ISSN 0008-3194 (p)/ISSN 1715-6181 (e)/2020/65–75/$2.00/©JCCA 2020

Locus of control in patients with Huntington disease: a cross-sectional study

Brynne E. Stainsby, BA, DC, FCCS(C)[1]
Silvano Mior, DC, FCCS(C), PhD[1]
Mark Guttman, MD, FRCPC[2]

Background: *Health locus of control (LOC) represents an individual's beliefs regarding one's ability to influence health outcomes. In patients with chronic and neurodegenerative diseases, greater internal LOC has been associated with lower levels of disability.*

Objective: *To examine LOC in patients with Huntington disease (HD).*

Methods: *A cross-sectional study of individuals affected by HD, stratified by disease status, was conducted. Participants completed a demographic questionnaire, the Internal Control Index (ICI), and the Hospital Anxiety and Depression Scales.*

Results: *Thirty-four subjects completed the study. All groups demonstrated greater internal LOC (measured by ICI scores), and significant differences between groups were observed. Secondary analysis demonstrated relationships between depressive symptoms and*

Contexte : *Le locus de contrôle de la santé (LCS) représente les croyances d'une personne sur sa capacité d'influer sur son état de santé. Chez les patients atteints de maladies chroniques et neurodégénératives, un locus de contrôle plus interne est associé à des degrés d'invalidité moindres.*

Objectif *: Observer le LCS chez des patients atteints de la maladie de Huntington.*

Méthodes : On a mené une étude transversale auprès de personnes atteintes de la maladie de Huntington, regroupées en fonction du stade de la maladie. Les participants ont rempli un questionnaire démographique, le questionnaire Internal Control Index (ICI) et le questionnaire HADS (Hospital Anxiety and Depression Scale).

Résultats : *Trente-quatre sujets ont participé à l'étude jusqu'à la fin. Dans tous les groupes, on a observé un locus de contrôle plus interne (mesuré par les scores ICI), et des différences significatives entre les groupes. Une étude secondaire a montré l'existence de liens entre les symptômes de la dépression et les symptômes de l'anxiété, de même qu'entre le score ICI et le temps*

[1] Canadian Memorial Chiropractic College, Toronto, Ontario, Canada
[2] Center for Movement Disorders, Toronto, Ontario, Canada

Corresponding author: Brynne E. Stainsby, Department of Clinical Education, Canadian Memorial Chiropractic College, 6100 Leslie Street, Toronto, ON M2H 3J1
Tel: 416.482.2340
E-mail: bstainsby@cmcc.ca

The authors have no disclaimers or competing interests to report in the preparation of this manuscript.
Funding for this study was provided by the Canadian Memorial Chiropractic College

anxiety symptoms, and ICI score and time from clinical diagnosis of HD.

Conclusion: *As patients with chronic pain and neurodegenerative diseases such as HD are likely to present for chiropractic care, identifying factors such as anxiety, depression and LOC may affect patients' response to care.*

(JCCA. 2020;64(1):65-75)

KEY WORDS: anxiety, chronic pain, depression, Huntington disease, internal-external control

écoulé à partir du diagnostic clinique de la maladie de Huntington.

Conclusion : *Les patients souffrant de douleurs chroniques et de maladies neurodégénératives, comme la maladie de Huntington, sont susceptibles de chercher de l'aide auprès des chiropraticiens. Certains facteurs comme l'anxiété, la dépression et le LCS peuvent influer sur la réponse des patients aux soins.*

(JCCA. 2020;64(1):65-75)

MOTS CLÉS : anxiété, douleur chronique, dépression, maladie de Huntington, contrôle interne-externe

Introduction

Chronic musculoskeletal pain is a complex problem affecting up to 85% of patients in chiropractic clinical practice.[1] Chronic pain is one of the leading burdens of illness in Canada with direct and indirect costs of $5.8 billion in 2008. Patients with chronic pain conditions frequently experience misdiagnosis, delayed diagnosis, unneccessary tests and referrals, frustration, and poor outcomes; all of which may lead to increased burden on the health care system.[1] Given the financial and societal burden, appropriate diagnosis and management of these complaints is critical, and understanding how patients respond to their diagnosis may assist clinicians in developing appropriate educational or manual interventions. For example, locus of control (LOC), based on Rotter's social learning theory[2], is a personality trait that influences human behaviour[2-4]. This theory posits that behaviour is influenced by an individual's expectation of reinforcement, the perceived value of the reinforcement, and the psychological context of the situation.[2] LOC is specifically related to the "expectation for reinforcement" component of this theory[2-4], as well as how an individual perceives and interprets an event, and how s/he then chooses to respond to the situation[3].

