Journal of Huntington's Disease 11 (2022) 17–24
DOI 10.3233/JHD-210519
IOS Press

Review

Social Withdrawal in Huntington's Disease: A Scoping Review

Jessie S. Gibson[a,*] and Kristen Springer[b]
[a]*University of Virginia School of Nursing, Charlottesville, VA, USA*
[b]*University of Virginia School of Education and Human Development, Charlottesville, VA, USA*

Pre-press 2 February 2022

Abstract.
Background: Huntington's disease (HD) commonly presents with impaired social functioning. Specifically, many patients exhibit social withdrawal, or decreased engagement in social activities. Despite the frequency of social withdrawal in HD, no review has been previously published on this subject.
Objective: The aim of this study was to conduct a scoping review of social withdrawal in HD.
Methods: Two searches were conducted to identify relevant literature. The articles were screened by title and abstract, followed by full text review for all remaining articles. Consistent with scoping review methodology, data extraction focused on identification of broad themes and knowledge gaps.
Results: Eight articles were identified that described social withdrawal in HD. Social withdrawal was exhibited by individuals with varying disease severity, and it occurred both within and outside of the home. Social withdrawal was associated with increased caregiver burden, behavioral issues, and psychiatric, cognitive, and physiological changes. Only one case study described an intervention that increased social participation in a previously withdrawn patient.
Conclusion: Although social withdrawal is commonly encountered in clinical settings, this review highlights the need for prospective studies to systematically evaluate social withdrawal in HD. These studies should be designed to consider disease stage and associated HD features as well as caregiver burden and potential interventions. Additionally, objective measures of social withdrawal should be used when possible, as existing instruments measure perceptions of participation levels rather than actual withdrawal behavior. Such studies will lay the groundwork to improve social functioning and quality of life for people with HD.

Keywords: Huntington's disease, social interaction, social participation, social isolation, illness behavior

INTRODUCTION

Impaired social functioning is a key feature of Huntington's disease (HD). In addition to motor limitations that prevent social participation (e.g., fall risk, driving cessation), personality changes caused by cognitive and psychiatric decline alter social functioning capacity in people with HD. Recent studies of resting-state connectivity have shown that the salience network, which is associated with social-emotional function, may have impaired connectivity with other brain regions in HD [1, 2]. Further, a recent qualitative study in HD patients and caregivers found that most participants reported patient social withdrawal compared to their baseline personality, attributed frequently to worsening anxiety or apathetic symptoms [3]. Social functioning deficits are commonly encountered in HD clinical settings, and these and related personality changes can cause more distress than other symptoms of HD [4].

*Correspondence to: Jessie S. Gibson, PhD, RN, 5008 McLeod Hall, PO Box 800792, Charlottesville, VA 22903, USA. Tel.: +1 434 924 0107; E-mail: js6zn@virginia.edu.

In the general population, studies have shown that social isolation has negative effects on a variety of health outcomes including early mortality [5]. Additionally, social well-being is a key feature of human health as defined holistically by the World Health Organization [6]. Despite this, there has been relatively little study of social functioning in HD. Under the umbrella of social functioning, various concepts have been studied, such as social withdrawal, social support, and social engagement, among others. This is important to note because subtle conceptual differences can have significant implications for the meaning of the results. For example, there is a difference between involuntary isolation and voluntary social withdrawal. In a longitudinal study of (non-HD) adults, anxiety and depression were more highly correlated with perceived isolation than social disconnectedness (fewer contacts) [7]. Additionally, studies have shown that social isolation and loneliness are not necessarily correlated [8]. Just as outcomes of unwanted social isolation may differ from those of voluntary social withdrawal, so too may interventions to address these issues. For example, strategies to address social isolation may target elimination of physical barriers preventing participation (e.g., gait instability), whereas interventions to reduce apathy or anxiety might more adequately target voluntary social withdrawal.

As noted above, social withdrawal has been identified as a particular social deficit in people with HD. For the purposes of this review, we will define social withdrawal as *decreased engagement in social activities* compared to a person's baseline level of engagement. Despite the acknowledgement of social withdrawal as a common clinical issue, no comprehensive review has been published on this subject. Thus, we completed a scoping review to synthesize existing literature and offer guidance for future research directions in this area. Unlike systematic reviews, which aim to offer specific evidence about intervention feasibility or effectiveness, scoping reviews provide a broad overview of the literature, allowing for identification of gaps in research, practice, and policy [9]. In this review, we aimed to describe what is known about social withdrawal in HD.

