximately 25% of the sample was 3.95 years or less from having a genetic test, 50% of the sample was 5.27 years or less, and 75% of the sample was 6.75 years or less. Basic demographic and medical data for both gene-expanded and non-expanded participants are presented in Table A1, and the number of participants from each research site is presented in Table A2.

The demographic characteristics of the current study's sample are similar to the larger PREDICT-HD study. Paulsen and colleagues (2006) first characterized 505 participants in the entire PREDICT-HD sample and found that it consisted of 64% women and 36% men, and it was 97% Caucasian. The average age of participants was 42 (9.9) years and slightly more educated than the general population, with 90% of

participants graduating from high school. Although the sample size of the PREDICT-HD study has grown, the demographic characteristics of the sample have remained consistent over time, and are reflected in the current study.

Preliminary Analyses

Data were analyzed with Predictive Analytics Soft Ware Statistics (PASW) Version 18 (SPSS, 2009). Descriptive data (means and standard deviations) were used to examine scale distributions. Frequency distributions, histograms, and box plots were utilized to identify outliers and check normality assumptions for demographic, clinical, and primary study variables. No imputations were used to correct for missing data. Raw scores for each variable were transformed into z-scores to examine outliers. A score was considered an outlier if it had a z-score with an absolute value greater than 3. No outliers were present among the demographic or posttraumatic growth (PTG) variables for the entire sample. For the clinical variables measured in the gene-expanded group (i.e., UHDRS, SDMT, SCL-90-R), the depression score from the SCL-90-R was the only variable to have outliers, with 3 participants having z-scores greater than 3. These outliers were examined to determine if they were different from the rest of the gene-expanded sample. Outliers' demographic and clinical characteristics were similar to the rest of the sample, suggesting that they were from the same population. Furthermore, analyses involving the SCL-90-R were conducted with and without the outliers to determine if their presence produced different results. Results were the same regardless of the outliers, so they were retained in the analysis.

Skewness and kurtosis values for the most of the variables were less than 1, indicating that they were normally distributed. The exceptions were the SCL-90-R

Depression score (skewness = 1.77, kurtosis = 2.42) and UHDRS Motor Score (skewness = 1.77, kurtosis = 3.36) which were positively skewed within the gene-expanded subsample. A log₁₀ transformation was performed because logarithmic transformations are well-suited for restoring normality in distributions with positive skew (Field, 2005). Skewness and kurtosis following the transformation indicated a normal distribution for both the SCL-90-R Depression score (skewness = -0.50, kurtosis = -.94) and the UHDRS Motor Score (skewness = --0.05, kurtosis = -0.83). Analyses were conducted with both the transformed and non-transformed scores. Differences in statistical results between the original data and log-transformed data were negligible; therefore, only the non-transformed data are presented.

Internal consistency reliability (i.e., Cronbach's alpha) was excellent for the PTGI total scale score ($\alpha = .96$). The subscales had high internal consistency reliabilities ranging from .87 (Personal Strength) to .93 (Spiritual Change). These coefficients are comparatively higher than most estimates reported in the literature (Taku et al., 2008; Tedeschi & Calhoun, 1996), indicating that the PTGI performed well within this study sample. Pearson product-moment correlations among the subscales ranged from $r = .51$ to .84, and subscale correlations with the PTGI total ranged from $r = .69$ to .93. Detailed information about zero-order correlations among the PTGI scales are presented in Table A3.

Data Screening

The dependent variables were examined to see if they were significantly related to the demographic variables. First, a series of independent sample *t*-tests were computed to determine if there were gender differences on the PTGI total scale and its five subscales.

The findings revealed gender differences for the PTGI total score, $t(117) = 2.15, p = .03$, with women ($M = 60.8, SD = 25.1$) having a higher mean PTGI total score than men ($M = 50.1, SD = 23.6$). Women also had higher scores on the Personal Strength, $t(117) = 2.28, p = .02$, and Spiritual Change subscales, $t(117) = 2.16, p = .03$). There were no gender differences (p 's $> .05$) on the Relating to Others, New Possibilities, and Appreciation for Life subscales. Because gender differences were found on the total score and subscales, gender will be controlled for in all analyses.

Two series of regression analyses were conducted to determine if age and education were related to any of the dependent variables in the combined sample of non-expanded and gene-expanded participants ($N = 119$). A total of six regression analyses were conducted with age as a predictor variable, one with the PTGI total score as an outcome variable and five with each of the PTGI subscales as single outcome variables. Education was examined in a similar manner, with the years of formal education entered as the predictor variable instead of age. Results indicated that age was only related to the New Possibilities subscale, $F(1, 117) = 5.70, p = .02$, and it accounted for 4% of the variance with a correlation of $r = -.22$. Education was not related to any PTGI scores (all p 's $> .05$). As a result, age will be included as a covariate in the MANCOVA exploring group differences on the five PTGI subscales, but not as a covariate for the ANCOVA exploring group differences for PTGI total score. Education will not be controlled for in any analysis.

One-way ANOVAs were conducted to ensure that potential cultural differences were not significantly related to PTGI scores. A comparison of PTGI total score and the five PTGI subscale scores based on country of origin revealed no differences in reported

growth between participants from the United States of America, Australia, and Canada. Therefore, country of origin was not controlled for in the analyses.

Primary Analyses: Aim #1

The first aim of this study was to characterize PTG following predictive genetic testing for HD. First, results of the descriptive statistical analyses are presented to characterize how much PTG gene-expanded and non-expanded participants report on the PTGI subscales and total score. The PTG reported in this sample is then compared to the PTG found in peer-reviewed studies of other disease populations. Comparisons between gene-expanded and non-expanded participants using a one-way ANCOVA for the PTGI total score and a MANCOVA for the PTGI subscales are then presented.

Descriptive Information for PTGI Variables

Descriptive statistics for study measures are presented in Table A4, and PTGI item means and standard deviations are presented in Table A5. Descriptive statistics were used to determine the level of growth participants reported as a result of their genetic testing experience. Participants' mean PTGI score was 57.6 ($SD = 25.0$, range = 0-105). The mean item rating was 2.74 ($SD = 1.2$, range = 0-5), indicating an overall scale rating just below a "moderate degree" of PTG following a genetic test result. The mean number of PTGI items with any endorsement (i.e., ≥ 1 on the 0-5 scale) was 17.6 ($SD = 5.1$, range = 0-21). The frequency of clinically meaningful growth was determined by calculating the number of items endorsed at a moderate degree or higher (i.e., ≥ 3 on the 0-5 scale), which is similar to what has been done in other PTG studies (Cordova et al., 2007; Widows et al., 2005). The mean number of items endorsed at a moderate degree or more was 13.1 ($SD = 6.7$, range = 0-21), which is consistent with what has been

found in breast cancer ($M = 13.1$, $SD = 6.3$; Cordova et al., 2008) and bone marrow transplant patients ($M = 14.7$, $SD = 5.2$, Widows et al., 2005).

Four PTGI items were endorsed at a moderate level or higher by more than 75% of participants: “My priorities about what is important in life” (83%), “An appreciation for the value of my own life” (77%), “Having compassion for others” (77%), and “Appreciating each day” (76%). Only two items were endorsed by less than 50% of participants, and they were the two items on the Spiritual Change subscale: “I have a better understanding of spiritual matters” (49%) and “I have a stronger religious faith” (38%). All other PTGI items were endorsed by 50% to 75% of participants. In summary, over three-quarters of participants endorsed the appreciation for life items at a “moderate” level or higher, indicating that learning their gene-status prompted growth in this domain. Furthermore, over half of all gene-expanded and non-expanded participants said they grew in their ability to relate to others, sense of self-efficacy, and pursuit of new opportunities in life.

The mean PTGI total score for all 119 participants in this study (i.e., gene-expanded and non-expanded combined) was compared to means reported for other medical populations. A systematic search of the health psychology literature was conducted to identify peer-reviewed studies that utilized the PTGI, reported means and standard deviations, and were conducted with English speaking participants who were 18 years or older. Potential studies were identified from a previous review of the PTG literature (Sawyer, Ayers, & Field, 2010) and a computerized search of articles on PubMed, Web of Science, and PsychInfo. Primary search terms included *posttraumatic growth*, *posttraumatic growth inventory*, and *benefit finding*. Search terms were crossed

with the following health-related terms: *disease, injury, cancer, HIV, AIDS, and traumatic brain injury (TBI)*. A total of 11 studies met criteria and they included 4 studies of breast cancer patients, 2 of bone marrow transplant patients, 2 of HIV/AIDS patients, 1 of a mixed cancer population, 1 of prostate cancer patients, and 1 of TBI patients. Eight of the 11 identified studies also reported enough descriptive information to briefly explore differences on the five PTGI subscales. Table A6 details the sample characteristics and mean PTGI scores of published PTG studies in other medical populations.

The mean PTGI for individuals receiving a predictive genetic test for HD was approximately 21 points higher than TBI patients 1 to 3 years post-injury (Powell et al., 2007) and about 10 points higher than men 1 year after having a prostatectomy for prostate cancer (Thornton & Perez, 2006). Interestingly, when TBI patients were 9-12 years post-injury, their PTGI scores reversed and were almost 11 points higher than the current sample (Powell et al., 2007). PTGI total scores in the current sample were also lower compared to bone marrow transplant (BMT) patients, regardless of whether they had the procedure recently (i.e., 2 years post-treatment; Widows et al., 2005) or long ago (9 years post-treatment; Tallman, Shaw, Schultz, & Altmaier, 2010). Both HIV-positive patients 6 years post-diagnosis (Milam, 2006) and a large sample of breast cancer survivors 7.5 years post-diagnosis (Brunet, McDonough, Hadd, Crocker, & Sabiston, 2010) had the highest PTGI total scores when contrasted with the current sample. Despite the different levels of growth that may exist between this study and some others, a comparison of this study with the health psychology literature revealed that HD-gene

testing prompted levels of growth that are largely similar to what has been reported in the majority of the PTG research.

Regarding the five PTGI subscales, the largest difference was found between the current sample and a large sample of breast cancer survivors examined by Brunet and colleagues (2010). Breast cancer survivors' mean PTGI item scores ranged from 2.61 ($SD = 1.5$) for the Spiritual Change subscale to 3.60 ($SD = 1.0$) for the Relating to Others subscale, versus HD-gene tested participants who had item means that ranged from 1.94 ($SD = 1.8$) for the Spiritual Change subscale to 3.35 ($SD = 1.3$) on the Appreciation for Life subscale. Unrelated-donor BMT patients had similarly higher scores in all PTG domains except for New Possibilities when compared to the current sample. The current sample was consistently lower than other medical populations on Spiritual Change with total subscale mean of 3.87 ($SD = 3.6$), which reflected little to no reported growth in this domain. In contrast, men who had a prostatectomy reported less growth in all five PTG domains compared to the current sample. There was considerable variability among studies in the subdomains of PTG, with this study finding greater growth in participants' appreciation for life and less growth in spirituality/religiosity compared to other studies.

Comparison of Gene-expanded and Non-expanded

Participants on PTGI Total

A one-way ANCOVA comparing gene-expanded and non-expanded participants was conducted to answer the following question: Are there group differences in the experience of overall PTG between those who will inevitably develop HD and those who will not? The results of the ANCOVA with PTGI total score as the dependent variable and gene-status as the independent variable (i.e., non-expanded vs. gene-expanded) are

presented in Table A7. The only covariate included in the analysis was gender since neither age or education was related to PTGI total score in the preliminary analyses. The adjusted mean PTGI total score for the non-expanded group was 60.7 ($SE = 4.1$) and the adjusted mean for the gene-expanded group was 56.0 ($SE = 2.7$). These means were similar to the unadjusted means for each group, which were 60.5 ($SD = 25.0$) for the non-expanded group and 56.3 ($SD = 25.1$) for the gene-expanded participants, indicating that the change in the means was negligible. The interaction of the gender covariate with gene-status was not statistically significant, indicating that the assumption of homogeneity of regression slopes was met. The covariate of gender had a significant effect on PTGI total score; however, the F -ratio for the main effect of gene status did not reach significance. These analyses did not find a difference in PTGI total score for gene-expanded and non-expanded participants.

Comparison of Gene-expanded and Non-expanded

Participants on PTGI Subscales

A MANCOVA was conducted to address the question of whether gene-expanded participants differ from non-expanded individuals with regard to the 5 domains of PTG identified by Tedeschi and Calhoun (1996, 2004). MANCOVA was selected to reduce the family-wise error rate and because of the correlations among the PTGI subscales in this sample, which ranged from $r = .51$ to $.84$ (see Table A3). These correlations suggest that the relationships between the subscales should be accounted for in the analysis. Gender and age were entered as covariates in the analysis because of their relationship to the five PTGI subscales as identified in the preliminary analyses.

Results of the overall MANCOVA were non-significant. The homogeneity of variance assumption was satisfied. The multivariate test indicated that gene-expanded and non-expanded participants did not differ on the five PTGI subscales, $\Lambda = 0.96$, $F(5, 111) = 1.06$, *ns*, even after controlling for gender and age. Differences between the adjusted means and unadjusted means were again negligible. These findings again indicate that the actual results of the genetic testing did not prompt differences in PTG between gene-expanded and non-expanded individuals, even among the sub-domains of growth.