In chronic diseases, health LOC represents an individual's beliefs regarding his/her ability to influence health outcomes.[3] Individuals with a greater internal LOC believe health outcomes are self-determined, via their actions or strategies, and demonstrate greater self-esteem, experience less depression, trait anxiety and neurotic symptoms.[3] Using measures including the Internal Control Index (ICI)[4], patients with HIV were divided into subtypes related to their mood, anxiety and ability to adapt to the disease[5]. Those in the 'highly adaptive' subtype were found to have greater internal LOC when compared with the 'average performing' and 'severely dysfunctional' subtypes.[5] In contrast, those with lesser LOC believe health outcomes are due to fate, luck or the decisions of doctors.[2-4]

While traditionally considered to be a personality trait that is stable over time, numerous authors have reported differences in LOC when examined in the context of illness or disease.[5-8] Gruber-Baldini *et al*. examined LOC relative to disability scores and quality of life in patients with Parkinson's disease.[6] In their cross-sectional study, greater internal LOC scores were associated with lower levels of disability.[6] In consideration of the psychological context variable of the social learning theory[3], the authors suggest those with greater internal LOC may have adopted behaviours and strategies to maintain functional abilities[6]. The authors further hypothesize that LOC may affect the course of disability as a consequence of a condition.[6]

Low back pain and neck pain are the most commonly reported conditions for seeking chiropractic care; however, those with Parkinson's disease, multiple sclerosis, stroke and diabetes may also seek care.[9] These chronic conditions may present with unique neuromusculoskeletal complaints, for which chiropractic care may be helpful. Huntington disease (HD) is an example of a neurodegenerative disease that may cause neuromusculoskeletal

complaints. HD is a fatal, autosomal dominant neurodegenerative disorder characterized by progressive motor dysfunction, decreased cognitive abilities, and psychiatric or behavioural disturbances (such as depression).[10-12] The prevalence of HD is 4-10 per 100,000 people; however, it impacts many more people. One of its most devastating effects is the impact on family life, including those at-risk, family members and caregivers.[13-17]

The genetic mutation that confirms the diagnosis is a cytosine-adenine-guanine (CAG) trinucleotide repeat expansion in the gene that encodes for the huntingtin protein on chromosome 4.[18,19] Typically, longer repeat lengths represent an earlier age of onset and more rapid progression of symptoms. While the length of the trinucleotide repeat accounts for 50-70% of the variability in these factors, little is known about how other genes or mechanisms influence the development or rate of progression of HD.[10,11,20-22] The role of non-genetic factors (such as coping strategies or behavioural modifications) in the delay of symptom onset and progression is believed to be important, but not well understood.[11]

In addition to assisting with prediction of the age of onset, the discovery of the DNA markers associated with the gene responsible for HD led to the development of predictive testing in those at-risk.[23,24] The risk of developing HD is considered a major stressor with tremendous influence on the life and major decisions of the at-risk population[14-16,25], yet only 10-20% have participated in predictive testing[14,16]. It has been suggested that the avoidance of testing may be related to passive or maladaptive coping strategies.[25]

Clinically, HD is recognized by the triad of motor, cognitive and psychiatric symptoms.[10-12] Clinical diagnosis of HD is a complex process based on the clinical impression of the treating physician and is not homogenous in clinical settings as there is no current consensus regarding clinical diagnostic criteria. The Unified Huntington Disease Rating Scale (UHDRS) diagnostic criterion is based on the motor assessment component of the UHDRS and requires the unequivocal presence of an extrapyramidal movement disorder, such as choreic movement, in a patient with a family history of HD.[10,27] In addition to its role in diagnosis, the UHDRS is the current gold standard measure used in research protocols; including clinical trials, as well as being used to stratify patients into groups based on stages of disease.[10,11,18,21,22,27] The UHDRS also includes a behavioural examination, which investigates symptoms such as depression and suicidal thoughts.[27] Behavioural examination is important as up to 63% of HD patients experience depressive symptoms, which have also been associated with decrease in functional abilities and quality of life.[28]

Beyond the obvious medical implications, an affected individual or their family member may also be required to cope with new financial burdens, social stigma, genetic discrimination, and the risk that children may inherit the disease.[14-16,29,30] To deal with this myriad of difficulties, patients and their families may adopt passive coping strategies. Passive coping strategies have been considered maladaptive, as the individual relinquishes control of their pain or situation and/or allows other areas of life to be adversely affected.[31-33] Such coping strategies have been linked to poorer adjustment in chronic health conditions, including chronic pain, rheumatoid arthritis and whiplash disorders.[6,31-33] Passive coping strategies have also been observed both in patients demonstrating lesser internal locus of control (LOC) and those with depression.[6,25]

The work by Gruber-Baldini provides new insight into the role of LOC in neurodegenerative diseases.[6] Specifically in HD patients, research has focused on physical and cognitive symptoms; however, little research has addressed the psychosocial aspects of the disease.[34] Based on the scarce research related to LOC and the results of Gruber-Baldini *et al*.[6], and in consideration of the potential for coping strategies or behavioural modifications to effect the course of disability, we aimed to examine the role of LOC in people affected by HD. Specifically, we examined:

1) the LOC in subjects affected by HD as measured by the Internal Control Index (ICI); and
2) their levels of depression and anxiety using the Hospital Anxiety and Depression Scale (HADS).