METHODS

Two literature searches were employed for this review. Because scoping reviews are intended to be flexible and iterative, search terms and exclusion criteria were revised prior to the second search, based on findings from the first. The first search, on 3/23/2020, included the following search terms, searched in PubMed, CINAHL, and PsycInfo: ((social* AND (withdraw* OR isolation OR connect* OR network OR engage* OR disengage*)) OR lonel*) AND (Huntington* OR Parkinson*)

The second search, on 2/28/2021, included the following search terms in the same databases: ("social behavior" [MESH] OR "social behaviour" [TIAB] OR "social behavior" [TIAB] OR "socialization" [MESH] OR "socializat*" [TIAB] OR "social isolation" [MESH] OR "social* isolate*" [TIAB] OR "social networking" [MESH] OR "social* network*" [TIAB] OR "social participation" [MESH] OR "social participa*" [TIAB] OR "social interaction" [MESH] OR "social* interact*" [TIAB] OR "social avoida*" [TIAB] OR "avoida*" [TIAB]) AND ("parkinson disease" [MESH] OR "parkinson disease" [TIAB] OR "parkinson's disease" [TIAB] OR "huntington disease" [MESH] OR "huntington disease" [TIAB] OR "huntington's disease" [TIAB]) NOT (review[pt] OR systematic review[pt] OR editorial[pt] OR guideline[pt] OR meta-analysis[pt])

For this review, articles were included that described social withdrawal or related concepts, such as social engagement, social network, social functioning, and social participation. Articles were excluded that exclusively described or measured irrelevant concepts such as social satisfaction, social support, involuntary isolation, loneliness, and stigma without explicit discussion of its effect on social withdrawal. However, because of inconsistencies in terminology, we included all potentially relevant (i.e., social-related) articles for full-text review, and those describing social withdrawal according to our definition were ultimately included, regardless of terminology used. For example, articles using the term "isolation" but actually describing social withdrawal behavior were still included (see Table 1 for specific terminology/concepts used in each article).

Both searches included Parkinson's disease terminology, and results were separated into two manuscripts for clarity of results presentation. As noted, results applying to HD are described in this manuscript. Basic exclusion criteria for both searches were as follows: not in an HD population, not in humans, not in English, reviews or commentaries, and studies exclusively in juvenile HD populations. For the first search, we also excluded studies that described social withdrawal explicitly in relation to motor symptoms (i.e., patients were physically unable to participate, rather than choosing to

Table 1
Articles describing social withdrawal in Huntington's disease (HD)