Primary Analysis: Aim #2

*Regression Analysis of Demographic and Time Variables
as Predictors of PTGI Scores*

The second aim of this study was to further explore the relationship between PTG and demographic variables, time since receiving a genetic test, and estimated proximity to diagnosis for gene-expanded individuals ($n = 82$) through regression analysis. To address this aim, three sets of six hierarchical regression analyses were conducted. The outcome variables within each set of hierarchical regressions were the five PTGI subscales and the PTGI total score. Predictor variables that were consistent in every set of regressions were age, gender, and time since receiving an HD-gene test. The predictor that changed for each set of regressions was the variable used to measure estimated proximity to HD diagnosis. The first set of regressions used YTD, the second set used Prob5yr, and the third set used the CAP to estimate time to diagnosis. Bivariate correlations among the variables for these regression analyses are presented in Table A8.

Regression coefficients for each set of regression analyses are presented in Tables A9, A10, and A11.

Because age and gender were related to the domains of posttraumatic growth in the published literature, and in the preliminary analysis of this study, they were entered into the first block of each regression. The number of years since receiving a genetic test was entered into the second block. The variable estimating time to diagnosis (i.e., YTD, Prob5yr, or CAP) was entered into the third block.

The step including demographic variables accounted for a significant amount of variance in scores for the PTGI total, the New Possibilities subscale, and the Personal Strength subscale in each of the three sets of regressions. Among the demographic variables, age was the only one that accounted for any variance in the outcome variables in all of the regressions. The first step of the regression for the Appreciation for Life subscale did not account for a significant amount of variance, but the β coefficient for age was significant. Spiritual change and Relating to Others were the only outcome variables that age was not related to in the regression analyses. For all other PTGI scores the β coefficients for age ranged from $-.25$ to $-.33$ (p 's $< .05$), which indicated that older individuals reported less general PTG, as well as less growth in the domains of Relating to Others, New Possibilities, Personal Strength, and Appreciation for life.

The number of years since receiving a genetic test, YTD, Prob5yr, and CAP was not related to any PTGI score. These findings indicate that time was not related to the amount of PTG experienced by gene-expanded individuals, and neither was approaching diagnosis.

Primary analyses: Aim #3

*Regression Analysis of Clinical Variables as Predictors
of PTGI Scores*

The third aim of the current study was to tentatively explore which clinical characteristics of HD (i.e., motor, cognitive, and psychiatric) were related to PTG for gene-expanded participants. A series of three separate hierarchical regressions were conducted, each with predictor variables of age, gender, time since testing, YTD, and a measure of one of the three clinical characteristics of prodromal HD. PTGI total score was the outcome variable for all three regressions. The UHDRS Motor Examination total score was the measure of motor functioning, SDMT total score was the measure of cognition, and SCL-90-R Depression score was the measure of psychiatric symptomatology. Age and gender were entered into the first block, time since testing into the second block, estimated years to diagnosis into the third block, and a single clinical variable of interest into the final block (i.e., UHDRS motor, SDMT, SCL-90-R Depression). Bivariate correlations between age, gender, time since testing, estimated years to diagnosis, and PTGI total are presented in Table A12. Results of the regression analysis with clinical variables as predictor variables for PTGI total score are presented in Table A13.

Demographic variables accounted for a statistically significant amount of variance in the PTGI total score in the first step of the regression analyses that included UHDRS Motor score and the SDMT. Gender was significantly related to PTGI total score in both analyses with β 's of -.24 and -.31 for the UHDRS Motor score and the SDMT, respectively. Age was only a significant related ($\beta = -.27$) in the regression that included the UHDRS Motor score as a variable. No other variables were related to PTGI total

score. Findings of the regression analyses indicate that time since HD-gene testing, YTD, UHDRS motor score, SDMT score, and SCL-90-R Depression score were not related to PTGI total score.

Descriptive data for the clinical variables are presented in Table A4 and revealed that participants' mean UHDRS Motor score was 8.7 ($SD = 9.7$) and 1.12 standard deviations higher than what was observed in non-expanded participants. The mean UHDRS Motor score was also 0.70 standard deviations higher than the mean UHDRS Motor score of 5.0 ($SD = 5.3$) reported by Biglan and colleagues (2009) in their sample of 733 gene-expanded individuals. Therefore, gene-expanded participants were not experiencing a high level of motor symptoms, but they were exhibiting more symptoms than what has been observed in non-expanded individuals and other gene-expanded participants in the literature. Participants' mean SDMT score of 47.3 ($SD = 12.4$) resulted in a z-score of -0.97 when compared to the mean score of 58.1 ($SD = 11.1$) for non-expanded participants in this study. Participants reported minimal depression symptoms on the SCL-90-R Depression scale with a mean score of 0.6 ($SD = 0.7$), which yielded a $z = 0.2$ when compared to non-expanded participants and a $z = -1.45$ when compared to psychiatric outpatients (Derogatis, 1994). In summary, the clinical measures used in this study found a higher level of motor symptoms and cognitive slowing in gene-expanded participants compared to non-expanded individuals, but the development of these symptoms was still not related to overall PTG.

CHAPTER V

DISCUSSION

This was the first study to quantitatively examine posttraumatic growth (PTG) as it relates to receiving a genetic test result for a fatal neurodegenerative disease. A cohort of gene-expanded and non-expanded individuals at-risk for Huntington disease (HD) were examined to address three research aims. The first aim was to identify and characterize PTG as a result of learning one's HD-gene status following predictive testing. This first aim considered how participants experienced PTG and whether gene-expanded and non-expanded individuals reported different levels of PTG as a result of being informed of their gene-status. The second aim was to determine the relationship between PTG and gender, age, time since receiving a genetic test, and estimated proximity to diagnosis. The third aim was to ascertain the relationship between the clinical symptoms of prodromal HD and PTG in gene-expanded participants. Because this study was exploratory in nature, no specific hypotheses were made regarding the study aims except that the clinical symptoms of prodromal HD would be positively related to PTG. The remainder of this chapter will summarize and explain the current findings with regard to the stated research aims. Implications for clinical practice, methodological limitations, and directions for future research will then be discussed.

Summary and Explanation of Findings

PTG Following Predictive Genetic Testing

The first aim of this study was to determine if any meaningful PTG occurred as a result of learning one's HD-gene status. Findings indicate that the majority of participants report growth as a result of their genetic test outcome. An examination of the number of

PTGI items endorsed at a clinically meaningful level (i.e., moderate degree of growth or more; Cordova et al., 2007; Widows et al., 2005) revealed that, on average, almost two-thirds of the items were endorsed as representing a considerable amount of PTG.

Reports of PTG in the present study are similar to what has been found in other health populations. Patients who received a diagnosis of HIV (Nightengale, Sher, & Hansen., 2010) or a variety of cancer diagnoses (Carboon et al., 2005; Cordova et al., 2007; Widows et al., 2005) also reported moderate to high levels of growth as a result of disease-related trauma. The reports of PTG in this sample, and their similarity with other health populations, indicates that PTG is a construct that warrants further attention from health professionals involved with genetic testing for HD. A paradigm shift is needed to move away from solely focusing on post-test distress to focusing a broader understanding of positive psychological change catalyzed by genetic testing.

Overall PTG in this sample was primarily driven by participants' new appreciation for life. Participants reprioritized what was important to them and developed a better understanding of the value of their own life. A substantial majority of participants also improved their ability to relate to people, with an increase in their compassion for others. People also experienced a greater sense of personal strength and realized that new opportunities were available to them. Interestingly, participants tended not to become more religious or spiritual. Reports of PTG in these domains are novel and expand the literature by considering more than just the practical benefits of testing, such as family and financial planning (e.g. Decruyenaere et al., 1995).

The present study converges with previous research by demonstrating that people experience a change in their appreciation of life after receiving a genetic test result.

Gene-expanded and non-expanded individuals in earlier qualitative studies have stated that genetic testing prompted them to be present-focused, take advantage of the time they had left, and reprioritize what was important in life (Bloch et al., 1992; Codori & Brandt, 1994). These themes from the qualitative research directly parallel what is demonstrated quantitatively in this study. The importance of a greater appreciation of life also coincides with Williams and colleagues (2010), who conducted the only study to explicitly examine benefit-finding following HD-gene testing. They demonstrated that gene-expanded and non-expanded people reported a greater sense of meaning and purpose in life, and that they were more certain about the direction their life was taking.

Changes in life priorities and values following testing do not appear to be limited to adults, either. Duncan and colleagues (2007) found that one of the most prominent benefits in people 15-25 years old was clarity about what matters in life and a desire to take advantage of every moment. Coupling Duncan and colleagues' work with the current study suggests that genetic testing for HD can catalyze a greater appreciation for life at any point in the life span. Although other studies have alluded to the notion that people grow in their appreciation for life, this is the first study to establish it as the primary area of psychological growth following a genetic test for HD.

The current study is also the first to demonstrate that PTG occurs in people's ability to relate to others following a genetic test result. The observed changes compliment what previous studies have found pertaining to post-test interpersonal relationships. With regard to romantic relationships, persons at-risk for HD have said that they developed better communication and empathy with their partners. One couple said the genetic test result led to "an increase of mutual understanding, support, and

acceptance in the relationship” (p. 28, Decruyenaere et al., 2004). Family relationships have also been shown improve as a result of genetic testing. Vamos, Hambridge, Edwards, and Conaghan (2007) studied the impact of HD on families and found that a third of their participants believed that being at-risk for HD brought their families closer together. Williams and colleagues (2010) found improved “connections” with family members, co-workers, and community members. The present study extends the literature by demonstrating that an intrapersonal change in a person’s ability to relate to others occurs in addition to stronger interpersonal relationships as a result of gene testing.

A lack of spiritual and religious PTG in this sample runs counter to the majority of the literature; although, previous studies on this topic are limited. Spiritual growth has been observed in the context of a variety of traumatic events, including AIDS diagnosis (Siegel & Schrimshaw, 2000), combat, and major disasters (Shaw et al., 2005). In one sample of patients 9 years post-bone marrow transplant, spiritual/religious growth was the second most endorsed domain of growth (Tallman, Shaw, Schultz, & Altmaier, 2010). Williams and colleagues (2010) found that at-risk individuals who benefited from gene testing in other domains also reported higher levels of religious and existential well-being compared to people who did not report benefits at all. There are two possible explanations for the differences between the current sample and the research on spirituality. First, differences in the assessment of spirituality may have contributed to the divergent findings. Much like other measures of benefit-finding, the PTGI only uses two items to assess spirituality/religiosity. A limited number of items prevent the scale from accurately capturing spiritual growth, which has resulted in some researchers calling for more sophisticated measures of PTG in this domain (Shaw et al., 2005; O’Rourke,

Tallman, & Altmaier, 2008). A second possible conclusion is that spiritual growth is not a common outcome following a genetic test, but only an important part of the process leading to PTG (Williams et al., 2010). Further research is necessary to determine which conclusion is more accurate.

Comparison of Gene-expanded and Non-expanded

Participants in PTG

A second major aim of this study was to determine if gene-expanded and non-expanded participants experienced differing levels of PTG as a result of their genetic test result. Ultimately, no difference in overall PTG was observed between gene-expanded and non-expanded individuals, even after controlling for demographic variables. Furthermore, people who learned they would develop HD did not experience any more or less PTG than non-expanded participants regarding their appreciation for life, pursuit of new possibilities, relating to others, spirituality/religiosity, or sense of personal strength. Gene-expanded participants learned that they would develop HD with 100% certainty, yet that knowledge did not yield growth beyond what was observed in people who did not face the threat of disease.

Despite the absence of other PTG studies in the predictive testing literature, the current results mirrored findings from other studies investigating general well-being and benefit-finding following genetic testing. For instance, a study utilizing the older genetic linkage analysis for the HD-gene found that those with a high-risk of developing HD (i.e., greater than a 75% chance of inheriting HD) had the same sense of well-being 12 months post-test as those who were low-risk (i.e., less than a 25% chance of inheriting HD; Wiggins et al., 1992). Moreover, both groups had an increased sense of well-being

compared to pre-test levels. A benefit-finding study aimed at assessing general benefit from HD-gene testing also found that both gene-expanded and non-expanded groups reported similar benefits (Williams et al., 2010). In an examination of post-test psychological outcomes for the genetic diseases of HD, familial adenomatous polyposis (FAP), and hereditary breast and ovarian cancer (HBOC), DudokdeWit, Tibben, Duivenvoorden, Niermeijer, & Passchier, (1998) found that test outcome did not contribute to post-test distress for the gene-carriers or non-carriers. This finding occurred despite the fact that FAP and HBOC have available treatments and incomplete penetrance across the lifetime, while HD is always fatal and has 100% penetrance across the lifetime. The findings from this study add to the preponderance of evidence rejecting the prima facie notion that genetic test results directly affect psychological outcomes.