Methods

Study design

We used a cross-sectional survey design. Given the number of ways that an individual may be affected by HD, we allocated subjects to four groups based on their HD status. We examined differences between 'at-risk' (positive family history of HD without genetic testing results), 'pre-symptomatic' (genetic test positive for CAG muta-

tion, without clinical diagnosis by HD physician), 'early symptomatic' (genetic test positive for CAG mutation, plus clinical diagnosis by HD physician), and 'genetic negative' (family history of HD with a negative genetic test result) groups at a given point in time. Despite a paucity of evidence to suggest that LOC may be linked to the stage of disease progression, individuals are commonly allocated to these groups in order to receive support in the HD community or participate in research.[10,11,18,21,22,27,34]

Sample specification

The target population was a convenience sample of males and females between 25 and 45 years who were affected by HD. The most recent clinical information provided by the patient's HD physician was used to allocate subjects into the pre-symptomatic or early symptomatic group. HD is not specifically associated with particular demographic variables; therefore, subjects representing a wide variety of ethnicities, education levels and socioeconomic status were eligible to participate. Subjects were excluded if they did not fit the sample specifications or were not competent to consent. Subjects were recruited from the Centre for Movement Disorders (Markham, ON) and via on-line communications through the Huntington Society of Canada (HSC) to its members.

Due to limited subject recruitment at six months, the protocol was amended to allow for online data collection. As those who provided data via online assessment did not undergo UHDRS testing, it was not possible to validate their correct allocation to the assigned study groups. However, we performed a post-hoc analysis to evaluate differences in results between the subjects who completed data collection in-person and those who completed it online to assess for differences in responses in these groups.

Finally, to increase participation in the study, we used a modification of a widely accepted framework for survey methods.[35] The HSC agreed to distribute only three emails to its membership at one week intervals to inform and remind members of the study and encourage participation. The study received institutional Research Ethics Board approval (REB approval 1007X05).

Description of outcome measures

Locus of control was evaluated using the ICI. The ICI was developed by Duttweiler in 1984 based on variables associated with internal LOC, such as cognitive processing, autonomy, resistance to influence attempts, delayed gratification and self-reliance.[4] It is a 28-item questionnaire and each item is rated on a 5-point scale, where higher scores indicate greater levels of internal LOC.[4,36] The maximal score (high internal response pattern) is 140, and the minimum score (low internal response pattern) is 28.[4] In follow-up studies, the ICI has been shown to be a reliable measure of LOC with an internal consistency of 0.85.[36] It is significantly correlated to the Beck Depression Inventory, the State-Trait Anxiety Inventory (Form Y), the Coopersmtih Self-Esteem Inventory (Form A), and the Eysenck Neuroticism Scale.[36] Further, convergent validity of this scale has been demonstrated against Rotter's Internal-External Scale.[36] While LOC is traditionally considered to be a personality trait that is stable over time, there have been reported changes in LOC when measured in the context of illness or disease.[5-8]

We used the Hospital Anxiety and Depression Scale (HADS) to address the secondary aim of the study.[38] The HADS has been used to assess the presence and severity of depression (HADS-D) and anxiety (HADS-A), and has been demonstrated to have good internal consistency.[38,39] It contains 14 questions, with scores ranging from zero to 42, where higher scores indicate greater levels of depression and anxiety.[38] The HADS has been validated for use in patients with HD with an area under curve of 0.90.[28] In this population, it has acceptable psychometric properties with a sensitivity of 1.00 and specificity of 0.79 using optimal cut-off values.[28]

Clinical features of HD were assessed using the UHDRS, a research tool produced and revised by the Huntington Study Group (HSG).[27] It was developed to provide a uniform assessment of the clinical features and disease progression, and allows for comparison of clinical signs, disease progression and the effects of therapy, within and between trials.[27] The UHDRS is composed of motor, cognitive, behavioural and functional assessments, an independence scale and a measure of total functional capacity.[27] The UHDRS was revised based on research experience and available evidence and refinements made to the cognitive and behavioural assessment sections.[27] The UHDRS is the current gold standard for research protocols, has undergone extensive reliability and validity testing, and has been used as a major outcome measure by the HSG in controlled clinical trials.[10,11,18,21,22]

Description of experimental maneuver

We included two strategies as noted above. The first strategy involved in-person interaction with the principal investigator (PI); the subject completed paper copies of the demographic questionnaire, ICI and HADS, and underwent complete UHDRS assessment. This strategy enabled the investigators to determine if the UHDRS scores obtained during the study were consistent with the most recent clinical information provided by an HD physician via the patient's self-reported HD status. The second strategy involved subjects completing only the demographic questionnaire (including clinical information for group allocation), ICI and HADS via an online survey tool.

Strategy I

Prior to data collection, a research assistant utilized a computer-generated random numbers table to label envelopes containing the two outcome measures (ICI and HADS), labelled with the same unique subject indentification (ID) number to code to ensure confidentiality for all subjects. After consenting to participate, the subjects underwent a brief interview with the PI to determine if they had undergone genetic testing, and if so, what the results were (negative or positive). Those with a positive genetic test were additionally asked if they had been diagnosed with HD by their physician. This information was used to allocate the subject into the appropriate group.

Subjects were provided with a coded envelope and led to a private area to complete the questionnaires and were instructed to return their completed surveys to the PI with the envelope sealed. Following the completion of the questionnaire, the PI assessed each subject via the UHDRS and recorded their scores. All data for each subject were gathered during one session lasting approximately one hour.

An independent research assistant scored both paper outcomes, and documented the UHDRS scores. The assistent then used a second computer-generated random numbers table to reassign subject numbers and provided the PI with the total scores for each of the three outcome measures for data analysis. The second random number served to further ensure anonymity for participants.