Author	Methods	Concept	Subjects	Instrument or Qualitative Data Collection Method	Relevant Results
Kowalski et al., 2015 [11]	Case Report	Inactivity, social isolation, "withdrawn and irritable"	$n = 1$ 34-year-old male with HD	N/A	HD patient with various psychiatric, cognitive, and physical manifestations displayed "general inactivity and social isolation" and "became more withdrawn and irritable" over time. Medication management (paroxetine and olanzapine) and psychotherapy improved his mood and irritability, but he remained resistant to support group participation.
Power 1982 [10]	Case Report	Inactivity, social isolation	$n = 1$ 46-year-old male patient with HD	N/A	HD patient withdrew unnecessarily from work and social activities after his diagnosis, and family felt embarrassed by his motor symptoms. Family counseling and education helped him to become productive again, returning to some social activity and part-time work.
Downing et al., 2012 [15]	Mixed-Methods	Decreased socializing, social withdrawal	$n = 23$ couples (adults with prodromal HD and companion)	Semi-structured interviews	In interviews with prodromal HD patients and companions, decreased socializing and relationship issues were two of the most common changes reported, though participants often did not attribute changes to HD; also, prodromal patients who attributed changes to HD used avoidance, including social withdrawal, as a coping strategy.
Gibson et al., 2022 [3]	Qualitative	Social withdrawal	$n = 15$ HD patients with neuropsychiatric symptoms and caregivers	Semi-structured interviews	Social withdrawal was endorsed by 14/15 (93%) of participants. Withdrawal from family in the home and from activities outside the home were described, and this often represented a change from the patient's baseline personality.
Ho & Hocaoglu, 2011 [12]	Qualitative	Going out for social occasions	$n = 31$ HD patients	Semi-structured interviews	HD participants in stages 1–4 reported that HD negatively impacted going out for social occasions.
Sherman et al., 2020 [14]	Qualitative	Limiting social interactions	$n = 82$; individuals with manifest HD ($n = 8$ early-stage HD; $n = 16$ late-stage HD), individuals at-risk or prodromal HD ($n = 16$), family HD caregivers ($n = 17$), and HD clinicians ($n = 25$)	Focus groups	Caregivers and providers reported that patients limit social interaction and become isolated, which is possibly due to chorea, inability to keep up with conversations, or "burning bridges" with others.
Williams et al., 2009 [13]	Qualitative	N/A	$n = 42$ adult carers of HD patients	Focus groups	In a focus group, one caregiver reported that her husband had decided to no longer see anyone socially, so she took on the "burden" of "keep[ing] him company". This was linked to mood and cognitive changes in the text.
Cruickshank et al., 2020 [16]	Quantitative	Social network size and diversity	$n = 29$ HD mutation carriers close to clinical onset and 15 healthy controls	Social Network Index [24, 25]	Greater social network size and diversity were associated with lower Nfl in HD patients, but not in controls, after controlling for gender and age.
Fritz et al., 2018 [17]	Quantitative	Social function	$n = 487$ HD patients ($n = 193$ prodromal, $n = 186$ early-stage manifest, $n = 108$ late-stage manifest)	NeuroQoL Satisfaction with Social Roles and Activities; NeuroQoL Ability to Participate in Social Roles and Activities [19, 20]	Better patient-reported social satisfaction and participation scores were associated with better apathy outcomes in multiple regression models.

withdraw), studies in people with a specific, uncommon genetic mutation, and manuscripts aiming to validate new measures. Exclusion criteria were revised for the second search to additionally exclude studies describing genetic testing and those assessing factors associated with participating in research interventions.

The original search, screening, and data extraction were done by JG. The second search and title and abstract screening were done by KS. Full text review and data extraction for the second search was done by both JG and KS, and the authors met to discuss any disagreements. Results, organized according to study type, are presented in the following section.

After the search was conducted, all potential articles were uploaded to Sciwheel in order to organize results and remove duplicates. The authors were able to screen articles independently and resolve disagreements using this software. Once all relevant articles were identified through title and abstract screening, full texts were reviewed again to ascertain pertinent data, and data extraction was recorded in Excel. The following variables were considered: article focus, study methods, concept (term used to indicate social withdrawal), subjects, instruments, and relevant results. The author(s), year of publication, journal, country, and database were also noted.

RESULTS

Study attributes

Search 1 yielded 795 results after removal of duplicates. Titles and abstracts of all results were reviewed for potential relevance, and those appearing to meet inclusion criteria were kept for further review ($n = 87$). Full text review identified 7 articles meeting inclusion criteria for the present review (i.e., in Huntington's disease). Search 2 yielded 894 results after removal of duplicates. Titles and abstracts of all results were reviewed for potential relevance, and those appearing to meet inclusion criteria were kept for further review ($n = 80$). Full text review identified 1 article meeting inclusion criteria for the present review (i.e., in HD). Three articles that were excluded on title and abstract review in search 2 were included for full text review in search 1 and were ultimately determined to meet inclusion criteria. An additional article, published by an author of this review after the second review search, was also added, as it included relevant findings and increased the breadth of this scoping review.

Characteristics of included articles are described in Table 1. Articles ($n = 8$) were published between 1982 and 2020, with the majority ($n = 6$) being published in the past 10 years. Articles described case reports ($n = 2$) and qualitative ($n = 3$), quantitative ($n = 2$), and mixed-methods studies ($n = 1$).

Characteristics of social withdrawal in HD

Description

Various manifestations of social withdrawal were described. In case reports, social withdrawal included stopping work and decreasing participation in family social activities [10, 11]. In qualitative studies, social withdrawal was often characterized by decreased participation in social activities outside the home, though withdrawal from family members in the home was also described [3, 12–14]. Other articles described withdrawal in more general or absolute terms, e.g., a patient who decided to no longer see anyone socially [13]. Additionally, social withdrawal was characterized in one study as a notable change from the patient's pre-HD personality [3].