Because there was no statistically significant difference in PTG between gene-expanded and non-expanded participants, this study's findings are consistent with theories that minimize the importance of an actual threat in the development of PTG. If gene-expanded participants had reported a larger degree of PTG than non-expanded participants, then the idea that PTG is mostly due to the presence of an *actual* threat would be supported; however, this was not the case. It may be counterintuitive to state that test outcome is not related to PTG or distress, but this suggestion is in harmony with Janoff-Bulman's (2006) conceptualization of traumatic experiences. She maintains that the actual threat of harm is not what causes a person's assumptive world to shatter, but the *meaning* of the trauma to the individual. If an event is perceived to be stressful enough, then people are forced to adjust their worldview and develop new beliefs about the world in order to accommodate the trauma. In the context of HD-gene testing,

Janoff-Bulman would suggest that non-expanded and gene-expanded persons experience similar levels of PTG because both groups perceive HD-gene testing to be equally stressful. Regardless of the test result, when people's assumptions about their gene-status are shattered by testing, then both gene-expanded and non-expanded people may be able to experience PTG as they rebuild their worldview (Calhoun & Tedeschi, 2006). In summary, the current study is consistent with Janoff-Bulman's theory of posttraumatic change, which suggests that the effect of the genetic test results on an individual's worldview is more salient to PTG than the test outcome itself.

Gender, Age, and PTG

Differences in PTG between men and women were examined to determine if gender was related to growth following predictive testing. Women in this study reported almost 20% more overall PTG than men, and they reported more growth in the personal strength and spiritual change domains as well. Even though there were differences in overall PTG, men and women experienced essentially the same amount of growth in the two domains that were most prevalent among gene-expanded and non-expanded individuals: a greater appreciation for life and improvement in relating to others.

Other studies have examined differences in PTG between men and women and have arrived at similar conclusions. Women have consistently exhibited more PTG than men, with varying magnitudes of difference between the two sexes (Milam, 2006; Park, Cohen, & Murch, 1996; Tedeschi & Calhoun, 1996; Zwahlen, Hagenbuch, Carley, Jenewein, & Buchi, 2010). Of the 74 people who benefited from predictive HD-gene testing in Williams and colleagues (2010) study 74% (n = 54) of them were women, which means that women were more inclined to report benefit than men after learning of

their HD status. Current results add further support to the body of literature that suggests women are more apt to experience overall PTG as a result of trauma.

In this study, age was related to most domains of PTG. When entered into a hierarchical regression model with gender, time since testing, and proximity to diagnosis, age had relationships with overall PTG and all the PTG sub-domains except for relating to others and spiritual growth. Age also predicted if participants experienced a desire to pursue new possibilities in a one-variable regression model; although, it only accounted for a small portion of the variance (4%). Negative correlations were observed in each instance, indicating that younger participants tended to report more growth than older participants.

The result that greater PTG occurs in young people contradicts Williams and colleagues (2010) study that found older participants reported more benefits as a result of their genetic test outcomes or HD family history. In contrast to Williams and colleagues, the current study supports the larger portion of the literature that indicates younger people tend to experience greater PTG (Bellizzi, 2004; Davis et al., 1998; Evers et al., 2001; Helgeson et al., 2006; Pietrzak, et al., 2010; Polatinsky & Esprey, 2000). Bellizzi (2004) studied PTG among middle aged cancer survivors with ages similar to the participants in the present study. He found that age and generativity were both strongly related to PTG, and that younger people were more likely to experience growth because they had not struggled with their own mortality to the degree that older participants had. Bellizzi's study implies that older participants in the present study may have already struggled with their own mortality and benefited from that struggle as much as possible, thus not gaining more PTG from the genetic test results. Another explanation for the relationship between

age and PTG could be that younger participants are less likely to have solidified their assumptions about the world, which results in greater malleability when traumatic events occur and allows for easier accommodation of trauma into their worldview (Tedeschi & Calhoun, 2004).

Time Since Testing and PTG

Another aim of this study was to examine the relationship between time since testing and PTG. Specifically, the goal was to answer the question: do people experience greater PTG as time passes following the receipt of their genetic test results? A hierarchical regression analysis demonstrated that there was no correlation between time and PTG in any domain of growth, even after controlling for covariates. These results indicate that time was not related to growth in either the positive or negative direction. The absence of a relationship between time and PTG in this study signifies that PTG can occur at any point post-test.

Findings from the broader literature examining the relationship between time and PTG have been mixed (Fromm et al., 1996; Helgeson et al., 2006; Milam et al., 2004; Widows et al., 2005). In one study, Nightengale and colleagues (2010) examined PTG following a diagnosis of HIV, which is similar to receiving a positive genetic test result for HD in that the symptoms of disease are likely to develop long after receiving the test results. The threat of harm is future-oriented in both diseases. Nightengale and colleagues found that participants in their study had been living with a diagnosis of HIV for an average of 11 years, but that time was not related to PTG or the perceived stressfulness of the diagnosis. These findings are consistent with what has been found in the rest of the HIV literature, in which time since diagnosis has yet to be correlated with

PTG (Milam, 2004; Milam, 2006; Siegel, Scrimshaw, & Pretter, 2005). Agreement among HIV studies and the present study signifies that time does not appear to be related to PTG in the prodromal phases of disease, which may be the case for all traumatic events with future-oriented threats.

The absence of a relationship between time and growth also suggests that theoretical models may need to be adjusted if they are to accurately describe the processes of PTG following genetic testing or the diagnosis of prodromal disease. Time is an essential component of Tedeschi and Calhoun's (1995, 2004) functional-descriptive model (FDM) because it is necessary for people to deliberately ruminate and reflect on the traumatic event (Figure B1). According to their model, if a person does not have time to ruminate, then the cognitive processes required for rebuilding schemas do not occur and PTG is inhibited (Stockton et al., 2011). In contrast to the FDM, the current study suggests that time is not required for people to ruminate and experience growth following predictive testing for HD, but this conclusion cannot be firmly stated. In this study, time may have been related to growth if PTG was assessed closer to genetic testing. The shortest amount of time that passed since testing for participants' was 1.10 years, with a mean time of 5.19 years. Previous studies of post-test affective symptoms have shown that people improve after approximately 1-2 years as they adapt to their gene status (Timman, Roos et al., 2004). Therefore, it may be that 1 year is plenty of time for rumination and for PTG to occur, which means that PTG may have fully developed in the current sample prior to their participation.. Indeed, studies that have examined PTG closer to traumatic events (i.e., within 1 year) have found that time is modestly and positively correlated with growth (Cordova et al., 2001a; Cordova et al., 2007); although,

the findings on this are mixed (e.g., Salsman, Segerstrom, Brechting, Carlson, & Andrykowski, 2009). Similarly, studies that have examined PTG long after health-related traumas have consistently found no relationship between time and PTG (Brunet et al., 2010; Tallman et al., 2010). There may be a dose-response relationship between time and PTG, where the effect of time is only noticeable soon after traumatic events.

Estimated Proximity to Diagnosis and PTG

Because many patients in the prodromal phase of HD are “waiting for the other shoe to drop” with the eventual diagnosis of the disease, another aim of this study was to ascertain whether or not estimated proximity to diagnosis was related to PTG in gene-expanded participants. Proximity to diagnosis was determined using objective data (i.e., age and CAG repeat length) rather than participants’ subjective assessment of when diagnosis might occur. Objective data was utilized because previous studies of psychological outcomes following genetic testing have used similar methodology (e.g., Codori et al., 1997).

In this sample, there was no relationship between proximity to diagnosis and overall PTG, even after using three different variables to measure to estimate time to diagnosis (i.e., YTD, Prob5yr, CAP). No other studies examine the relationship between benefit-finding and estimated proximity to diagnosis; however, the current study’s findings mirror the research on psychological distress following testing. For example, Codori and colleagues (1997) longitudinally examined the relationship of estimated years to diagnosis with hopelessness and depression after genetic testing, and they found that no relationship existed between proximity to diagnosis and psychological distress. The

present results ultimately suggest that overall PTG is not hindered or advanced by an approaching HD diagnosis.

Clinical Symptoms in Prodromal HD and PTG

The third and final aim of this study was to briefly explore the relationships between PTG and the triad of signs and symptoms that typically develop in prodromal HD: cognitive decline, psychiatric changes, and motor dysfunction (Paulsen, 1999). Like estimated proximity to diagnosis, prodromal HD signs and symptoms signal an approaching HD diagnosis, only they do so more concretely since they are directly related to striatal degeneration in HD (Aylward et al., 2004; Paulsen et al., 2001) and they are readily observable to gene-expanded individuals. It was hypothesized that the manifestation of prodromal HD symptoms would be related to greater PTG. Prodromal manifestations of HD were expected to rekindle the trauma of genetic testing and also introduce the new trauma of HD itself. In the end, the study hypothesis was not supported because none of the clinical measures were related to overall PTG. Despite being some of the earliest prodromal HD symptoms identified in the literature, slowed cognitive processing speed (Paulsen et al., 2001; Verney et al., 2007; Stout et al., 2010), depressive symptoms (Duff et al., 2007), and increased motor dysfunction (Biglan et al., 2009) were not related to PTG.

The absence of a relationship between PTG and prodromal HD signs and symptoms may indicate that the prodrome of HD does not progress to the degree necessary for changes in PTG to occur. The most prominent manifestations of prodromal HD (e.g., cognitive slowing, mild motor symptoms) were not related to PTG in this sample despite the fact that gene-expanded participants had symptoms that were

significantly worse than non-expanded participants, statistically speaking. Nonetheless, no firm conclusions about the relationship between clinical symptoms and PTG can be reached because there was a lack of marked pathology in this sample. Motor symptoms in the current sample were higher than non-expanded participants' scores but the level of symptoms was still relatively low. Gene-expanded participants had a mean motor score of 9 on a scale that has a maximum total score of 124, which means that motor symptoms were present but minimal. The SCL-90-R Depression scores were also low for both non-expanded and gene-expanded participants and indicated that neither group was exhibiting depressive symptoms. It is likely that the prodromal symptoms of HD do not reach a level of severity that prompts PTG.

Clinical Implications

Much of the work done by psychotherapists and genetic counselors with individuals at-risk for HD understandably focuses on helping clients prepare for and cope with the negative aspects of the genetic testing process. With a propensity for at-risk individuals to develop depression (Codori et al., 2004), subclinical affective distress (Hayden & Bombard, 2005; Timman et al., 2004), social isolation, grief, (Bloch et al., 1992), intrusive memories, and avoidance (Codori & Brandt, 1994; Hayden & Bombard, 2005; Timman et al., 2004), good reasons exist for the therapeutic process to concentrate on treating the emotional turmoil that may result from testing. However, professionals who focus on the detrimental aspects of testing neglect the beneficial half of the genetic testing experience.

A steadily growing body of research has started to explore the benefits of PTG for mental and physical health outcomes. For instance, Helgeson and colleagues (2006)

found that PTG was related to more positive affect and less depression. Sawyer and colleagues (2010) also found in their large meta-analysis of cancer and HIV/AIDS patients that greater PTG had a positive relationship with healthy psychological adjustment, subjective physical health, and a negative relationship with poor psychological adjustment and psychiatric dysfunction. Milam (2006) found that HIV/AIDS patients with PTG were less depressed and used illicit drugs less frequently regardless of their stage of disease. PTG has also led to better physical functioning (Danoff-Burg & Revenson, 2005), positive health behaviors (Milam et al., 2004; Siegel & Schrimshaw, 2000), increased optimism and positive affect (Hart et al., 2008), and a higher quality of life (Stanton et al., 2006).

Two important conclusions for counseling gene-expanded and non-expanded individuals can be drawn from the present study. The first conclusion is that predictive genetic testing provides a unique opportunity for mental health providers to foster PTG, which can subsequently lead to favorable physical and mental health outcomes. Second, both gene-expanded and non-expanded individuals can benefit equally from therapy aimed at facilitating PTG. Intuitively, therapists may feel inclined to focus most of their efforts on those who receive a positive genetic test result because of the certainty of HD for that group. However, the outcome of genetic testing does not appear to strongly impact the development of PTG, so mental health providers would do well to direct their efforts towards gene-expanded and non-expanded individuals equally. The question now becomes: how is PTG facilitated during the predictive genetic testing process?

Before discussing practical recommendations for treating gene-expanded and non-expanded patients, there are unique advantages and caveats related to the HD genetic

testing process that need to be considered. One advantage of the genetic testing process is that it allows people to proactively address their reactions to the trauma (i.e. genetic testing) before the event occurs. The majority of traumatic experiences—such as assault, diagnosis of terminal disease, and car accidents—only allow for the facilitation of PTG post-trauma. Any therapy aimed at facilitating growth for survivors of these traumas are necessarily reactive because of the trauma's sudden and unexpected onset. Since individuals can choose when they undergo genetic testing, and because the genetic test for HD is so accurate, patients and therapists have the unique opportunity to actively defend against the pitfalls of genetic testing while also setting the foundation for psychological change.