The PI was blinded to the participants' survey responses as described above. Compliance was assessed by recording the number of eligible subjects who participated, the number who provided demographic information and the number not willing to participate.

Strategy II

Strategy II was introduced to increase the number of eligible participants and allow for the recruitment of subjects across Canada. All data (including demographic information) were collected online. Identical subject inclusion and exclusion criteria applied in both strategies. All subjects consenting to participate were provided survey questions as described above from the demographic questionnaire, the ICI and the HADS. The same randomized coding procedure as described in Strategy I was undertaken by an independent research assistant. All data were returned to the PI for analysis.

Sample size estimation

The sample size, based on Cohen's f for an ANOVA[40] and calculated via the R-Project software (R Project, version 2.10.0)[41], was 15 per group for a total of 60 subjects. Standard deviations (SD) obtained from previously cited studies[5,42] suggested a great degree of variability. Therefore, the pooled SD (13.52) from the Smith *et al*. study[42] was used to calculate the sample size based upon methodological similarity to our study. This calculation was based on an effect size (f) of 0.49, accounting for a 10% change that was arbitrarily deemed as clinically relevant. To compensate for non-compliance and errors in completing the outcome measures, an additional 20% was added to each group, for a total sample size of 18 per group and a total study size of 72.

Data analysis

In order to assess for any differences in responses between the subjects who completed Strategy I (in-person), and those who completed online assessment (Strategy II) of the ICI and HADS, analysis of variance was performed. The ICI scores for each group were descriptively analyzed to provide means, standard deviations, minimum and maximum values. To address the primary aim of this study, a one-way ANOVA with Bonferroni correction was used to assess mean differences in the ICI scores. All calculations were based on a Type I error of 0.05 and a Type II error of 0.2. To address the secondary aim of this study, the scores for the HADS were analyzed using a Kruskal-Wallis test, as the data violated the assumptions for ANOVA use (assessed by the Bartlett test).

We calculated Spearman's correlation test to assess the relationships between the outcome measures. Specifically,

Table 1.
Demographic characteristics of subjects.

	Negative	At-risk	Pre-symptomatic	Early Symptomatic
Total number	8	10	9	7
Average age (yrs)	30.0 (3.8)	29.0 (5.2)	35.4 (7.2)	38.7 (6.1)
Female subjects (%)	87.5	70	66.7	42.9
Subjects from Strategy 1 (%)	50.0	60.0	44.4	57.1
Avg years from genetic result (sd)	2.0 (2.3)	N/A	8.1 (6.5)	7.6 (5.1)
Avg years from clinical diagnosis (sd)	N/A	N/A	N/A	3.6 (2.9)

we assessed the relationship between HADS-anxiety and HADS-depression scores, ICI score and length of time in years from HD clinical diagnosis, ICI score and length of time in years from HD genetic result, and depression and length of time in years from genetic result, and the length of time in years from the clinical diagnosis. All data were analyzed with STATA (STATA, version 10.0) and SPSS (IBM SPSS Statistics for Windows, Version 26.0) statistical software.

Results

Thirty-four subjects completed all the questionnaires, while 16 completed the UHDRS assessment (Strategy 1). Subjects were similarly distributed across each of the four groups. They ranged in age from 25 to 45, with greater proportion being female; however, this finding is consistent with other HD studies (Table 1).[38] There were no significant differences in ICI and HADS scores of subjects recruited in-office and on-line. Therefore, the data sets were merged and all scores used in the analysis.

The grouped ICI scores are summarized in Table 2. All groups demonstrated mean scores above the scale midpoint of 84, indicating increased levels of internal LOC.[4] Post-hoc Bonferroni-corrected contrasts demonstrated a significant difference between the at-risk and early symptomatic groups ($p < 0.01$), and the early and pre-symptomatic groups ($p < 0.02$) (Table 3).

Results from the Kruskall-Wallis test of the HADS-D indicated a significant difference between groups (Adjusted $H = 12.2$, $df=3$, $p < 0.01$). Table 4 provides the means and standard deviations of these scores. Subjects in the at-risk category had the lowest scores (fewest depres-

Table 2.
Descriptive statistics of ICI scores by group.

Group	Mean	SD	Minimum	Maximum
Negative	104.4	12.8	80	124
At-risk	109.3	5.5	101	118
Pre-symptomatic	107.0	9.4	92	117
Early symptomatic	90.6	12.0	74	107

Table 3.
ICI scores contrasted between groups as calculated by Bonferroni-corrected comparison.

Group	Negative	At-risk	Early symptomatic
At-risk	4.9		
Pre-symptomatic	2.6	–2.3	16.4 (p<0.02)
Early symptomatic	–13.8	–18.7 (p<0.01)	

Table 4.
Median scores and ranges for HADS-D. Adjusted H = 12.2, p<0.0

Group	Score
Negative	2.0 (0-10)
At-risk	0.5 (0-3)
Pre-symptomatic	3.0 (0-9)
Early symptomatic	6.0 (1-10)

Table 5.
Median scores and ranges for HADS-A. H = 6.8, p=0.08

Group	Score
Negative	5.5 (3-9)
At-risk	5.0 (1-8)
Pre-symptomatic	6.0 (3-15)
Early symptomatic	8.0 (4-15))

sive symptoms), while the early symptomatic subjects averaged the highest scores. There were no significant differences between groups (Adjusted H = 6.8, df=3, p = 0.08). Descriptive results by group are provided in Table 5.

