Prevalence of convergence insufficiency-type symptomatology in Parkinson's disease

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Running title: Convergence insufficiency in Parkinson

Word count (abstract): 231
Word count (text) : 2360

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Abstract

Background : Individuals with Parkinson's disease (PD) often present visual symptoms (eg. difficulty in reading, double vision) that can also be found in convergence insufficiency (CI). The objective was to estimate the prevalence of CI-type visual symptomatology in individuals with PD, in comparison with controls.

Methods : Participants ≥ 50 yrs with (n= 300) and without (n= 300) PD were recruited. They were administered the Convergence Insufficiency Symptom Survey (CISS-15) over the phone. A score of ≥ 21 on the CISS-15, considered positive for CI-type symptomatology, served as cut-off. Data from individuals (n= 87 with, n= 94 without PD) who were approached but who reported having a known oculovisual condition were analyzed separately. Student t test and Chi-square at the 0.05 level were used for statistical significance.

Results : 29.3% of participants with vs 7.3% without PD presented a score of ≥ 21 on the CISS-15 (p= 0.001). Of the participants having a known oculovisual condition, 39.1% with vs 19.1% without PD presented a score of ≥ 21 on the CISS-15 (p= 0.01).

Conclusion : The prevalence of CI-type visual symptoms is higher in individuals with vs without PD whether or not they have a co-existing oculovisual condition. These results suggest that PD *per se* places individuals with the disease at greater risk of visual symptomatology. These results further underline the importance of providing regular eye exams to individuals with PD.

Introduction :

Patients with Parkinson's disease (PD) have a variety of non-motor symptoms that are becoming more recognized[1]. Among these are oculovisual symptoms such as dry eyes[2], difficulty reading and double vision[1,3] that can affect quality of life in PD patients. Alterations in some visual functions have also been documented in PD, among which is convergence insufficiency (CI), a decreased ability to converge both eyes on an object located at near distance[2]. When present, CI can lead to blurred vision, tearing, ocular fatigue, double vision and make it difficult or impossible for a person to read comfortably. This can be detrimental to many aspects of a person's life in modern countries where the ability to read efficiently permeates the educational, working or even recreational environments.

Over the last two decades, a few studies have addressed CI-type symptomatology in individuals with PD[2-6]. The CI-related symptoms most frequently cited in PD were difficulty reading and diplopia. All of these studies, however, were conducted on limited numbers of participants and none used a questionnaire developed and validated for CI. Our objective was to estimate the prevalence of CI-type symptomatology in a systematic fashion, in a large population of individuals with PD, compared to age-matched controls.

Methods :

This study was conducted in collaboration with the Institut universitaire de gériatrie de Montréal (IUGM), the Centre hospitalier de l'Université de Montréal (CHUM) and the Montreal General Hospital (MGH). The study protocol was approved by the Research Ethics Committee of each of the three hospitals and the study was conducted according to the Declaration of Helsinki.

Participants signed an informed consent in accordance with the requirements of the various ethics committees.

A total of 300 participants ≥ 50 yrs of age with a clinical diagnosis of PD were recruited from the Movement Disorder Clinics (MDC) of the neurology department at the CHUM and MGH (Figure 1). They were each matched for age (± 5 yrs) and opposite sex to a control participant without PD. Opposite sex was used in trying to facilitate recruitment in case spouses would be interested in participating and knowing that a gender-related prevalence of CI has not been documented[7]. A control was chosen among the spouse, family or friends of each participant with PD and if none was found, then the control was recruited from the bank of participants at the IUGM. A few controls had to be recruited from a third alternative source, i.e. the Clinique universitaire de la vision de l'Université de Montréal. The matching was done with a spouse (20.0%), a family member (0.3%) or another unrelated adult (79.7%).

A review of clinical charts excluded individuals where binocular dysfunction other than CI (eg. strabismus), known ocular disease/decreased visual acuity (eg. glaucoma, age-related macular degeneration, amblyopia), other forms of neurodegenerative disease (eg. Huntington's disease, dementia) or diseases likely to affect the extraocular muscles (eg. Graves' thyroid disease, myasthenia gravis) or visual function (eg. diabetes) were reported.

Individuals who met the study criteria based on their clinical chart review were contacted by mail and provided the following documents: research neurologist's letter explaining the study, ethics documents including the information and consent, answer codes for the convergence

insufficiency symptom survey (CISS-15) questionnaire. Approximately 10 days later the research assistant (RA) called each individual to answer any questions and determine if they were interested in taking part in the study. If individuals did not want to participate no other contact was made. If a person was interested in participating, he/she was first allowed to ask any question related to the study, and was then given the choice to answer the phone questionnaires right away or at any other convenient time. The participant was asked to sign the consent form and mail it to the research team, according to each Ethic committee's requirement.