Frequency

Articles included descriptions and/or measurement of social withdrawal in persons across the spectrum of HD severity. In a sample of persons with prodromal HD, Downing et al. (2012) reported that decreased socializing was one of the most common changes described by participants and their companions [15]. Almost all participants reported social withdrawal in one qualitative study of neuropsychiatric symptoms [3]. According to Ho and Hocaoglu (2011), participants from premanifest to stage 4 HD endorsed concerns about going out for social occasions [12]. Further, social withdrawal was found to be more common in HD compared to controls, even in patients with preserved motor function [12]. Cruickshank et al. (2020) reported that HD mutation carriers with a mean Total Functional Capacity score of 13 (the maximum possible) had fewer high contact roles, social contacts, and embedded social networks than controls [16].

Associations and negative outcomes

Social withdrawal was associated with a variety of neuropsychiatric, cognitive, and even motor changes. In case reports and qualitative studies, psychiatric changes such as mood swings, irritability, impulsivity, and anxiety were described as co-occurring with and/or exacerbating social withdrawal behaviors [10,

13]. Similar changes were also endorsed by participants in the Ho and Hocaoglu (2011) study, though associations between these features were not reported [12]. Fritz et al. (2018) found that better scores on Satisfaction with Social Roles and Activities and Ability to Participate in Social Roles and Activities measures were associated with lower apathy burden on multiple regression [17]. The two case reports and Ho et al. (2011) also reported cognitive symptoms (e.g., processing speed and attention deficits) as co-occurring with social withdrawal [10–12]. Sherman et al. (2020) additionally noted that cognitive and motor features of HD, such as speech changes and difficulty "keeping up" with conversations, precipitated social withdrawal for some people with HD [14].

Only one study examined physiological changes associated with social withdrawal. Serum neurofilament light protein (Nfl) is an emerging biomarker for HD, potentially predicting HD onset and increasing with disease progression [18]. Cruickshank and colleagues (2020) found that lower levels of serum Nfl were associated with greater size and diversity of social networks in people with HD after controlling for age and gender [16].

Behavioral issues may also contribute to social withdrawal in HD. Two articles reported examples of social withdrawal in prodromal or early-stage HD as related to the person's awareness of their HD diagnosis. In Power's case report, the HD subject chose to withdraw from social interactions after his unexpected HD diagnosis [10]. Despite the patient's early disease stage and preserved functional capacity, he was resistant to restart social activities as recommended by his healthcare providers. In Downing et al.'s (2012) study of coping strategies in prodromal HD, HD participants who attributed functional changes to HD (rather than to benign or other medical reasons) used avoidance, including social withdrawal behaviors, as a coping strategy [15]. Similarly, Sherman et al. (2019) noted that increased watchfulness for progression of HD symptoms (i.e., chorea) precipitated decreased independence and worsening interpersonal relationships [14].

Finally, social withdrawal by HD patients was linked to caregiver burden for family caregivers and others. When HD patients withdraw from social interaction outside the home, family caregivers may feel burdened by the pressure of being the only person to attend to the patient's physical and social needs. One spouse caregiver reported feeling responsible for all of her husband's social interactions, since he refused to leave home [13]. This burden can be exacerbated when a patient has comorbid psychiatric issues (i.e., irritability, aggression) that are also borne by the caregiver alone. In Sherman et al.'s (2020) qualitative study, one HD provider noted that many HD patients become "very isolated" and "burn bridges with everybody around them" [14]. On the other hand, one article described a case where family members disengaged from the socially withdrawn patient due to lack of understanding about HD [10]. Family members were initially embarrassed to be seen with the patient after his diagnosis and did not understand the importance of continued social participation; this encouraged the patient's continued withdrawal.

Alleviating factors

Only one case report described an intervention for social withdrawal. In Power's (1982) report, an eight-week direct rehabilitation intervention was trialed to mitigate social withdrawal in one HD patient [10]. The rehabilitation intervention was facilitated by a counselor and included the HD patient and family members. The intervention encouraged discussion of emotional needs, educated the patient and family about HD, and assigned homework activities for family members to complete with the patient each week. Assignments included daily walks of progressively increasing length, performing household tasks together, and eventual attendance at larger social outings (e.g., going to see a movie). The intervention successfully increased social participation in and outside of the home, culminating in the patient's voluntary return to part-time work [10]. No other case reports or studies in this review described interventions or alleviating factors for social withdrawal in HD.