Secondary analysis demonstrated HADS-D was significantly related to HADS-A, r_s = 0.63, 95% Bias Corrected accelerated (BCa) Confidence Interval (CI) [0.42, 0.74], p < 0.01. The ICI scores were not significantly related to the length of time (in years) from the time of genetic testing, r_s = -0.59, 95%BCa CI [-0.43, 0.31], p = 0.78. The ICI scores were significantly related to length of time (in years) of clinical diagnosis r_s = 0.89, 95%BCa CI [0.16, 1.00], p < 0.01. The HADS-D scores were not significantly related to the length of time (in years) from the time of genetic testing, r_s = 0.02, 95%BCa CI [-0.41, 0.44], p = 0.93, nor were the HADS-D scores significantly related to the length of time (in years) from the time of clinical diagnosis, r_s = 0.22, 95%BCa CI [-0.50, 0.73], p = 0.63.

Discussion

Our data suggests differences in LOC may exist between groups of subjects affected by HD, such that those in the early symptomatic group had greater internal LOC than the at-risk and pre-symptomatic groups. Additionally, we observed a significant difference in depression scores between the at-risk and early symptomatic groups. We observed a trend of increasing anxiety from the at-risk to the pre-symptomatic groups, which appeared to decrease in the early symptomatic groups. We also observed increased anxiety levels in the negative group compared to those at-risk.

Locus of control

Our results suggest that differences in LOC may exist within groups of subjects affected by HD. Specifically; the at-risk group had a significantly lower LOC score than the early symptomatic group. Although we did not evaluate changes in LOC as the disease progresses within an individual with HD, one may hypothesize that because those in the at-risk group have not yet received the genetic test results, they may perceive a lack of ability to control their future. Alternatively, those in the early symptomatic group may recognize the disease process has begun and may adopt active coping behaviours, as demonstrated in those with greater internal LOC.[2-4,6,31-33]

Helder *et al*. identified a similar trend in their cross-sectional study.[34] They found that a sample of patients with clinically diagnosed HD scored significantly higher on the "acceptance" subscale of the COPE inventory compared to a convenience sample of healthy adults.[34] Interestingly, these patients scored significantly lower on other subscales such as "suppression of competing activities" and "mental disengagement".[34] This may suggest a difference in coping strategies related more to personality traits (such as LOC) rather than the cognitive decline associated with HD.[8,34]

Furthermore, our secondary analysis demonstrated a relationship between higher ICI scores and time from first clinical diagnosis of HD in the early symptomatic group. Again, this is consistent with the findings of Helder *et al*., where their subjects had a meantime elapsed of 5.1 years from first diagnosis.[34] Although we had a small group (n = 7) in our study, a future longitudinal study is warranted to confirm this trend.

The early symptomatic group also had a significantly higher internal LOC than the pre-symptomatic group. Again, it is possible that those in the pre-symptomatic stage of HD experience a sense of uncertainty in waiting for the onset of their disease and thus are more likely to feel that future health outcomes are related to luck or fate.[2,4,6] McAllister *et al*. reported that anxiety is commonly experienced in patients affected by genetic conditions; however, it often becomes more intense during times of disease change, such as a new diagnosis or genetic testing.[45] With respect to those specifically affected by HD, they commonly experience greater levels of distress following a genetic diagnosis in anticipation of the onset of HD, due to previous experiences of observing the effects

of HD and concern for how such effects will affect their own life.[34,45]

Depression

Since up to 63% of patients with HD demonstrate depressive symptoms that may be related to passive coping and poorer health outcomes[8,28], we also examined the scores of the HADS-D scale. Previous studies suggest that depressive symptoms in patients with HD are associated with impaired function and decreased quality of life.[28] Paulsen *et al*. found that those with an expanded CAG repeat upon genetic testing demonstrated greater levels of distress on psychiatric testing than those without the expansion.[44] We observed a significant difference in depression scores between the at-risk and early symptomatic groups. Our findings reinforce the presence of depressive symptoms in patients with early symptomatic HD, and encourage early evaluation and treatment.[28]

While our findings support the presence of depression in patients with HD, we cannot comment upon how it is affected by the progression of symptoms over time. We found a trend toward a negative correlation between the HADS-depression score and the elapsed time since receiving a genetic result. It is important to interpret these results with caution as this relationship was observed within a small and specific group. If confirmed in a larger study, these results may suggest that within the pre-symptomatic stage of HD, individuals may become less affected by depressive symptoms the longer they have to accept the result. When dealing with patients with terminal illnesses, Kubler-Ross described a dynamic cycle involving denial, anger, bargaining, depression and acceptance states of grief.[45] In consideration of this process, it may be hypothesized that simply the confirmation of a genetic diagnosis may evoke similar emotional responses and cause an individual to progress through the process of grief, eventually resulting in greater acceptance.