Phone interviews lasted about 30 minutes on average. Four questionnaires were filled over the phone by the RA, in the following order: 1) Adult Lifestyles Function Interview (ALFI), 2) Ocular history, 3) General health, and 4) CISS-15. The first three questionnaires were used to further assess the eligibility of study participants. The ALFI is a telephone-administered version of the Mini-Mental State Examination (MMSE), that comprises 22 items aimed at screening for cognitive impairment[8]. A score below 14 was used as an exclusion criterion[9]. The ocular history and general health questionnaires were developed by the clinician/researcher specialists on our team, to ensure that the conditions specified by our inclusion/exclusion criteria were met. The CISS-15 questionnaire[10] was designed to estimate the frequency and severity of CI symptoms and has been shown to be a valid and reliable instrument for CI treatment outcomes[11]. It contains 15 items with a 5 digit scale from 0 to 4. The response to each item expresses the frequency of symptom occurrence (0= never; 4= always) and the potential total score, obtained by adding the individual response scores, ranges from 0 to 60, higher scores indicating greater symptom severity. A score of 21 has been shown to distinguish between symptomatic ($\geq$ 21) *vs* asymptomatic (< 21) individuals[11] and served as the cut-off for CI-type symptomatology in this

study. All individuals who consented to participate were asked to answer the 4 questionnaires over the phone. Some had to be excluded from the main study because they indicated having a binocular dysfunction other than CI or an ocular disease. Their data were kept and entered in a different Excel spreadsheet.

The statistical average differences and percentage differences between two independent groups were respectively determined using the Student *t* test and Chi-square at the 0.05 level of significance.

Results :

The PD group included 121 women and 179 men with an average age of 67.3 ± 8.9 yrs, while the control group comprised 179 women and 121 men with an average age of 67.2 ± 8.7 yrs ($p > 0.05$). The participants with PD had an average of 2.9 ± 1.7 diseases, were taking 5.1 ± 2.8 medications, including 2.3 ± 1.1 PD-related medications, while the controls had an average of 1.6 ± 1.4 diseases and were taking 2.1 ± 2.2 medications ($p < 0.001$). The mean duration of PD was 8.4 ± 5.9 yrs. The group-average score on the ALFI was 19.5 ± 2.3 for PD participants and 20.3 ± 1.9 for controls ($p = 0.001$). The group-average score on the CISS-15 was 15.7 ± 9.3 for PD participants and 10.3 ± 7.0 for controls ($p = 0.001$). 29.3% ($n = 88$) of PD participants and 7.3% ($n = 22$) of controls ($p = 0.001$) had scores on the CISS-15 of ≥ 21.

87 participants with (36 women) and 94 without (68 women) PD were excluded from the main study for known ocular disease (n= 51 PD; n= 57 controls) or binocular vision anomaly other than CI (n= 36 PD; n= 37 controls). (Figure 2) Their average age was 70.5 ± 9.7 yrs for the PD

participants and 70.7 ± 8.9 yrs for the controls (p> 0.05). The participants with PD had an average of 3.8 ± 2.0 diseases, were taking 5.9 ± 2.6 medications, including 2.3 ± 1.1 PD-related medications, while the controls had an average of 2.0 ± 1.9 diseases and were taking 2.5 ± 2.0 medications (p< 0.01). The mean duration of PD was 9.0 ± 6.3 yrs. The group-average score on the ALFI was 18.9 ± 2.4 for PD participants and 20.1 ± 1.8 for controls (p= 0.001). The group-average score on the CISS-15 was 19.3 ± 11.2 for PD participants and 13.7 ± 9.2 for controls (p= 0.001). A score on the CISS-15 of ≥ 21 was obtained for 39.1% (n= 34) participants with and 19.1% (n= 18) without PD (p= 0.01).

An analysis of individual CISS symptoms in participants having positive CI symptomatology, revealed that "eyes feel tired" and "eyes feel uncomfortable" when reading or doing close work stood out the most for PD and non-PD participants. (Table 1) Those that emerged least were "headache" for "included/excluded" PD / "included" non-PD participants, and "double vision" for "excluded" non-PD participants.

Discussion :

This study indicates that CI-type visual symptomatology: 1) is higher in PD *vs* non-PD participants, 2) remains higher in PD *vs* non-PD participants, for those having a known oculovisual condition, and 3) is higher in PD and non-PD participants having *vs* not having a known oculovisual condition. Overall, these results indicate that having a known oculovisual condition is accompanied by a high prevalence of visual symptoms and they further suggest that having PD *per se* places individuals with the disease at higher risk of visual symptomatology.