Another advantage that mental health professionals have in genetic testing is that patients have frequent contact with genetic counselors and psychologists throughout the process. Unlike patients facing other conditions, such as cancer or cardiovascular disease, at-risk individuals are practically mandated to receive mental health treatment. The Huntington Disease Society of America's (HDSA; United States Huntington's Disease Genetic Testing Group, 2003) predictive genetic testing guidelines state that at-risk individuals must meet with a genetic counselor to review the risks and benefits of the test and discuss the applicant's perceptions of HD. Additionally, applicants must have a formal psychological assessment completed to assess their emotional state and provide recommendations on their susceptibility to adverse psychological outcomes after learning their gene-status. Moreover, the guidelines emphasize that the primary aim of mental health providers is to discuss the unpredictable dangers of testing to self-esteem, psychological health, relationships with family and friends, employability, and social

standing. Interestingly, each of these areas of discussion directly parallel the types of PTG that the present study identified in gene-expanded and non-expanded individuals. When the risks of testing are discussed with patients, it is just as incumbent on psychologists and genetic counselors to foster growth as it is to prepare patients for negative psychological outcomes. As a matter of speculation, fostering growth may actually have a greater protective effect against the negative consequences of genetic testing than simply preparing people for the worst.

In addition to the advantages of the genetic testing for the development of PTG, a few caveats also bear mentioning. Cordova (2008) offers a number of cautions to therapists who wish to facilitate PTG, and many of his warnings are relevant to the context of genetic testing. The first caveat is that not all genetic testing applicants will need psychotherapeutic intervention to foster PTG. As evidenced by the literature, most people spontaneously experience growth since nearly all studies measure PTG as it naturally occurs without any therapeutic intervention. In fact, some researchers have suggested that PTG not only occurs spontaneously, but also unintentionally (Zoellner & Maercker, 2006a). At best, overly enthusiastic providers who intervene unnecessarily may actually undermine the natural development of PTG. At worst, patients may infer that they are deficient if they do not experience PTG as suggested by their therapist (Calhoun & Tedeschi, 2008). A second caveat is that explicitly discussing PTG in therapy may be perceived as patronizing and invalidating. Like many people facing serious illnesses, patients are likely to be encouraged to “keep their head up” and “stay positive” by other well-meaning people. As a result, blatant attempts to promote PTG may be taken as a minimization of their suffering. Lastly, although theories of PTG

abound, and research supporting those theories is growing exponentially, our understanding of PTG is still nascent. The processes and variables that mediate the development of PTG are not fully understood, so any attempt to facilitate growth may falter due to a lack of understanding. With those caveats aside, what follows are some suggestions for fostering PTG in gene-expanded and non-expanded individuals based on the present study and findings in the extant literature.

Facilitating PTG is a delicate endeavor because of the sensitive nature of genetic testing. Providers run the risk of being misperceived as celebrating the genetic testing experience because of the psychological growth it can bring about. Certainly no traumatic experience should be celebrated, especially not genetic testing for HD. To avoid appearing Pollyannaish or insensitive, Calhoun and Tedeschi (1999) suggest that therapists take the stance of an *expert companion*. This therapeutic stance acknowledges that therapists are experts in the treatment of trauma while also recognizing that gene-expanded and non-expanded patients are the experts in the emotional experience of what it is like to face the threat of HD. As an expert companion, therapists should not attempt to directly induce PTG in patients (Calhoun & Tedeschi, 2008). Instead, they should listen for themes of PTG in what people say and then simply highlight them through active listening. For instance, if a person says, "I find that I have a better understanding of what my father with HD went through," the therapist simply needs to observe, "You seem more compassionate towards your family members than you used to be." Such a statement would subtly highlight themes of growth and prompt patients to engage in patterns of thinking that lead to PTG (i.e., deliberative rumination and reflection; Stockton et al., 2011).

Based on the recommendations of Tedeschi and McNally (2011), once counselors establish themselves as an expert companion they should focus on reducing the distress associated with genetic testing, encouraging constructive self-disclosure, and building a narrative of the testing experience that includes the five domains of PTG. Managing the stress, anxiety, and intrusive nature of genetic testing is a necessary first step because it blunts the negative effects of brooding while also setting the stage for deliberative rumination. With the foundation for PTG laid, at-risk individuals should be encouraged to disclose how the testing process has impacted their perceptions of themselves, others, and the world. Through self-disclosure patients will reveal how threatening they perceive testing to be, as well as the degree to which their previous assumptions about the world have been shattered (Janoff-Bulman, 2006). Once the impact of the trauma has been assessed, therapists can help patients reconfigure their understanding of the genetic testing experience to include PTG. Tedeschi and McNally suggest that this “reconfiguration” should begin with organizing the genetic testing process into a coherent story that identifies the genetic test result as the fulcrum of the narrative. Then, reflective listening can be employed to encourage patients to engage in paradoxical thinking that allows them to see that loss and gain are not diametrically opposed to each other. Once patients have started to engage in all of these processes, their attention can be drawn to the five domains of PTG. As the current study suggests, therapists should be especially careful to listen for growth that occurs in gene-expanded and non-expanded individuals’ appreciation for life and relationships with others.

Teaching Implications

Educating mental health professionals about PTG following predictive genetic testing is necessary at the national and local levels to modify and improve healthcare for people facing HD, or other fatal genetic diseases. At the national level, changes need to be made to how professionals are guided during the genetic testing process. The Huntington Disease Society of America's (United States Huntington's Disease Genetic Testing Group, 2003) predictive genetic testing guidelines are the primary reference for genetic counselors, but they do not mention the possibility of psychological growth. The guidelines often highlight the frequency of "adverse emotional responses" and the need to identify those who require "greater emotional support." No guidelines are offered for how to maximize growth following the test results, but only to minimize negative psychological reactions. Findings from the current study suggest that the predictive testing process outlined by HDSA guidelines should include a statement educating professionals about the possibility of growth. Making mental health professionals aware of the potential for PTG would be a tremendous catalyst since one of the reasons providers do not actively foster PTG is a lack of awareness. PTG is not neglected in the genetic testing process because providers are callous or incompetent; it is because they are simply unaware of the possibility for growth.

Local action can also be taken by professors of health psychology at the graduate level. Student psychologists and genetic counselors can be taught how to foster PTG through didactics and clinical supervision. Effective didactic training would incorporate sessions about PTG into classes on psychopathology and counseling methods. Classroom discussions on the five domains of growth, their correlates, and their integration into

various theoretical orientations would help students begin to critically think about how to view patients holistically. Such discussions are particularly well suited for counseling psychologists with their emphasis on strengths, positive psychology, and psychological health. Didactics can then be followed up with clinical supervision. As students develop their skills in the “common factors” of psychotherapy, listening for themes of PTG can be one of the active listening skills developed alongside empathy, reflective statements, and others. Students could then be taught to reflect PTG themes as an *expert companion* and subsequently foster growth.

Limitations

As with any investigation, the findings of this study should be considered in light of certain limitations. The first limitation of this study is that participants were asked to rate PTG retrospectively and judge the level of personal growth they experienced as the result of an event that happen long ago—8 years ago in some cases. Frazier and colleagues (2009) have correctly pointed out that retrospectively assessing PTG appears simple at first, but it is actually a complex task that requires participants to:

(a) evaluate their current standing on a dimension (e.g., closeness to other people), (b) recall their previous standing on the same dimension, (c) compare their current and previous standings, (d) assess the degree of change, and (e) determine how much of that change can be attributed to the traumatic event. (p. 913)

Because of the complexity involved with retrospectively assessing PTG, many participants may have misperceived the amount of growth they actually experienced. Others may have misattributed PTG to their genetic test results when other struggles since that time were responsible for the personal change they experienced.

Another limitation is that the results of the current study may not be fully generalizable to other genetic disorders or other people at-risk for HD. Generalizing to other disorders may be difficult because no other fatal condition has a genetic test that is as accurate as the test for the HD-gene expansion. Furthermore, most other genetic disorders do not have the same heritability as HD (50/50), and those that do are not fully penetrant across the lifespan (DudokdeWit et al., 1998).

Applying the present study to minority populations or non-western cultures will also be difficult because the sample is well-educated, 99% Caucasian, and 100% from westernized countries. The homogeneity of the study sample complicates the generalizability of PTG findings because African-Americans and Hispanics have consistently demonstrated higher levels of growth than Caucasians in the literature (Bower et al., 2005; Helgeson et al., 2006; Stanton et al., 2006).

Further limiting generalizability is the overall well-being of the current sample. Participants who undergo genetic testing tend to be psychologically healthier than people who avoid testing (Decruyenaere et al., 1995). Therefore, the reports of PTG in this study can only be directly applied to the minority of people who are at-risk for HD and complete genetic testing. Those who are less willing to complete testing may report different levels of PTG than what was observed in this study because they tend to be less resilient and experience greater distress than test completers (Codori et al., 1994). In fact, some authors might suggest that people who resist testing may actually experience more PTG from their experience because of their lack of coping skills (e.g. Tedeschi & McNally, 2011).

Implications for Future Research

This study has expanded the literature because it is the first quantitative investigation to demonstrate that PTG occurs as a result of predictive genetic testing. Furthermore, this is the first study to examine PTG in a neurodegenerative condition (although other studies have examined the related concept of benefit-finding in HD; Williams et al., 2010). In the present study, similarities between gene-expanded and non-expanded individuals were observed across every type of PTG. Age and gender related to PTG in varying degrees, which contributes to the debate about the relationship between demographic factors and growth. Neither time since testing nor estimated proximity to diagnosis were related to PTG in this sample. Lastly, exploration of the relationships between PTG and cognitive, psychiatric, and motor signs and symptoms indicated that the prodromal manifestation of HD may not relate to the growth experienced by gene-expanded participants. Each of these findings has numerous implications for future research. What follows is a discussion about the most salient recommendations that can be offered in order to build on the current study and expand the broader PTG literature.

First and foremost, the reported PTG in this sample suggests that an expanded study of PTG following HD-gene testing should be conducted. A cross-sectional design was chosen for the current study because it was best suited for the exploratory nature of the research questions, and because between-group differences (e.g., gene-expanded vs. non-expanded) were the primary focus of the study. Ideally, a follow-up study would be longitudinal and have a larger sample size. A longitudinal study would allow the trajectories of PTG in gene-expanded and non-expanded participants to be compared.

Similarities or differences observed in the pattern of growth between the two groups could have important implications for the clinical and theoretical literature.

A larger sample size would be helpful for powering analyses aimed at exploring how additional variables unique to prodromal HD might predict, mediate, or moderate the course of PTG following genetic testing. Such variables might include: indicators of prodromal functional decline, perceptions of HD in parents, experience of genetic discrimination, and others. Furthermore, a larger sample size would allow for a broader assessment of the relationship between prodromal clinical symptoms and PTG. Due to the exploratory nature of this study, only a few clinical measures (i.e., SDMT, SCL-90-R Depression Scale) were examined because of their sensitivity to prodromal changes. These measures do not encompass all of the various cognitive and psychiatric domains that are affected prior to diagnosis. A variety of psychiatric changes have been found in prodromal HD (Beglinger et al., 2008; Duff et al., 2007) and they may have differing relationships to PTG than what was observed with depression in this study. Different cognitive domains, such as time perception, psychomotor performance, emotion recognition, and working memory, have all have also been observed to decline early in the HD prodrome (Stout et al., 2010). Finding a relationship between PTG and these early cognitive symptoms would benefit the literature by providing ecological validity for neuropsychological measures and also by clarifying the relationship between symptom onset and PTG.

Qualitative studies investigating the underlying processes of PTG following a genetic test are recommended because they can elucidate differences in how non-expanded and gene-expanded participants arrive at similar levels of PTG. The vast

majority of participants indicated that learning of their HD gene-status gave them a greater appreciation for life; however, growth in this domain may have developed along different lines of reasoning depending on one's gene-status. Gene-expanded individuals may have developed an appreciation for life because they knew their time was limited and they needed to take advantage of it (Codori et al., 1994). In contrast, non-expanded participants may have felt that they received a "new lease on life" and wanted to capitalize on their new hope (Huggins et al., 1992). Although the 'appreciation for life' domain illustrates the point, differences in the process leading up to PTG in other domains may have occurred and qualitative research methods (e.g., CQR; Hill, Thompson, & Williams, 1997) are ideally suited for uncovering these processes.

Prospective assessment of PTG related to predictive genetic testing is also needed to clarify the true impact of genetic test results on PTG. This study chose to focus on the disclosure of the test result as the most traumatic part of genetic testing; however, some pre-test PTG could have potentially occurred from two other stressors surrounding the genetic testing process. First, PTG may occur when an individual learns that they have a family history of HD. Williams and colleagues (2010) demonstrated this possibility when people at-risk for HD derived benefits from the knowledge that their parents or grandparents had the disease. Second, struggling with the initial decision to complete testing may also lead to PTG. Undergoing testing forces people to acknowledge that they have a 50/50 chance of developing HD and some people jump to the conclusion that they have the disease (Duncan et al., 2007). Acknowledging the risk of HD may be traumatic in its own right. Pre-/post-test assessments of PTG would be an excellent first step towards dismantling how different aspects of predictive testing may elicit PTG.