Anxiety

Anxiety is considered a common neuropsychiatric symptom in patients with HD, and the evaluation of its presence is considered important in a comprehensive examination of a patient with the disease.[21] Although we observed no significant differences between groups, our findings suggested a trend of increasing anxiety from the at-risk to the pre-symptomatic, which then decreased in the early symptomatic groups. As hypothesized above, perhaps the distress associated with receiving a positive genetic test leads to greater anxiety than the actual development of the disease due to LOC and the belief that future health will be determined by fate.[2,4,6,34]

Increased anxiety levels were also observed in the negative group compared to the at-risk. In addition to the challenges that may present to all members of an affected family[14-16], those who receive a negative genetic test result are commonly affected by "survivor's guilt"[45]. This concept speaks to the guilt associated with not inheriting the CAG expansion, while other family members may not yet know about their future, may have tested positive, and/or may already demonstrate symptoms.[45] Studies suggest those receiving negative genetic test results demonstrate this phenomenon, in addition to a period of emotional numbness and difficulties developing new perspectives for life.[45,47-51] Future studies with a larger sample may elucidate if this finding changes over time.

Finally, when examining the pooled data from all subjects, a positive relationship was observed between depression and anxiety, suggesting that these symptoms may be linked. This finding is supported by previous research that has identified a wide spectrum of neuropsychiatric symptoms and disorders in patients with HD.[10,11,27,28]

Limitations and future research

Our study included a small convenience sample that may not be representative of the general HD population. It is important, therefore, to interpret the results with caution. It is also possible that data collected online were completed by participants with assistance from a second party. In the future, a study involving multiple sites to recruit a larger sample may confirm the observed results of this study.

Recruitment was limited to individuals prior to the onset of moderate to severe symptoms in order to ensure that all subjects were competent to provide consent. While this limitation was intended to protect the rights of the research subjects and increase internal validity, it may have resulted in the recruitment of a younger population and limited the generalizability to the entire population affected by HD. In patients without neurodegenerative disease, internal LOC was associated with hippocampal volume in young and elderly subjects[52] ; however, this relationship has not been examined in patients with HD or other neurodegenerative diseases. Future research may

attempt to measure this. It should also be noted that there was a high percentage of females who participated in this study. Given there is no relationship between inheritance and patient sex, the findings of this study must be interpreted with caution with respect to the generalizability to the entire population affected by HD.

It is important to consider that disease progression in patients with HD has historically been evaluated based on motor dysfunction; however, changes in behaviour and cognition may be observed as a patient approaches symptomatic diagnosis.[53] Duff *et al*. have found a greater prevalence of apathy, disinhibition and executive dysfunction ("frontal behaviours") in patients with the CAG expansion, and also noted that these behaviours are associated with motor and cognitive markers of HD progression.[53] These findings reinforce the need for further research with a more robust population and may also suggest that the group stratification could be modified given the association between the Frontal System Behavioral Scale scores and the probability of diagnosis within five years.[52] It is possible that those in the pre-symptomatic category could perhaps be considered in the early stage using expanded diagnostic criteria. Future longitudinal research with a more robust population and diverse outcome measures may provide further insight into the role of LOC as the disease progresses.

Despite numerous attempts using various forms of communication through both the PI and the HSC, subject recruitment was a significant challenge. The HSC has documented that many Canadians affected by HD prefer to remain independent from affiliations with the disease, avoid participation with volunteer or support groups, and decline to participate in research studies.[4] Utilizing Dillman's method as it is described may have resulted in a greater response rate; however, we felt our modified approach balanced the need for email communications and respecting the time and willingness of a charitable organization and its volunteers, donors and members to participate.[35]

Given the difficulties with recruitment, we recognize our study was underpowered based on our sample size estimation. This may have impacted our results and increased the potential for type II error, thus our findings should be cautiously interpreted. Given the lack of current studies on LOC in patients with HD, we used the pooled SD of a study with similar methodology[42], as well as arbitrarily assuming a 10% difference in scores would be clinically relevant. In the initial estimation of required number of subjects, it was decided to include an additional percentage (20%) to account for the possibility of non-compliance and errors in completing the outcome measures. In retrospect this appeared to be a gross over-estimation of the actual number of incomplete returns, which was zero. Despite these comments, the authors acknowledge the failure to recruit the number of subjects recommended by the power calculation, and encourage care in interpretation of the results. Future studies should consider a multisite strategy in effort to facilitate subject recruitment.

Further, it is also important to recognize the potential for selection bias in the current study. It is possible that the participants in our study may have had greater levels of internal LOC compared to the general population affected by HD. Those who demonstrate more active coping strategies (including those with greater levels of internal LOC) commonly seek out information regarding their disease process[30], thus they may be more likely to participate in research. It may also be possible that those with fewer depressive symptoms and lower levels of anxiety would also be more likely to participate in research. However, it can be assumed that selection bias would affect each group equally, and thus relationships observed between groups may be realistic.

Finally, our study was cross-sectional in design and did not allow for evaluation of change in LOC over time. It does provide the basis for hypothesis generation and future longitudinal studies. In particular, this study aimed to inform future research that examines an individual's LOC as it relates to coping ability and strategies, quality of life and/or functional abilities.