DISCUSSION

In this review, few studies and case reports were identified which examined or described social withdrawal in HD. This is surprising given the high frequency of social withdrawal seen clinically and noted by HD patients and caregivers [3]. Overall, social withdrawal was common and evident across disease stages. It was associated with symptomatic and physiological markers of disease progression and caused particular burden for family caregivers. Although a successful counseling intervention was described, no prospective studies have evaluated interventions for addressing social withdrawal in

HD. Results revealed additional gaps that may be addressed in future work.

Gaps identified

Limitations in study design, instrumentation, and analysis were noted for the included articles. Only two quantitative studies were identified, and both were cross-sectional [16, 17]. As a result, the directions of the relationships of social functioning measures with apathy and serum Nfl concentrations are unclear. Longitudinal observational studies or randomized controlled trials would be more appropriate to clarify the direction of these effects. Additionally, such studies could systematically assess the effects of other patient variables that might modify social withdrawal in HD patients (e.g., sex, medication use, functional capacity).

Further, caregiver burden was a clear outcome of patient social withdrawal in qualitative studies and case reports, but it was not included as an outcome in either of the quantitative studies in this review. Future studies should attempt to quantify the scope of the effect of social withdrawal on caregiver burden. In such studies, researchers should also consider disease stage in study design and analyses. Results from the current review revealed that people with later stage HD are more dependent, requiring increased caregiver vigilance and safety monitoring [14]. Thus, these caregivers may have more frequent interactions with and responsibility for HD patients- an issue that is exacerbated for caregivers of patients who refuse outside social interaction [13, 14].

In addition to implications for caregiver burden, stratification by disease stage will be critical in future social withdrawal research. It is likely that social withdrawal varies according to disease stage, but existing studies were not designed or powered to assess for statistically significant group differences. In Ho and Hocaoglu's (2011) study, decreased socialization was endorsed by many participants, but was not specifically reported for those in premanifest and stage 5 groups [12]. Additionally, several studies supported the idea that people with prodromal and early-stage HD might intentionally increase social participation. Early-stage participants in Sherman et al.'s (2020) study reported increasing activity (e.g., joining a gym or participating in volunteer opportunities) as a method of coping with their disease [14]. Similarly, some prodromal participants in Downing et al.'s (2012) study went "out of [their] comfort zone" to make social connections or find sustainable work [15]. Future studies should assess group differences by disease stage and examine modifiers of increased versus decreased social participation in early HD. These studies should also consider potential confounding effects based on who is completing social withdrawal measures (patient, caregiver, or clinician), as proxy report is more likely in later stages.

Instrumentation should be carefully considered for future work in this area. Instruments intended to measure social functioning in HD may not actually capture this concept. To measure social functioning in their study, Fritz et al. (2018) used NeuroQoL patient reported outcome measures, including Satisfaction with Social Roles and Activities and Ability to Participate in Social Roles and Activities instruments [17, 19, 20]. However, these instruments more precisely measure patient feelings about current levels of social participation (i.e., satisfaction or disappointment) and patient perception of their ability to participate in social activities, respectively. If attempting to capture levels of actual social functioning or withdrawal, use of these measures is problematic for several reasons. First, socially withdrawn and particularly apathetic patients are likely unbothered by their decreased social participation, thus having little effect on reported levels of satisfaction. Second, patient ability to participate in activities and actual participation are distinct. An HD patient thinking concretely could rate himself as fully able to participate while being socially withdrawn in reality. Finally, the frequency of anosognosia in HD may affect the validity of patient reported outcome measures [21]. These limitations must be considered when interpreting results of the Fritz et al. (2018) study and other studies that use these instruments to measure social functioning or withdrawal. For future quantitative studies, in the absence of a social withdrawal-specific instrument, measures of social network activity and/or objective measures of participation (e.g., geolocation data) are recommended.