The prevalence of CI-type visual symptomatology in individuals with PD (29.3%) was found to be 4 times greater than for those without PD (7.3%), and 2 times higher in PD (39.1%) *vs* non-PD (19.1%) for individuals with a pre-existing oculovisual condition. These results are rather strong and deserve some interpretation. It is important to point out that the CISS-15 questionnaire used in the present study was originally designed by experts to address the symptoms most likely to be present in individuals having a diagnosis of CI, to serve as an outcome measure of success for CI treatment. In other words, this questionnaire was to be used in people already having a diagnosis of CI, and was not meant to serve as a screening tool for CI. Knowing this limitation, the CISS-15 questionnaire was used here since it was the only existing validated tool to at least enquire about "CI-type" symptoms that could be used in a large number of participants. The similarity of symptoms found in CI and in other oculovisual conditions could have increased the prevalence of symptoms found in the present study. The elevation of CISS scores in those having a known oculovisual condition is consistent with this. The present results confirm those obtained in our previous report[12], indicating that "eyes feel tired or uncomfortable while reading or doing close work" is a more prevalent/severe symptom than "double vision" in that population and suggest that this item could be added in non-motor screens to better identify PD individuals with vision problems. It is important also to point out that our data showing a higher prevalence of CI-type symptomatology in PD does not indicate that a *diagnosis* of CI is more prevalent in PD. Further research that would include a complete eye exam is needed to address this issue and has been pursued in view of the strength of the results obtained here. Although the limited resources available for the present study prevented the provision of an eye exam for all participants, we have been able to perform eye exams in a subset of 80 PD and 80 non-PD participants. Results from this research have shown that a clinical diagnosis of CI is in

fact more prevalent in PD (43.8%) *vs* non-PD (16.3%) participants[12]. Taken together, these prevalence data underline the importance of evaluating oculovisual symptomatology and CI in individuals with PD. Oculovisual symptomatology being particularly prevalent in PD, it is important to provide these individuals with regular eye exams and treat any underlying oculovisual condition if at all possible. If symptoms were to be linked with a diagnosis of CI, in patients experiencing significant discomfort and decreased quality of life, then it could be possible to offer them some form of treatment such as prism or orthoptic therapy. These therapies would have to be decided upon based on the stability of the clinical findings however and, if judged of potential benefit, would have to be well explained and reserved to highly motivated patients, since they are known to work for older individuals[13-15] but have not been formally evaluated in PD.

Another limitation to this study is that we could not stage the severity of PD since the UPDRS ratings or Hoehn and Yahr staging were not available. Although this does not allow a comparison between severity of PD *vs* severity of CI-type symptomatology, it does not change the results that indicate a higher prevalence of CI-type symptomatology in PD *vs* non-PD individuals. In addition, using clinical charts to identify and recruit PD participants may have affected the population representativity of our sample but it would be difficult to give an opinion on the direction or magnitude of any potential selection bias. However, the strength of the data suggests that similar results would likely have been obtained in another PD population recruited under a different mode of selection.

Despite acknowledged limitations, the higher prevalence of symptoms found in those having PD certainly stresses the impact the disease has on the oculovisual system. It has been reported that ocular changes take place early on in the course of PD, likely a result of the disease itself[2]. Our results further suggest that particular care should be provided to patients with PD during an eye exam, to verify the extent of their symptoms and address them if at all possible. Similarly, as mentioned by Chaudhuri et al[1], neurologists should also pay special attention to non-motor symptoms, including the oculovisual ones, in the care of their PD patients. This is particularly important knowing that PD medications can have a positive effect on visual function[6,16]. To that effect, it is worth mentioning that day-time somnolence has been linked with diplopia[3]. The authors suggested that drowsiness may alter the ability to maintain fusion[3], a condition that may or may not be helped by PD medications, depending on whether the drowsiness is induced by a symptomatic undiagnosed binocular vision problem, by the medication itself, or due directly to the disease process itself (i.e. degeneration of wake-promoting nuclei). It is interesting to add that the issue of how ocular pathology contributes to disability in PD has been raised in a review paper addressing the retina in PD[17]. Although our results cannot provide any answer to that question, they certainly demonstrate that symptoms are higher in the presence of an ocular pathology or a visual dysfunction and they reinforce the importance of pursuing research aimed at better understanding vision in PD.

In conclusion, our data have shown that CI-type symptomatology is higher in individuals with PD having or not a concurrent visual dysfunction or ocular pathology. Our results further stress the importance of providing regular eye exams for individuals affected by the disease.

Acknowledgements:

Conflict of interest :

The authors have no conflict of interest to report.

Authors' roles :

Conception of the project (EC, MJK, BSL, MP, ELI, HK); data acquisition (CL, EC); expertise in various aspects of participant's recruitment (MJK, MP, ELI, RP, SC, HK); writing and critical review of the manuscript (all co-authors); statistical analyses (BSL).

Disclosure :

C Law has no conflict to report.

E Chriqui has no conflict to report.

MJ Kergoat received grants from the Fonds de la Recherche en Santé Québec-Fonds d'innovation Pfizer sur la maladie d'Alzheimer et les maladies apparentées, the Canadian Institute of Health Research and the Canadian Consortium on Neurodegeneration in Aging, the Comité aviseur pour

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