Conclusion

As patients with chronic pain and neurodegenerative diseases such as HD are likely to present for chiropractic care, it is important that chiropractors recognize the psychosocial factors that may affect patients' clinical presentation and response to care. In addition to manual care, chiropractors may consider evaluating LOC, screening for symptoms of anxiety and depression, and/or identifying passive coping strategies, which may be associated with poorer outcomes in chronic health conditions. Assisting patients with the development of active coping strategies (or referring for this when appropriate)

may benefit patients and their prognoses. Future research could have important implications in informing disease management programs and coping strategies for individuals affected by HD.

Acknowledgements

The authors wish to thank Dr. Marion McGregor for her assistance with the development of this study and statistical analysis, and the Canadian Memorial Chiropractic College for funding for this study.

References

1. Bourgaize S, Newton G, Kumbhare D, Srbely J. A comparison of the clinical manifestation and pathophysiology of myofascial pain syndrome and fibromyalgia: implications for differential diagnosis and management. J Can Chiropr Assoc. 2018;62(1): 26-41.
2. Rotter JB. Some problems and misconceptions related to the construct of internal vs. external control of reinforcement. J Consult Clin Psych. 1975; 48: 56-67.
3. Rotter JB. Some implications of a social learning theory for the prediction of goal directed behaviour from testing procedures. Psychol Rev. 1960; 67: 301-316.
4. Duttweiler PC. The Internal Control Index: a newly developed measure of locus of control. Educ Psychol Meas. 1984; 44: 209-221.
5. Combs DR and Livingston RB. Psychological sub-types among persons with HIV infection: an empirical study. AIDS Care. 2001;13: 157-162.
6. Gruber-Baldini AL et al. Effects of optimism/pessimism and locus of control on disability and quality of life in Parkinson's disease. Parkinsonism Related D. 2009; 15: 665-669.
7. Oberle K. A decade of research in locus of control: What have we learned? Journal Adv Nurs. 1991;16: 800-806.
8. Fishbain DA, Cole B, Cutler RB, Lewis J, Rosomoff HL and Rosomoff RS. Chronic pain and the measurement of personality: Do states influence traits? Pain Med. 2006;7(6): 509-529.
9. Beliveau PJH, Wong JJ, Sutton DA, Simon NB, Bussieres AE, Mior SA and French SD. The chiropractic profession: a scoping review of utilization rates, reasons for seeking care, patient profiles, and care provided. Chiropr Man Therap. 2017;25: 35-52.
10. Tabrizi SJ, Langbehn DR, Leavitt BR, Roos RA, Durr A, Craufurd D et al. Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data. Lancet Neurol. 2009; 8: 791-801.
11. Paulsen J. Early detection of Huntington disease. Neurol. 2010;5(1): 85-104.
12. Hedreen JC, Peyser CE, Folstein SE, Ross CA. Neuronal loss in layers V and VI of cerebral cortex in Huntington's disease. Neurosci Lett. 1991;133: 257-261.
13. Huntington Society of Canada [homepage on the Internet]. Kitchener, ON; c2010 [cited 2010 January 24]. Available from: http://www.huntingtonsociety.ca.
14. Etchegary H. Coping with genetic risk: living with Huntington Disease (HD). Curr Psychol. 2009;28: 284-301.
15. Forrest Keenan K, Miedzybrodzka Z, van Teijlingen E, McKee L, Simpson SA. Young people's experiences of growing up in a family affected by Huntington's disease. Clin Genet. 2007;71: 120-129.
16. Vamos M, Hambridge J, Edwards M, and Conaghan J. The impact of Huntington's disease on family life. Psychosomatics. 2007; 48: 400–404.
17. Statistics Canada [homepage from the Internet]. Address; c2010 [cited 2010 January 24]. Available from http://www.statcan.gc.ca
18. Witjes-Ane MW, Mertens B, van Vugt JP, Bachoud-Levi AC, van Ommen GJ, and Roos RA. Longitudinal evaluation of "presymptomatic" carriers of Huntington's disease. J Neuropsychiatry Clin Neurosci. 2007; 19: 310-316.
19. The Huntington's Disease Collaborative Research Group. A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. Cell. 1993; 72: 971-983.
20. Li JL, Hayden MF, Almqvist EW, Brinkman RR, Durr A, Dode C et al. A genome scan for modifiers of age at onset in Huntington Disease: The HD MAPS study. Am J Hum Genet. 2003; 73: 682-687.
21. Paulsen JS, Zhao H, Stout JC, Brinkman RR, Guttman M, Ross CA et al. Clinical markers of early disease in persons near onset of Huntington's disease. Neurol. 2001; 57: 658–662.
22. Duff K, Paulsen JS, Beglinger LJ, Langbehn DR, Stout JC et al. Psychiatric symptoms in Huntington's Disease before diagnosis: The Predict-HD Study. Biol Psychiatry. 2007; 62: 1341-1346.
23. Babul R, Adam S, Kremer B, Dufrasne S, Wiggins S, Huggins M et al. Attitudes toward direct predictive testing for the Huntington disease gene: relevance for other adult-onset disorders. The Canadian Collaborative Group on Predictive Testing for Huntington Disease. J Am Med Assoc. 1993;270: 2321–2325.
24. Fox et al. Predictive testing for Huntington disease: description of a pilot project in British Columbia. Am J Med Genet. 1989; 32: 211-216.
25. Pakenham KI, Goodwin VA and MacMillan JC. Adaptation to being at-risk for Huntington's disease and the availability of genetic testing: application of a stress and coping model. Psycho Health Med. 2004; 9: 380-397.
26. Hayden MR. Predictive testing for Huntington's disease: the calm after the storm. Lancet. 2000; 356: 1944-1945.