Review limitations

A limitation of this review is the nuanced differentiation between social withdrawal versus subjective or perceived isolation. We limited inclusion criteria intentionally because social withdrawal and involuntary social isolation by patients with HD may be related to different factors and may have different effects on patients and their caregivers. In quantitative studies included for full-text review, many of

the instruments used to measure social function or a related concept assessed subjective loneliness or satisfaction with social support; these studies were not relevant for the purposes of this review. Although we reviewed full texts of all potentially relevant articles and included those describing social withdrawal as we defined it, it is still possible that we missed relevant results.

On the other hand, we chose to include studies assessing social network size and diversity, such as the Cruikshank et al. (2020) study [16]. Given the lack of appropriate instruments to measure social withdrawal in HD, we agreed that social network activity would be a reasonable proxy measure for social withdrawal. However, social network size and diversity can also be influenced by external factors, such as driving restrictions or limited social support [14].

Apathy is another concept that can be difficult to distinguish from social withdrawal. Measures of apathy often include items assessing social withdrawal behavior. For example, one FrSBe apathy item assesses frequency of spontaneous involvement in activities [22]. Although apathy may precipitate social withdrawal in HD, the two concepts are distinct. Apathy refers to a neuropsychiatric manifestation of HD, whereas social withdrawal is an observable behavioral phenomenon. We did not include apathy as a proxy for social withdrawal in this review because social withdrawal can also be related to other factors (i.e., anxiety or perceived stigma) [3, 14]. Despite these differences, studies of apathy in HD may offer additional insights regarding the nature of social withdrawal in this population. For example, when measured using FrSBe, apathy has been associated with worse emotion recognition in people with HD [23]. It is logical that emotion recognition and related theory of mind deficits may play a role in the mechanisms underlying social withdrawal in HD. However, studies are needed that specifically assess these deficits in relation to social withdrawal. Future research can clarify how apathy and other cognitive changes (e.g., cognitive inflexibility) moderate this relationship.

Additionally, we did not include studies that specifically assessed outcomes associated with the genetic testing process in HD. This was intentional in order to separate social withdrawal as a manifestation of the disease from withdrawal as a coping response. However, based on our results, gene-positive HD patients may be more likely to socially withdraw as a result of diagnosis or symptom attribution to HD. Thus, withdrawal after genetic diagnosis may similarly be related to HD, rather than to the testing process alone, and an exploration of genetic testing literature could add to this understanding.

CONCLUSION

Although social withdrawal is a common manifestation of HD, its description in the literature is limited. Studies are generally small and/or have significant limitations in design or instrumentation. Further, we identified no prospective studies testing interventions to reduce social withdrawal in HD. Valid measures are needed to accurately capture social withdrawal in HD, and much more research is needed to determine associated factors and potential modifiers. Only then can interventional trials be implemented to address this pressing clinical issue.

ACKNOWLEDGMENTS

JSG is supported as an iTHRIV Scholar under Award Numbers KL2TR003016/ULTR003015 through the National Center for Advancing Translational Sciences of the National Institutes of Health and has received additional research funding from University of Virginia; she has also received research funding and personal fees for consulting from Teva Branded Pharmaceutical Products, R&D, Inc. KS has no conflicts to declare.

CONFLICT OF INTEREST

The authors have no conflict of interest to report.

REFERENCES

[1] Seeley WW. The salience network: A neural system for perceiving and responding to homeostatic demands. J Neurosci. 2019;39(50):9878-82.

[2] Pini L, Jacquemot C, Cagnin A, Meneghello F, Semenza C, Mantini D, et al. Aberrant brain network connectivity in presymptomatic and manifest Huntington's disease: A systematic review. Hum Brain Mapp. 2020;41(1):256-69.

[3] Gibson JS, Rhoten BA, Ridner SH, Claassen DO. Perceived effects of neuropsychiatric symptoms on functional status in early-stage Huntington disease. West J Nurs Res. 2022;44(2):141-50.

[4] Glidden AM, Luebbe EA, Elson MJ, Goldenthal SB, Snyder CW, Zizzi CE, et al. Patient-reported impact of symptoms in Huntington disease: PRISM-HD. Neurology. 2020;94(19):e2045-e2053.

[5] Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: A meta-analytic review. Perspect Psychol Sci. 2015;10(2):227-37.