Future research may also want to modify how PTG is assessed. Indeed, the lack of spiritual growth in the current sample indicates that a change in assessment methods is warranted. Items on the PTGI are all worded positively, which does not allow participants the opportunity to report posttraumatic declines. In this sample, the limited endorsement of spiritual growth may actually reflect a decrease in spirituality for some individuals. Cole, Hopkins, Steel, Tisak, and Carr (2008) suggest that bi-directional measures be developed to assess spiritual change so that both growth and decline are measured post-trauma. Future studies of PTG following HD-gene testing would do well to extend Cole and colleagues suggestions to the measurement of all PTG by developing bi-directional scales for each domain of PTG.

Lastly, the findings in this study have implications for the broader predictive testing literature. HD is a unique genetic condition because it is autosomal dominant, fully penetrant across the lifetime, incurable, insidious, detrimental to multiple systems, and fatal. Nonetheless, portions of this study can be replicated in a number of other genetically-linked disorders, such as hereditary breast and ovarian cancer, familial adenomatous polyposis, and spinocerebellar ataxia (Broadstock et al., 2000), to assess for PTG in those conditions as well. Findings from the current study also have implications for patients with a diagnosis of amnesic mild cognitive impairment (aMCI). People who receive a diagnosis of aMCI progress into dementia at ten times the rate of healthy individuals (Petersen et al., 1999). Although the certainty of disease following aMCI is equivocal compared to HD, people who are diagnosed with MCI may experience PTG if they perceive the diagnosis and its implications to be traumatic.

APPENDIX A

Tables

Table A1. Demographics for gene-expanded and non-expanded participants

Characteristics	Gene-expanded ^a	Non-expanded ^b	Total ^c
Gender (<i>n</i> , %)			
Female	58 (70.7)	25 (67.6)	83 (69.7)
Male	24 (29.3)	12 (32.4)	36 (30.3)
Age (<i>M</i> , <i>SD</i>)	43.1 (12.4)	46.1 (14.4)	44.0 (13.1)
Ethnicity (<i>n</i> , %)			
Caucasian	81 (98.8)	37 (100)	118 (99.2)
More than one race	1 (1.2)	0 (0)	1 (0.8)
Education (<i>M</i> , <i>SD</i>)	14.1 (2.4)	14.6 (2.2)	14.3 (2.3)
Country (<i>n</i> , %)			
United States	53 (64.6)	31 (83.8)	84 (70.6)
Australia	19 (23.2)	4 (10.8)	23 (19.3)
Canada	10 (12.2)	2 (5.4)	12 (10.1)
Time since receiving a genetic test (<i>n</i> , %)			
< 5 years	35 (42.7)	19 (51.3)	54 (45.4)
≥ 5 years	47 (57.3)	18 (48.7)	65 (54.6)
YTD ^d	13.3 (7.5)	NA	NA
Prob5yr ^d	0.2 (0.2)	NA	NA
CAP ^e	328.2 (83.8)	NA	NA

Note. CAP = CAG/Age Product; HD=Huntington disease; Prob5yr = probability of receiving a diagnosis of Huntington disease within 5 years; YTD = expected years to receiving a diagnosis of Huntington disease

^a *n* = 82

^b *n* = 37

^c *N* = 119

^d Estimates were calculated using the Langbehn et al.(2004) formula based on CAG repeat and age.

^e Estimates were calculated using the Zhang et al. (2011) formula for CAG/Age Product.

Table A2. Number of study participants from each PREDICT-HD research site

<u>Research Site</u>	<u><i>n</i></u>	<u>% of sample</u>
University of Rochester Medical Center Rochester, New York, USA	5	4.2
Columbia University New York, New York, USA	3	2.5
Baylor University Waco, Texas, USA	3	2.5
University of Iowa Iowa City, Iowa, USA	32	26.9
Washington University St. Louis, Missouri, USA	22	18.5
University of British Columbia Vancouver, British Columbia, Canada	12	10.1
Colorado Neurological Institute Englewood, Colorado USA	1	.8
Westmead Hospital Sydney, New South Wales, Australia	4	3.4
University of California San Francisco San Francisco, California, USA	6	5.0
Hereditary Neurological Disease Centre Wichita, Kansas, USA	10	8.4
Cleveland Clinic Cleveland, Ohio, USA	2	1.7
St. Vincent's Aged Psychiatric Service Kew, Victoria, Australia	15	12.6
Graylands Selby-Lemnos & Special Care Services Mt. Claremont, Western Australia, Australia	4	3.4
<u>Total</u>	<u>119</u>	<u>100.0</u>

Table A3. Zero-order correlations among the PTGI subscales and total score

PTGI scales	1	2	3	4	5	6	Items	Range
1. Relating to Others	--						7	0-35
2. New Possibilities	.80*	--					5	0-25
3. Personal Strength	.81*	.80*	--				4	0-20
4. Spiritual Change	.55*	.58*	.58*	--			2	0-10
5. Appreciation for Life	.73*	.71*	.84*	.51*	--		3	0-15
6. PTGI total score	.93*	.91*	.92*	.69*	.86*	--	21	0-105

Note. PTGI=Posttraumatic Growth Inventory

* $p < .01$

Table A4. Descriptive statistics for study measures based on HD-gene status

Measures	Range	Gene-expanded ^a		Non-expanded ^b		Total sample ^c		α
		<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
PTGI scale scores								
Relating to Others	0-35	19.5	8.4	19.7	9.2	19.5	8.6	0.90
New Possibilities	0-25	12.4	7.0	13.5	6.6	12.7	6.9	0.88
Personal Strength	0-20	11.1	5.4	12.2	5.3	11.4	5.3	0.87
Spiritual Change	0-10	3.7	3.7	4.3	3.5	3.9	3.6	0.93
Appreciation for Life	0-15	9.7	4.0	10.7	3.5	10.1	3.9	0.88
PTGI total score	0-105	56.3	25.1	60.5	25.0	57.6	25.0	0.96
PTGI item scores								
Relating to Others	0-5	2.79	1.19	2.81	1.32	2.79	1.23	--
New Possibilities	0-5	2.47	1.40	2.71	1.32	2.54	1.37	--
Personal Strength	0-5	2.77	1.34	3.05	1.33	2.86	1.34	--
Spiritual Change	0-5	1.84	1.84	2.16	1.74	1.94	1.81	--
Appreciation for Life	0-5	3.24	1.34	3.58	1.18	3.35	1.30	--
PTGI total score	0-5	2.68	1.19	1.17	1.19	2.74	1.19	--
HD clinical variables								
UHDRS motor	0-47	8.7	9.7	3.9	4.3			0.92
SDMT	17-74	47.3	12.4	58.1	11.1			NA
SCL-90-R Dep	0.0-3.2	0.6	0.7	0.5	0.5			0.95

Note. α = Cronbach's alpha; HD = Huntington disease; NA = Not applicable; PTGI = Posttraumatic Growth Inventory; SCL-90-R Dep = Symptom Checklist 90-Revised depression subscale; SDMT = Symbol Digit Modalities Test; UHDRS = Unified Huntington's Disease Rating Scale

^a $n = 82$

^b $n = 37$

^c $N = 119$

Table A5. Means and standard deviations of PTGI items for gene-expanded and non-expanded participants^a

PTGI items	Gene-expanded ^b		Non-expanded ^c		Total sample ^d	
	<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>
My priorities about what is important in life...	3.37	1.35	3.59	1.14	3.44	1.29
An appreciation for the value of my own life...	3.30	1.55	3.73	1.42	3.44	1.52
I developed new interests...	2.34	1.71	2.43	1.63	2.37	1.68
A feeling of self-reliance...	2.43	1.72	2.92	1.71	2.58	1.73
I have a better understanding of spiritual matters...	2.09	1.93	2.30	1.82	2.15	1.89
Knowing that I can count on people in times of trouble...	3.09	1.46	2.73	1.61	2.97	1.51
I established a new path for my life...	2.27	1.75	2.43	1.88	2.32	1.78
A sense of closeness with others...	2.62	1.57	2.73	1.69	2.66	1.60
A willingness to express my emotions...	2.28	1.57	2.27	1.39	2.28	1.51
Knowing I can handle difficulties...	2.79	1.59	3.27	1.50	2.94	1.57
I am able to do better things with my life...	2.55	1.60	2.89	1.41	2.66	1.55
Being able to accept the way things work out...	2.98	1.49	3.14	1.27	3.03	1.42
Appreciating each day...	3.07	1.56	3.41	1.48	3.18	1.54
New opportunities are available which wouldn't have been otherwise.	2.33	1.74	2.68	1.62	2.44	1.70

Note. PTGI = Posttraumatic Growth Inventory

^a Item scale range = 0-5: 0 = did not experience change, 1 = very small degree of change, 2 = small degree of change, 3 = moderate degree of change, 4 = great degree of change, 5 = very great degree of change

^b $n = 82$

^c $n = 37$

^d $N = 119$

Table A5. Continued

PTGI items	<u>Gene-</u> <u>expanded</u> ^b		<u>Non-</u> <u>expanded</u> ^c		<u>Total</u> <u>sample</u> ^d	
	<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>	<i>M</i>	<i>(SD)</i>
Having compassion for others...	3.16	1.52	3.54	1.43	3.28	1.50
Putting effort into my relationships...	2.88	1.60	3.32	1.42	3.02	1.55
I am more likely to try to change things which need changing...	2.87	1.67	3.11	1.47	2.94	1.61
I have a stronger religious faith...	1.59	1.88	2.03	1.77	1.72	1.85
I discovered I am stronger than I thought I was...	2.90	1.65	2.89	1.60	2.90	1.63
I learned a great deal about how wonderful people are...	2.72	1.58	2.70	1.54	2.71	1.56
I accept needing others...	2.71	1.65	2.38	1.62	2.61	1.64

Note. PTGI = Posttraumatic Growth Inventory

^a Item scale range = 0-5: 0 = did not experience change, 1 = very small degree of change, 2 = small degree of change, 3 = moderate degree of change, 4 = great degree of change, 5 = very great degree of change

^b $n = 82$

^c $n = 37$

^d $N = 119$

Table A6. Comparisons of PTGI total scale ($M = 57.6$, $SD = 25.0$) or item mean ($M = 2.74$, $SD = 1.19$) to published summary statistics for various health conditions

Study	Event	N	Age	Gender	Time since Event	PTGI
Powell, Ekin-Wood, & Collin (2007)	TBI	23	41.1 (13.8)	M = 19; F = 4	1-3 years	36.5 (18.7)
Powell, Ekin-Wood, & Collin (2007)	TBI	25	43.6 (13.5)	M = 20; F = 5	9-12 years	68.1 (16.6)
Milam (2006) ^a	HIV-positive	412	39.0 (7.9)	M = 36; F = 49	6.4 (4.2) years from diagnosis	4.1 (0.7)
Nightengale, Sher, & Hansen (2010)	HIV-positive	112	44.9 (8.9)	M = 82; F = 30	10.9 (5.7) years since diagnosis	61.1 (28.5)
Cordova, Cunningham, Carlson, & Andrykowski (2001)	Breast cancer	70	54.7 (12.1)	F = 70	23.6 (16.2) months post treatment; ≤ 5 years post- diagnosis	64.1 (24.8)
Sears, Stanton, & Danoff-Burg (2003)	Early-stage breast cancer	58	51.6 (10.3)	F = 58	28.5 (13.4) weeks from diagnosis	58.4 (25.8)
Widows, Jacobsen, Booth-Jones, & Fields (2005)	BMT	72	47.6 (10.0)	M = 19; F = 53	24.1 (10.0) months since post-BMT	64.7 (21.3)

Note. BMT = bone marrow transplant; HIV = Human immunodeficiency virus; PTGI = Posttraumatic Growth Inventory; TBI = traumatic brain injury

^a Item mean is presented, not scale means

Table A6. Continued

Study	Event	N	Age	Gender	Time	PTGI
Carboon, Anderson, Pollard, Szer, & Seymour (2005)	Various cancer diagnoses	62	43.4 (14.3)	M =36; F = 26	184 days post-diagnosis	55.1 (24.7)
Thornton & Perez (2006)	Prostate cancer	82	61.3 (7.19)	M=82	1 year post prostatectomy	46.6 (25.6)
Cordova, Giese-Davis, Golant, Kronenwetter, Chang, & Spiegel (2007)	Breast cancer	65	52.3 (9.3)	F=65	9.4 (6.4) months post-diagnosis	57.8 (25.4)
Brunet, McDonough, Hadd, Crocker, & Sabiston (2010) ^a	Breast cancer survivors	47 0	57.3 (7.8)	F=470	7.46 (5.34) years post diagnosis; 5.91 (4.97) years post treatment	4.51 (0.92)
Tallman, Shaw, Schultz, & Altmaier (2010)	Unrelated donor BMT	25	37.2 (10.3)	M=12; F=13	8.68(1.78) years post treatment	74.2 (18.1)

Note. BMT = bone marrow transplant; HIV = Human immunodeficiency virus; PTGI = Posttraumatic Growth Inventory; TBI = traumatic brain injury

^a Item means are presented, not scale means

Table A7. Analysis of covariance of PTGI total score based on gene-status^a

Source of variation	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>
Covariate				
Gender	2872.94	1	2872.94	4.72*
Gene-status	517.61	1	517.61	.851
Error	70546.06	116	608.16	
Total	468860.00	119		

Note. PTGI = Posttraumatic Growth Inventory

^a non-expanded $n = 37$; gene-expanded $n = 82$

* $p < .05$

Table A8. Bivariate correlations among age, gender, time variables, and PTGI scales for gene-expanded participants (n = 82)

Variables	1	2	3	4	5	6	7	8	9	10	11
1. Gender	--										
2. Age	.11	--									
3. Time Since Testing	.08	.18	--								
4. YTD	-.24 ⁺	-.43*	-.22 ⁺	--							
5. Prob5yr	.27 ⁺	.48*	.10	-.82*	--						
6. CAP	.27 ⁺	.46*	-.02 ⁺	-.89*	.94*	--					
7. Relating to Others	-.19	-.19	-.00	.01	-.04	-0.08	--				
8. New Possibilities	-.18	-.26*	-.04	.03	-.09	-0.10	0.84*	--			
9. Personal Strength	-.15	-.24*	-.06	.00	-.06	-0.07	0.80*	0.79*	--		
10. Spiritual Change	-.20	-.03	-.05	.05	-.06	-0.04	0.51*	0.57*	0.56*	--	
11. Appreciation for Life	-.10	-.23*	-.00	-.01	-.07	-0.08	0.74*	0.70*	0.85*	0.46*	--
12. PTGI Total	-.19	-.23*	-.03	.02	-.07	-0.09	0.93*	0.92*	0.92*	0.67*	0.85*

Note.; CAP = CAG/Age Product; Prob5yr = probability of receiving a diagnosis of Huntington disease within 5 years; PTGI = Posttraumatic Growth Inventory; YTD = expected years to receiving a diagnosis of Huntington disease.