27. Kieburtz K et al. The Unified Huntington's Disease Rating Scale: reliability and consistency. Mov Dis. 1996;11: 136-142.
28. De Souza J, Jones LA and Rickards H. Validation of Self-Report Depression Rating Scales in Huntington's Disease. Mov Dis 2010; 25: 91-96.
29. Bombard Y et al. Managing genetic discrimination: Strategies used by individuals found to have the Huntington disease mutation. Clin Genet. 2007; 71: 220–231.
30. Bombard Y et al. Engagement with genetic discrimination: concerns and experiences in the context of Huntington disease. Eur J H Genet. 2008;16: 279-289.
31. Snow-Turek AL, Norris MP and Tan G. Active and passive coping strategies in chronic pain patients. Pain. 1996;64: 455-462.
32. Brown GK, Nicassio PM, and Wallston KA. Pain coping strategies and depression in rheumatoid arthritis. J Consult Clin Psych. 1989;57(5): 652-657.
33. Carroll LJ, Cassidy JD, and Cote P. The role of pain coping strategies in prognosis after whiplash injury: Passive coping predicts slowed recovery. Pain. 2006;124: 18-26.
34. Helder DI, Kaptein AA, van Kempen GMJ, Weinman J, van Houwelingen HC and Roos RAC. Living with Huntington's disease: Illness perceptions, coping mechanisms and patients' well-being. Br J Health Psych. 2002; 7: 449-462.
35. Hoddinott SN and Bass MJ. The Dillman Total Design survey method: A sure-fire way to get high survey return rates. Can Fam Phys. 1986;32: 2366-2368.
36. Meyers LS and Wong DT. Validation of a new test of locus of control: the Internal Control Index. Educ Psychol Meas. 1988; 48: 753-761.
37. Jacobs KW. Psychometric properties of the Internal Control Index. Psychol Rep. 1993;73: 251-255.
38. Zigmond AS and Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67: 361-370.
39. Djukanovic I, Carlsson J and Arestedt K. Is the Hospital Anxiety and Depression Scale (HADS) a valid measure in a general population 65-80 years old? A psychometric evaluation study. Health Qual Life Out. 2017: 15: 193.
40. Cohen J. (1998) Statistical power analysis for the behavioural sciences (2nd ed), New Jersey: Lawrence Erlbaum Associates.
41. R project
42. Smith VL. Analysis of locus of control and education level utilizing the Internal Control Index. Marshall University Graduate College 2003.
43. Amrhein PC et al. Locus of control and the age difference in free recall from episodic memory. J Gen Psychol. 1999, 126:149-164.
44. Paulsen JS, Magnotta VA, Mikos AE, Paulson HL, Penziner E, Andreasen NC and Nopoulos PC. Brain structure in preclinical Huntington's disease. Biol Psychiatry. 2006;59: 57-63.
45. McAllister M, Davies L, Payne K, Nicholls S, Donnai D and MacLeod R. The emotional effects of genetic diseases: Implications for clinical genetics Am J Med Genetics. 2007;143A: 2651-2661.
46. Kubler-Ross E (1969). On death and dying, Routledge.
47. Meiser B and Dunn S. Psychological impact of genetic testing for Huntington's disease: an update of the literature. J Neurol Neurosurg Psychiatry. 2000;69: 574-578.
48. Maat-Klerit A, Vegter-van der Vlis M, Zoeteweij M, Losekoot M, van Haeringen A and Roos R. Paradox of a better test for Huntington's disease. J Neurol Neurosurg Psychiatry. 2000;69: 579-583.
49. Tibben A, Duivenvoorden HJ, Vegter-van der Vlis M, Niermeijer MF, Frets PG, van de Kamp JJP et al. Presymptomatic DNA testing for Huntington disease: identifying the need for psychological intervention Am J Med Genet. 1993;48: 137-144.
50. Tibben A, Timman R, Bannink EC and Duivenvoorden HJ. Three-year follow-up after presymptomatic testing for Huntington's disease in tested individuals and partners. Health Psychol. 1997;16(1): 20-35.
51. Wiggins S, Whyte P, Huggins M, Adam S, Theilmann J, Bloch M et al. The psychological consequences of predictive testing for Huntington's disease. N Engl J Med. 1992;327: 1401-1405.
52. Pruessner J, Baldwin MS, Dedovic K et al. Self-esteem, locus of control, hippocampal volume, and cortisol regulation in young and old adulthood. NeuroImage. 2005;28: 815-826.
53. Duff K, Paulsen JS, Beglinger LJ et al. "Frontal" behaviors before the diagnosis of Huntington's disease and its relationship to markers of disease progression: Evidence of early lack of awareness. J Neuropsychiatry Clin Neurosci. 2010; 22(2): 196-207.