[6] World Health Organization. Constitution of the World Health Organization [Internet]. 1946. Available from: https://apps.who.int/gb/bd/PDF/bd47/EN/constitution-en.pdf?ua=1

[7] Santini ZI, Jose PE, York Cornwell E, Koyanagi A, Nielsen L, Hinrichsen C, et al. Social disconnectedness, perceived isolation, and symptoms of depression and anxiety among older Americans (NSHAP): A longitudinal mediation analysis. Lancet Public Health. 2020;5(1):e62-e70.

[8] Coyle CE, Dugan E. Social isolation, loneliness and health among older adults. J Aging Health. 2012;24(8):1346-63.

[9] Pollock D, Davies EL, Peters MDJ, Tricco AC, Alexander L, McInerney P, et al. Undertaking a scoping review: A practical guide for nursing and midwifery students, clinicians, researchers, and academics. J Adv Nurs. 2021;77(4): 2102-13.

[10] Power PW. Family intervention in rehabilitation of patient with Huntington disease. Arch Phys Med Rehabil. 1982;63(9):441-2.

[11] Kowalski PC, Belcher DC, Keltner NL, Dowben JS. Biological perspectives: Huntington's disease. Perspect Psychiatr Care. 2015;51(3):157-61.

[12] Ho AK, Hocaoglu MB. Impact of Huntington's across the entire disease spectrum: The phases and stages of disease from the patient perspective. Clin Genet. 2011;80(3):235-9.

[13] Williams JK, Skirton H, Paulsen JS, Tripp-Reimer T, Jarmon L, McGonigal Kenney M, et al. The emotional experiences of family carers in Huntington disease. J Adv Nurs. 2009;65(4):789-98.

[14] Sherman CW, Iyer R, Abler V, Antonelli A, Carlozzi NE. Perceptions of the impact of chorea on health-related quality of life in Huntington disease (HD): A qualitative analysis of individuals across the HD spectrum, family members, and clinicians. Neuropsychol Rehabil. 2020;30(6):1150-68.

[15] Downing NR, Williams JK, Leserman AL, Paulsen JS. Couples' coping in prodromal Huntington disease: A mixed methods study. J Genet Couns. 2012;21(5):662-70.

[16] Cruickshank T, Bartlett D, Govus A, Hannan A, Teo WP, Mason S, et al. The relationship between lifestyle and serum neurofilament light protein in Huntington's disease. Brain Behav. 2020;10(5):e01578.

[17] Fritz NE, Boileau NR, Stout JC, Ready R, Perlmutter JS, Paulsen JS, et al. Relationships among apathy, health-related quality of life, and function in Huntington's disease. J Neuropsychiatry Clin Neurosci. 2018;30(3):194-201.

[18] Byrne LM, Rodrigues FB, Blennow K, Durr A, Leavitt BR, Roos RAC, et al. Neurofilament light protein in blood as a potential biomarker of neurodegeneration in Huntington's disease: A retrospective cohort analysis. Lancet Neurol. 2017;16(8):601-9.

[19] Cella D, Lai JS, Nowinski CJ, Victorson D, Peterman A, Miller D, et al. Neuro-QOL: Brief measures of health-related quality of life for clinical research in neurology. Neurology. 2012;78(23):1860-7.

[20] Carlozzi NE, Hahn EA, Goodnight SM, Kratz AL, Paulsen JS, Stout JC, et al. Patient-reported outcome measures in Huntington disease: Quality of life in neurological disorders (Neuro-QoL) social functioning measures. Psychol Assess. 2018;30(4):450-8.

[21] Isaacs D, Gibson JS, Stovall J, Claassen DO. The impact of anosognosia on clinical and patient-reported assessments of psychiatric symptoms in Huntington's disease. J Huntingtons Dis. 2020;9(3):291-302.

[22] Stout JC, Ready RE, Grace J, Malloy PF, Paulsen JS. Factor analysis of the frontal systems behavior scale (FrSBe). Assessment. 2003;10(1):79-85.

[23] Kempnich CL. Emotion recognition correlates with social-neuropsychiatric dysfunction in Huntington's disease. J Int Neuropsychol Soc. 5;24(5):417-23.

[24] Cohen S. Social supports and physical health: Symptoms, health behaviors, and infectious disease. In: Life-span developmental psychology: Perspectives on stress and coping. Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc; 1991. pp. 213-34.

[25] Cohen S, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JMJ. Social ties and susceptibility to the common cold. JAMA. 1997;277(24):1940-4.