⁺ $p < .05$, * $p < .001$

Table A9. Regression coefficients for demographic variables, time since testing, and estimated years to diagnosis predicting PTGI total and subscale scores for gene-expanded participants ($n = 82$)

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>PTGI Total Score</u>							
Step 1: Demographics				.28	.08	.08	3.45 (2,79)*
Gender	-10.78	6.12	-.20				
Age	-0.55	0.24	-.27*				
Step 2: Time testing	-0.01	1.61	-.00	.28	.08	.00	2.28 (3,78)
Step 3: YTD	-0.50	0.41	-.15	.31	.10	.02	2.08 (4,77)
<u>Relating to Others</u>							
Step 1: Demographics				.26	.07	.07	2.80 (2,79)
Gender	-3.66	2.06	-.20				
Age	-0.16	0.08	-.24				
Step 2: Time testing	0.12	0.54	.03	.26	.07	.00	1.89 (3,78)
Step 3: YTD	-0.15	0.14	-.14	.29	.08	.01	1.73 (4,77)
<u>New Possibilities</u>							
Step 1: Demographics				.30	.09	.09	3.84 (2,79)*
Gender	-2.71	1.70	-.18				
Age	-0.17	0.07	-.30*				
Step 2: Time testing	-0.01	0.45	-.00	.30	.09	.00	2.54 (3,78)
Step 3: YTD	-0.13	0.12	-.14	.32	.10	.02	2.24 (4,77)

Note. PTGI = Posttraumatic Growth Inventory; YTD = expected years to receiving a diagnosis of Huntington disease

* $p < .05$

Table A9. Continued

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>Personal Strength</u>							
Step 1: Demographics				.27	.08	.08	3.19 (2,79)*
Gender	-1.87	1.31	-.16				
Age	-0.13	0.05	-.29*				
Step 2: Time testing	-0.11	0.35	-.04	.27	.08	.00	2.10 (3,78)
Step 3: YTD	-0.12	0.09	-.17	.31	.10	.02	2.06 (4,77)
<u>Spiritual Change</u>							
Step 1: Demographics				.20	.04	.04	1.63 (2,79)
Gender	-1.59	0.92	-0.20				
Age	-0.00	0.04	-0.01				
Step 2: Time testing	-0.08	0.24	-0.04	.20	.04	.00	1.11 (3,78)
Step 3: YTD	-0.01	0.06	-0.01	.20	.04	.00	0.82 (4,77)
<u>Appreciation for Life</u>							
Step 1: Demographics				.24	.06	.60	2.46 (2,79)
Gender	-0.95	0.99	-.11				
Age	-0.09	0.04	-.29*				
Step 2: Time testing	0.06	0.26	.03	.25	.06	.00	1.68 (3,78)
Step 3: YTD	-0.08	0.07	-.16	.28	.08	.02	1.65 (4,77)

Note. PTGI = Posttraumatic Growth Inventory; YTD = expected years to receiving a diagnosis of Huntington disease

* $p < .05$

Table A10. Regression coefficients for demographic variables, time since testing, and probability of diagnosis in 5 years predicting PTGI total and subscale scores for gene-expanded participants ($n = 82$)

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>PTGI Total Score</u>							
Step 1: Demographics				.28	.08	.08	3.45 (2,79)*
Gender	-10.45	6.21	-.19				
Age	-0.53	0.25	-.26*				
Step 2: Time testing	0.28	1.60	.02	.28	.08	.00	2.28 (3,78)
Step 3: Prob5yr	12.85	16.29	.10	.30	.09	.01	1.86 (4,77)
<u>Relating to Others</u>							
Step 1: Demographics				.26	.07	.07	2.80 (2,79)
Gender	-3.67	2.08	-.20				
Age	-0.16	0.09	-.24				
Step 2: Time testing	0.21	0.54	.04	.26	.07	.00	1.89 (3,78)
Step 3: Prob5yr	5.17	5.45	.12	.28	.08	.01	1.65 (4,77)
<u>New Possibilities</u>							
Step 1: Demographics				.30	.09	.09	3.84 (2,79)*
Gender	-2.59	1.72	-.17				
Age	-0.16	0.07	-.28*				
Step 2: Time testing	0.07	0.45	.02	.30	.09	.00	2.54 (3,78)
Step 3: Prob5yr	3.08	4.52	.09	.31	.09	.01	2.01 (4,77)

Note. Prob5yr = probability of receiving a diagnosis of Huntington disease within 5 years; PTGI = Posttraumatic Growth Inventory

* $p < .05$

Table A10. Continued

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>Personal Strength</u>							
Step 1: Demographics				.27	.08	.08	3.19 (2,79)*
Gender	-1.78	1.33	-.15				
Age	-0.11	0.05	-.28*				
Step 2: Time testing	-0.04	0.34	-.01	.27	.08	.00	2.10 (3,78)
Step 3: Prob5yr	3.04	3.49	.11	.29	.08	.01	1.76 (4,77)
<u>Spiritual Change</u>							
Step 1: Demographics				.20	.04	.04	1.63 (2,79)
Gender	-1.57	0.93	-.20				
Age	-0.00	0.04	-.01				
Step 2: Time testing	-0.07	0.24	-.03	.20	.04	.00	1.11 (3,78)
Step 3: Prob5yr	0.01	2.45	.00	.20	.04	.00	0.82 (4,77)
<u>Appreciation for Life</u>							
Step 1: Demographics				.24	.60	.60	2.46 (2,79)
Gender	-0.84	1.01	-.10				
Age	-0.09	0.04	-.26				
Step 2: Time testing	0.11	0.26	.05	.25	.06	.00	1.68 (3,78)
Step 3: Prob5yr	1.56	2.65	.08	.26	.07	.00	1.34 (4,77)

Note. Prob5yr = probability of receiving a diagnosis of Huntington disease within 5 years; PTGI = Posttraumatic Growth Inventory

* $p < .05$

Table A11. Regression coefficients for demographic variables, time since testing, and CAP predicting PTGI total and subscale scores for gene-expanded participants ($n = 82$)

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>PTGI Total Score</u>							
Step 1: Demographics				.28	.08	.08	3.45 (2,79)*
Gender	-10.22	6.23	-.19				
Age	-0.51	0.25	-.25*				
Step 2: Time testing	0.41	1.62	.03	.28	.08	.00	2.28 (3,78)
Step 3: CAP	0.02	0.04	.08	.29	.09	.01	1.79 (4,77)
<u>Relating to Others</u>							
Step 1: Demographics				.26	.07	.07	2.80 (2,79)
Gender	-3.49	2.09	-.19				
Age	-0.15	0.09	-.22				
Step 2: Time testing	0.26	0.54	.05	.26	.07	.00	1.89 (3,78)
Step 3: CAP	0.01	0.01	.07	.27	.07	.00	1.49 (4,77)
<u>New Possibilities</u>							
Step 1: Demographics				.30	.09	.09	3.84 (2,79)*
Gender	-2.55	1.73	-.17				
Age	-0.16	0.07	-.28*				
Step 2: Time testing	0.10	0.45	.03	.30	.09	.00	2.54 (3,78)
Step 3: CAP	0.01	0.01	.07	.30	.09	.00	1.97 (4,77)

Note. CAP = CAG age product; PTGI = Posttraumatic Growth Inventory

* $p < .05$

Table A11. Continued

Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
<u>Personal Strength</u>							
Step 1: Demographics				.27	.08	.08	3.19 (2,79)*
Gender	-1.75	1.33	-.15				
Age	-0.12	0.05	-.27*				
Step 2: Time testing	0.00	0.35	.00	.27	.08	.00	2.10 (3,78)
Step 3: CAP	0.01	0.01	.10	.29	.08	.01	1.72 (4,77)
<u>Spiritual Change</u>							
Step 1: Demographics				.20	.04	.04	1.63 (2,79)
Gender	-1.60	0.93	-.20				
Age	0.00	0.04	-.01				
Step 2: Time testing	-0.07	0.24	-.03	.20	.04	.00	1.11 (3,78)
Step 3: CAP	0.00	0.01	.02	.20	.04	.00	0.82 (4,77)
<u>Appreciation for Life</u>							
Step 1: Demographics				.24	.60	.60	2.46 (2,79)
Gender	-0.83	1.01	-.10				
Age	-0.09	0.04	-.26*				
Step 2: Time testing	0.13	0.26	.05	.25	.06	.00	1.68 (3,78)
Step 3: CAP	0.00	0.01	.07	.26	.06	.00	1.32 (4,77)

Note. CAP = CAG age product; PTGI = Posttraumatic Growth Inventory

* $p < .05$

Table A12. Bivariate correlations among age, gender, time variables, clinical measures, and PTGI scales for gene-expanded participants

Variables	1	2	3	4	5	6	7
1. Gender	--						
2. Age	.11	--					
3. Time Since Testing	.09	.18	--				
4. YTD	-.24 ⁺	-.43**	-.23 ⁺	--			
5. UHDRS Motor Exam ^a	-.00	.32*	-.07	-.36*	--		
6. SDMT ^b	-.15	-.45**	-.06	.54**	-.57**	--	
7. SCL-90-R Depression ^c	-.18	-.04	-.18	.02	.29*	.00	--
8. PTGI Total ^d	-.19	-.23 ⁺	-.03	.02	.07	-.04	-.10

Note. PTGI = Posttraumatic Growth Inventory; SCL-90-R Depression = Symptom Checklist 90- Revised Depression Scale; SDMT = Symbol Digit Modalities Test; YTD = expected years to receiving a diagnosis of Huntington disease; UHDRS = Unified Huntington's Disease Rating Scale

^a $n = 76$

^b $n = 67$

^c $n = 81$

^d $n = 82$

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

Table A13. Regression coefficients for demographic variables, time since testing, estimated years to diagnosis, and clinical variables predicting PTGI total score in gene-expanded participants.

Predictor Variables	<i>B</i>	<i>SE B</i>	β	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i> (<i>df</i>)
Step 1: Demographics				.29	.08	.08	3.22 (2,73)*
Gender	-13.31	6.43	-.24*				
Age	-0.55	0.26	-.27*				
Step 2: Time testing	0.15	1.66	.01	.29	.08	.00	2.13 (3,72)
Step 3: Time diagnosis	-0.54	0.44	-.16	.33	.11	.03	2.20 (4,71)
Step 4: UHDRS Motor ^a	0.26	0.32	.10	.34	.12	.01	1.88 (5,70)
Step 1: Demographics				.30	.09	.09	3.25 (2,64)*
Gender	-16.53	6.68	-.31*				
Age	-0.41	0.27	-.21				
Step 2: Time testing	0.51	1.68	.04	.31	.10	.00	2.20 (3,63)
Step 3: Time diagnosis	-0.35	0.47	-.11	.34	.12	.02	2.03 (4,62)
Step 4: SDMT ^b	-0.24	0.29	-.12	.35	.13	.01	1.75 (5,61)
Step 1: Demographics				.27	.07	.07	3.00 (2,78)
Gender	-13.65	6.06	-.26				
Age	-0.45	0.24	-.23				
Step 2: Time testing	-0.39	1.59	-.03	.27	.07	.00	1.99 (3,77)
Step 3: Time diagnosis	-0.57	0.40	-.18	.30	.09	.02	1.94 (4,76)
Step 4: SCL-90-R Dep ^c	-5.26	3.68	-.16	.34	.12	.02	1.98 (5,75)

Note. PTGI = Posttraumatic Growth Inventory; SCL-90-R Dep = Symptom Checklist 90-Revised Depression Subscale; SDMT = Symbol Digit Modalities Test; UHDRS Motor = Unified Huntington's Disease Rating Scale Motor Exam

^a*n* = 76

^b*n* = 67

^c*n* = 81

* *p* < .05

APPENDIX B

Figure

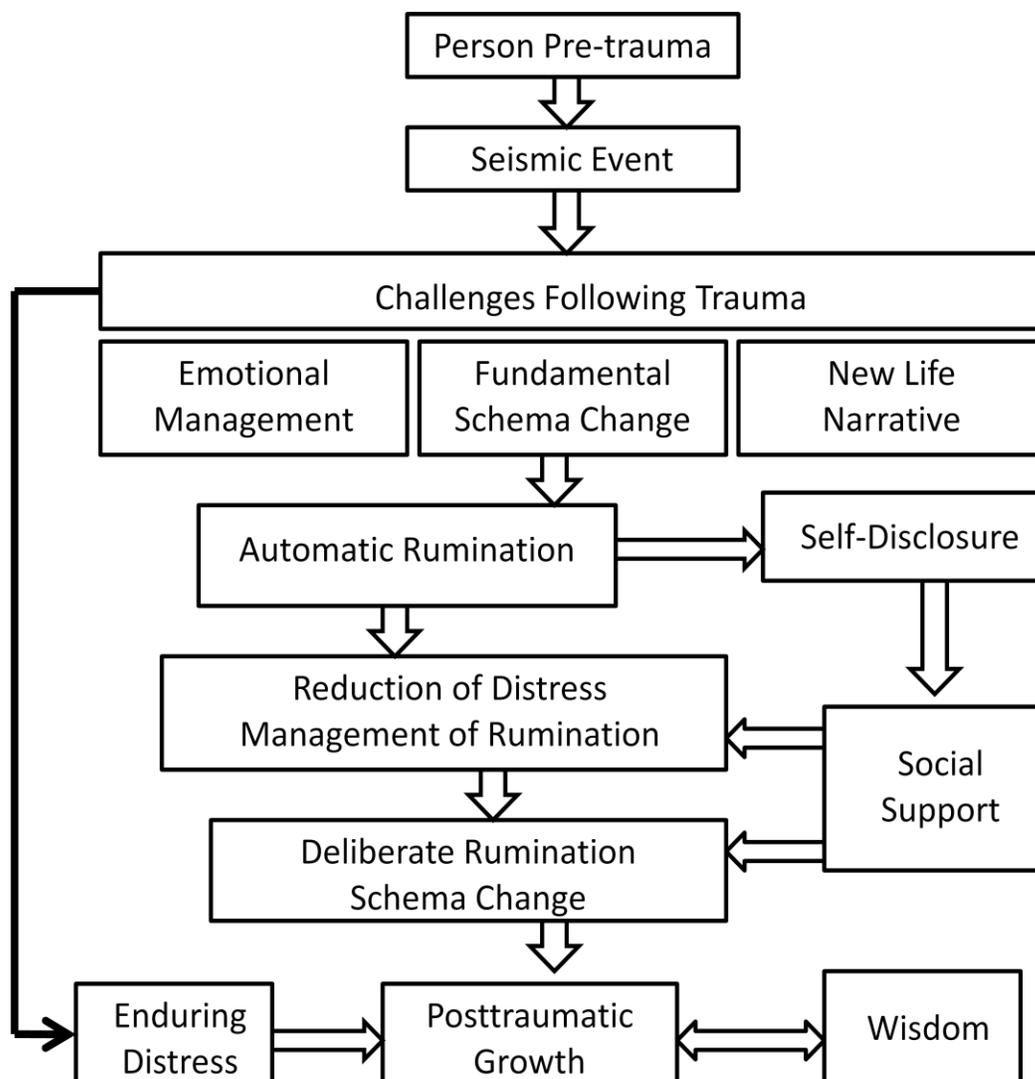


Figure B1. Functional-descriptive model of posttraumatic growth

Adapted from: Tedeschi, R. G., & Calhoun, L. G. (2004). Posttraumatic growth: Conceptual foundations and empirical evidence. *Psychological Inquiry*, 15, 1-18.

APPENDIX C

*Patient Consent Form***INFORMED CONSENT DOCUMENT**

Project Title: **Neurobiological Predictors of Huntington's Disease Version 2.0**

Investigators: This research study is conducted by a group of scientists called the Huntington Study Group (HSG), which seeks to develop new treatments for Huntington's disease (HD).

Study Chair: Dr. Jane S. Paulsen
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Other Personnel: Jane Paulsen, PhD; Leigh Beglinger, PhD; Kevin Duff, PhD; Ergun Uc, MD; Stacie Vik, BA; Nicholas Doucette, BA; Teri Thomsen, MD; Christine Anderson, BA; Anne Leserman, MSW, LISW; William Adams, BA; Jessica Schumacher, BA; Andrew Juhl, BS; Kelsey Vitense, BA; Stephen Cross, BA; Nancy Hale, BA, RN; Robert Rodnitzky, MD; Justin O'Rourke, MA; Elijah Waterman, BA; Mycah Kimble, BA, Pat Ryan, BS, MA, MSW

This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.

- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have been tested for the expanded HD gene and are not showing signs of HD.

The purpose of this research study is to characterize the earliest changes in HD so that experimental drug therapies to slow or alleviate early HD symptoms can be studied and tested. Before we can begin studies of experimental drugs in persons who do not have symptoms, however, we must answer some critical questions:

1. What are the earliest changes in blood, urine, thinking skills, motor signs, behavior or brain structure that take place as a person starts to transition from health to HD?
2. What are the typical rates of change for these measures, against which we can measure whether a new treatment is beneficial or harmful?

To answer these questions, the Huntington Study Group (HSG) is conducting the PREDICT-HD Version 2.0 study. PREDICT-HD 2.0 is a unified research effort by approximately 30 HSG centers around the world to study persons at-risk for HD who are aware of their gene status. We completed the initial goals of our study of over 1000 persons with predictive gene testing in 2008. The National Institutes of Health has decided to continue the research for at least 5 more years. The ultimate goal of the PREDICT-HD 2.0 study is to define the earliest biological and clinical features of HD before at-risk individuals have diagnosable symptoms of the disease. Completion of this research will make it possible to test possible treatments to delay or prevent the onset of HD. We will be including people who have tested gene positive and gene negative. It is an observational study. This means that as a research participant in the study, you will be examined periodically, but you will receive no experimental drugs or treatments. It is a study that is expected to give us essential information to help design future studies of experimental drugs aimed at slowing or postponing the onset of HD in healthy persons at-risk for developing HD. As possible drugs are developed, you will be invited to participate with separate consents and protocols.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 300 people will take part in this study conducted by investigators at the University of Iowa. PREDICT-HD 2.0 will involve more than 1000 at-risk individuals from locations around the world.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for a minimum of 5 yearly visits. This study is ongoing and has been renewed several times by the government and other funding agencies, so we may ask you if you would like to continue

past this minimum estimate in the future. Visits will occur approximately every 12 months. Visits will last from 3 to 6 hours.

WHAT WILL HAPPEN DURING THIS STUDY?

Study Entry: The first study visit (Visit 1) will determine whether you meet the necessary criteria for participation in the study. If you are at-risk for HD, 18 years of age and older, have completed predictive testing (and have tested either positive or negative), have never been diagnosed with definite HD, and meet all the necessary criteria, you may enter PREDICT-HD 2.0. If you were previously in the initial phase of PREDICT-HD (1.0), we would appreciate your continued participation in advancing knowledge of early HD. Continued participation in the study would be helpful in designing the best study for preventive clinical trials. Your site investigator, Dr. Kevin Duff, will perform an evaluation at each visit and will manage all of the activities of PREDICT-HD 2.0. He can address any concerns you might have about the study.

Study Overview: As a research participant in PREDICT-HD 2.0, you will be examined every 12 months and receive phone calls that will occur between visits at 6 month intervals for a minimum of 5 years. Phone call length will vary, but you should expect this to take no more than 10 minutes. Visits will last 3-6 hours. During each visit a blood draw, an update of medications you are taking and an examination of motor (movement), intellectual (thinking), and behavioral features of the disease will be conducted. You will also be asked to complete questionnaires that assess your opinions and feelings. During each phone call, your next scheduled visit will be confirmed along with an update of contact information (change of address and phone number). We ask that you provide us with a means of contacting you between visits, (e.g. to confirm appointments). We will not identify ourselves as having any connection with a medical facility if we contact you, to preserve privacy. Participation in the PREDICT-HD 2.0 study will not prevent you from seeking care from other healthcare providers, though we may ask you to tell the site investigator if you are prescribed medications. While you are a research participant in PREDICT-HD 2.0, we ask that you inform the site investigator immediately if you are admitted to the hospital. **MRI imaging (a scan of your brain done without the use of radiation or x-rays) will occur at odd year visits (first visit and then every other yearly visit). The MRI will last no longer than one hour and only one scan will be needed at each odd-year visit.**

As part of the research study, you will be asked to identify a companion who will give firsthand knowledge of you by answering some questions (surveys). The companion will be given these questions on a yearly basis, during annual visits or, when travel hardships pose a significant problem for the companion, these questions (surveys) may be completed outside the visit and returned via mail. The companion may also be contacted by the site for updated contact information (change of address or phone number) if other means have failed.

First Visit- Study Identifier: The first visit will consist of some evaluations which will only occur once in the study, but may be updated at each visit. First a random number

will be assigned to you as your study identification. This unique code will identify you and all coded clinical information will be kept separate from your name. In addition, you will be given an HSG unique identification number that will connect your research information obtained in PREDICT-HD 2.0 to the other HSG studies in which you may participate. To receive this number, you and the site coordinator will go to a secure internet website on a computer at the research clinic and enter pieces of information about you (last name at birth, sex at birth, day, month and year of birth, city and country of birth, and mother's maiden name). You will receive the Unique ID number as soon as you are finished entering the information and can print your ID number so that you and your site will have a copy. Once you receive the unique ID, you will be able to get it again at a later date by going to the website and entering the same pieces of information. If you have participated in a previous HSG study and already have an existing Unique ID number, you can use this number for the study. Participation in PREDICT-HD 2.0 will allow the HSG to link your data in this research project with other research projects in which you volunteered.

First Visit- History and Physical: Your first study visit will include a medical history and a physical examination. If you are already enrolled in the initial phase of PREDICT (1.0), these exams will not be repeated. However, your medical information will be updated at each visit. Please keep in mind that these general health and vitals questions are for research purposes and are not being used to evaluate your health or identify medical issues. These values will not be reviewed by a physician.

First Visit- Genetic Data: We will collect a blood sample (about 4 teaspoons or 20 ml) from a vein in your arm. The research lab of Dr. Marcy MacDonald at Harvard Medical School and the Broad Institute in Boston will receive your sample. Your blood cells will be used to create a copy of the DNA in your cells that will be available for researchers in the future to study the CAG repeat length in the HD genotype. We will create a cell line from your DNA for genetic research (such as looking for other modifiers of HD onset). Under no circumstances will the individual results of the DNA cell line ever be disclosed to anyone by name. This includes the researchers involved in PREDICT-HD 2.0, your family and even you. The coded samples will be kept in a confidential biobank and the purpose of keeping genetic materials is for future medical research.

First Visit- Brain Donation: All participants will be invited to donate their brain to research should an untimely death occur. The New York Brain Bank at Columbia University will receive all donations and the brain bank will analyze and store the samples. Researchers who have had their research reviewed by an Institutional Review Board (IRB) can request samples from Dr. Jean Paul Vonsattel with the approval of the PREDICT-HD 2.0 PI and Steering Committee. All clinical data, blood, and genetic data can be combined and made available to the researchers using the appropriate data banks.

All visits- biobank: We will collect blood samples (about 4-5 teaspoons or 27 ml) from a vein in your arm and a urine sample (approximately ¼ cup or 50 ml) at each visit. All samples will only be labeled with your PREDICT-HD 2.0 ID code. Your blood and urine samples will never be labeled with your name and will be kept separately from files

linked to your name. Your blood and urine will be frozen and stored at the Coriell Institute for medical research indefinitely and samples will only be released under the review of the PREDICT-HD 2.0 PI and Executive Committee. Storage in the biobank allows future researchers to acquire samples and clinical data from PREDICT-HD 2.0 to further study the disease markers or mechanisms of HD as new technology becomes available. Under no circumstances will the individual results of the samples ever be disclosed to anyone by name. This includes the researchers involved in PREDICT, your family and even you. All coded samples will be kept confidential in the biobank and the only purpose to store them is for future medical research.

All Visits- Thinking, Feeling, Behavior and Movement Assessments: At each annual visit, you will undergo evaluation of your thinking, feelings, behaviors and movement abilities. The length of the thinking examination will be less than 2 hours, the length of the feeling and behavior interviews will be less than 2 hours, and the movement (motor) exam will take about 15 minutes. You will be asked to be audio and video taped for some portions of the study to ensure consistency among raters. These tapes will be used for educational purposes by HD researchers and your name will not be disclosed to anyone. At each visit, we will inquire about your general health and update our records on any prescribed medications and over-the-counter supplements you are taking. In addition, we will ask your opinion about life decisions, research volunteering and treatment options.

Every Other Visit- Brain Scan: An MRI picture of brain tissue, which is taken without any radiation (x-ray) exposure and without any contrasting agent. During an MRI, you lie on your back on a table positioned inside a tube. You will be asked to lie very still when the MRI imaging is being performed. The MRI procedure will take 1 hour each time. An MRI will happen at odd-year visits starting with your first yearly visit (so a scan will happen at every other research visit, not at each yearly visit).

Tissue/Blood/Data Storage for Future Use

As part of this study, we are obtaining blood, urine and other data samples from you. We would like to study your blood, urine and data in the future, after this study is over.

Blood cells removed from the blood samples will be used to make a cell line and DNA. Cell lines are produced by growing blood cells in a laboratory and allow us to have a source of the DNA without having to redraw your blood. These blood cells can be stored for decades or more. The cell lines and DNA and data will be made available to researchers trying to learn more about the cause of diseases.

The tests we might want to use to study your blood, urine and data may not even exist at this time. Therefore, we are asking for your permission to store your blood, urine and data so that we can study them in the future. These future studies may provide additional information that will be helpful in understanding Huntington's Disease, but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your blood, urine or data might be used to develop products or tests that could be

patented and licensed. There are no plans to provide financial compensation to you should this occur.

If you agree now to future use of your blood, urine and data but decide in the future that you would like to have it removed from future research, you should contact Dr. Kevin Duff at (319) 353-6640. However, if some research with your blood, urine or data has already been completed, the information from that research may still be used.

By initialing or marking below, I understand that my blood, urine and other data may be stored/shared for future research.

_____ **Yes**, I give my permission for my blood, urine and data to be stored/shared for future research.

_____ **No**, I do not give my permission for my blood, urine and data to be stored/shared for future research.

Genetic Research

One purpose of this study is to look at genes (DNA) and how they affect health and disease. Genes are the instruction manual for the body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment.

You are being asked to give a blood sample for genetic research. What we learn about you from this sample will not be put in your health record. Your test results will not be shared with you or your doctor. No one else (like a relative, boss, or insurance company) will be given your test results, including the study PI and research team.

A single blood sample of about 4 teaspoons (or 20 ml) will be drawn from a vein in your arm using a needle. This will take about 5-10 minutes of your time.

Audio Recording/Video Recording

One aspect of this study involves making audio and video recordings of you. These recordings will be used to help us correctly evaluate your movements and speech, as well as to help keep our research team correctly trained as they give you the tests described above. **Recordings will only be accessible to the PREDICT research team and those at the data center responsible for reviewing and housing them. Recordings will be stored/shared for future research depending on what you choose above. Destruction of recordings will take place after the study has closed and all data are analyzed if you choose not to give your permission for future storage/sharing.**

Yes **No** I give you permission to make audio recordings of my testing during this study.

Yes **No** I give you permission to make video recordings of my motor (movement) examination during this study.

Yes **No** I give you permission to make a video recording of all my testing during this study visit.

Contact For Future PREDICT-Related and HD Research

In addition to the primary PREDICT-HD 2.0 project, we are conducting several additional studies to advance future preventive clinical trials. We and our partners in the HSG are currently conducting other HD-related research and plan to conduct more in the future. Some of the additional studies we are planning include a) developing new or better measures of HD; b) gathering survey data about ethical, legal and social considerations of being genetically at-risk for disease; c) trying new imaging techniques for better measures of the brain; and d) testing new drugs to understand possible side effects or benefits in pre-HD. We are always in need of PREDICT volunteers to participate in these smaller studies. By checking “yes” below, we will be able to contact you about additional research pertaining to PREDICT-HD, or additional HSG studies on HD. Any time you are contacted for additional research you are free to consider your time commitments and the proposed study before agreeing to participate. Choosing to participate or not to participate will not affect your ability to continue in the main PREDICT-HD 2.0 study. Participation in this study does not obligate you to participate in any future study. A separate Consent Document would be signed to participate in any future study. Thank you for your consideration.

_____ **Yes**, I give my permission for the PREDICT-HD 2.0 coordinating site at the University of Iowa (Jane Paulsen, PI) to contact me in the future for additional HD-related research purposes.

_____ **No**, I do not give my permission for the PREDICT-HD 2.0 coordinating site at the University of Iowa (Jane Paulsen, PI) to contact me in the future for additional HD-related research purposes.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Confidentiality is a concern in PREDICT-HD 2.0. Every possible effort will be made to keep research information in the strictest confidence, but we cannot absolutely guarantee that accidental disclosure will not happen. We remind you that the responsibility for confidentiality rests with everyone involved: you should think carefully before mentioning your role in PREDICT to anyone, since the effects of disclosure on insurance,

employment, relationships, etc. cannot be predicted for any individual. You may skip any question you prefer not to answer.

The chance of developing HD will not be changed by participating in this study, nor will the progression of the disease. The uncertainties of not knowing when HD will start may cause distress. Some of the surveys you will complete ask you about your outlook of the future and your mood. We will talk with you and the participant at each visit, and if you feel at any time you could benefit from an expert opinion, treatment or additional support, you can be referred to a specialist. There is some evidence in the literature that persons at genetic risk for disease may have higher than usual suicidal tendencies. If the PREDICT staff are concerned about your mental health or level of distress we will recommend you see a professional to address the concerns.

Some people experience nervousness, fatigue, or boredom during the testing and surveys. Frequent rest breaks are provided and staff are trained to offer assurance and to discontinue testing if necessary.

During the collection of blood samples, you may feel pain at the site on the arm where the blood is taken, and bruising may occur. Infections or fainting can also happen, but they are rare. If you experience fainting, you should lie down immediately to avoid possible injuries and notify our study staff. All collection of blood is done by trained staff who are educated to prevent infections or other pain as much as possible.

The MRI images for this study are not being used to evaluate your health. The images obtained for the study are for specific research purposes and are not being used to find medical abnormalities. These images will not be reviewed by a radiology physician to diagnose existing abnormalities. Persons with any concerns about findings from the study examinations or MRI scan will receive assistance in arranging for an evaluation outside of the study if they wish. This would occur at their own cost. Even though the MRI is well lit, open at both ends, ventilated, and has an intercom, some people undergoing brain scans feel anxious about being in the MRI scanner. You may request a mild sedative ahead of time if you expect to be uncomfortable.

The general physical and medical information, yearly vitals collection and updates to your medical information are not being used to evaluate your health. These pieces of information are obtained for the study for specific research purposes and a physician will not be reviewing them to diagnose existing abnormalities or to refer you for medical care. Persons with concerns about any of these pieces of information will be assisted in arranging for an evaluation outside of the study if they wish. This would occur at their own cost.

Genetic Research

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. To prevent this, these samples will be given a code. Only the study staff will know the code.

The name that belongs to the code will be kept in a locked file or in a computer with a password. Only Dr. Kevin Duff and the PREDICT research team will have access to your name.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study. However, we hope that in the future other people might benefit from this study because your participation may provide information that is useful to our understanding of HD onset in persons at-risk for the illness.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study. There will be no charges for scheduled visits or laboratory tests that are part of this study. You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

Participants will be reimbursed at \$150 for visits involving assessments only and \$200 for visits involving a brain scan. Travel and lodging costs incurred by your participation will be reimbursed. You will not share in any profits from the development of any commercial properties resulting from the research, if any.

WHO IS FUNDING THIS STUDY?

The National Institute of Neurological Disease and Stroke (NINDS) and Cure Huntington's Disease Initiative (CHDI), Inc. are funding this research study. This means that the University of Iowa is receiving payments from NINDS and CHDI to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from NINDS or CHDI for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.

- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

It is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)
- the sponsors, **NINDS and CHDI, Inc.**

To help protect your confidentiality, we will limit access to your personal information to Dr. Kevin Duff and the PREDICT research team. All data, including identifying information, will be kept in locked cabinets within locked offices, or on password protected computer files only accessible to the PREDICT research team. All data with identifying information will be kept separate from research data only labeled with ID codes. No names or other identifiable information will be attached to the data. The samples you give will be given a randomly assigned code number. An anonymous coded blood sample will be submitted to the Coriell Cell Repositories, a research resource supported by the National Institutes of Health/The National Institute for Neurological Disease and Stroke. The blood will be used for the preparation of a cell line from the DNA will be prepared. The cell line and DNA and accompanying data including genotyping data will be distributed to scientists including those in research, teaching, and industry. The sample will be kept indefinitely. The sample and accompanying information, including clinical and genetic information, will be used for the study of many disorders, not just the one that you may have. The clinical data and genetic data will be housed anonymously in a public database at the National Institutes of Health.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate means that the researchers cannot be forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the researcher from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you or your legally authorized representative request in writing that information about you or your participation in the research be released to an insurance company, the researcher may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own

privacy. Finally, the researcher is not prevented from taking steps, including reporting to appropriate authorities, to prevent serious harm to yourself or others. You may receive a copy of the Certificate of Confidentiality upon request.

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires your health care provider to obtain your permission for the research team to access or create “protected health information” about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study. Once your health care provider has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under “Confidentiality.”

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff, and the data coordination center. The sponsors, NINDS or CHDI, Inc. may also inspect parts of your medical record for the purposes of auditing the conduct of this study.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes your healthcare provider to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to Dr. Kevin Duff **at**:

Dr. Kevin Duff
The University of Iowa
Department of Psychiatry

1-308 MEB
Iowa City, IA 52242

However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I Decide to Drop Out of the Study?

Leaving the study early will not cause you any harms or discomforts, and you will still have access to all of the medical care and healthcare to which you are entitled. If you choose to end participation early, we may contact you to determine if additional final assessments can be completed.

Will I Receive New Information About the Study while Participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can Someone Else End my Participation in this Study?

Under certain circumstances, the researchers, NINDS or CHDI might decide to end your participation in this research study earlier than planned. This might happen because:

- You have done or experienced something listed in the "exclusion criteria" of this study
- Dr. Kevin Duff or other staff believe you are a threat to yourself or others
- You have become permanently institutionalized
- All reasonable attempts to contact you for a study visit or follow-up have failed
- You have been diagnosed with HD by our study staff
- Funding for the research study has ended
- The sponsors have decided to stop the research
- You are clearly unable to continue study procedures due to an increase in HD symptoms or other medical or psychiatric illness/difficulty.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself or if you have a research-related injury, please contact either Dr. Jane Paulsen at

(319) 353-4551 or Dr. Kevin Duff at (319) 353-6640. Their e-mail and fax contacts are also listed on the front of this document, and you will receive a copy to take home and keep for your records.

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 340 College of Medicine Administration Building, The University of Iowa, Iowa City, Iowa, 52242, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, <http://research.uiowa.edu/hso>. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Participant's Name (printed):

Do not sign this form if today's date is on or after \$STAMP_EXP_DT.

(Signature of Participant)

(Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the participant or, where appropriate, with the participant's legally authorized representative. It is my opinion that the participant understands the risks, benefits, and procedures involved with participation in this research study.

(Signature of Person who Obtained Consent)

(Date)

APPENDIX D

The Posttraumatic Growth Inventory

INSTRUCTIONS: Indicate for each of the statements below the degree to which this change occurred in your life as a result of being informed about your HD gene status. Please use the scale below.

	Did Not Experience	Very Small Degree	Small Degree	Moderate Degree	Great Degree	Very Great Degree
1. My priorities about what is important in life.	0	1	2	3	4	5
2. An appreciation for the value of my own life.	0	1	2	3	4	5
3. I developed new interests.	0	1	2	3	4	5
4. A feeling of self-reliance.	0	1	2	3	4	5
5. A better understanding of spiritual matters	0	1	2	3	4	5
6. Knowing that I can count on people in times of trouble	0	1	2	3	4	5
7. I established a new path for my life.	0	1	2	3	4	5
8. A sense of closeness with others.	0	1	2	3	4	5
9. A willingness to express my emotions.	0	1	2	3	4	5
10. Knowing I can handle difficulties.	0	1	2	3	4	5
11. I am able to do better things with my life.	0	1	2	3	4	5
12. Being able to accept the way things work out	0	1	2	3	4	5

	Did Not Experience	Very Small Degree	Small Degree	Moderate Degree	Great Degree	Very Great Degree
13. Appreciating each day.	0	1	2	3	4	5
14. New opportunities are available which wouldn't have been otherwise.	0	1	2	3	4	5
15. Having compassion for others.	0	1	2	3	4	5
16. Putting effort into my relationships	0	1	2	3	4	5
17. I am more likely to try to change things which need changing.	0	1	2	3	4	5
18. I have a stronger religious faith.	0	1	2	3	4	5
19. I discovered I am stronger than I thought I was.	0	1	2	3	4	5
20. I learned a great deal about how wonderful people are.	0	1	2	3	4	5
21. I accept needing others.	0	1	2	3	4	5

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