Recognizing visual complaints in people with multiple sclerosis: Prevalence, nature and associations with key characteristics of MS

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ABSTRACT

Keywords: Multiple sclerosis Vision Prevalence

Background: Visual disturbances are common in multiple sclerosis (MS), but visual complaints may be underestimated. While these complaints decrease quality of life, they may not be discussed during clinic visits. People with MS (pwMS) may not be referred to appropriate care. We therefore investigated the prevalence, nature and associations of visual complaints of pwMS.

Methods: We performed a cohort study with a comparison group. PwMS (n = 493) and healthy controls (n = 661) filled out the Screening Visual Complaints questionnaire (SVCq). Primary outcomes were the percentage of pwMS and controls that reported the 19 complaints, and total scores of the SVCq. We also compared the scores on the SVCq between different groups of pwMS.

Results: In general, the complaints were reported more often by pwMS than by controls. PwMS especially reported experiencing complaints ‘often/always’, while controls reported the complaints primarily ‘sometimes’. PwMS with and without a history of optic neuritis showed similar complaints. PwMS with a longer disease duration and those with SPMS reported more complaints. EDSS score and disease duration only showed a limited association with discomfort of visual complaints.

Conclusion: The prevalence of visual complaints among pwMS is high and any person with MS may experience a wide array of different visual complaints anywhere along the disease course, regardless of a history of optic neuritis. Using the SVCq may help detect pwMS’ visual complaints and may facilitate referrals to appropriate care.

ARTICLE INFO

1. Introduction

Since a large part of the cerebral cortex is involved in processing visual information, visual disturbances are common among people with acquired brain injury or a neurodegenerative disease, such as stroke (Hepworth et al., 2016), traumatic brain injury (Armstrong, 2018), Parkinson’s disease (Davidsdottir et al., 2005) and dementia (Colligaris et al., 2018). MS may also affect the brain and visual disturbances are common in MS (Salter et al., 2013). Moreover, MS may affect all parts of the visual system.

Diminished visual functions that are commonly described among people with MS (pwMS) are reduced visual acuity, altered color vision, a decreased contrast sensitivity, visual field defects and eye movement abnormalities, such as nystagmus or internuclear ophthalmoplegia (Hoff et al., 2019; Hickman et al., 2014; Costello, 2016; Francis, 2013; Balcer et al., 2015). PwMS may also show visuo-perceptual abnormalities (Vleugels et al., 2000).

Besides diminished visual functions, pwMS may report visual complaints such as blurred vision, difficulty seeing in bright light or diplopia (Jasse et al., 2013; Ma et al., 2002). These complaints may well reduce the quality of life and pwMS regard good visual functioning as highly valuable (Jasse et al., 2013; Heesen et al., 2008). However, contrary to...
the visual functions assessed in pwMS, visual complaints are hardly described in the literature. There could be several reasons why visual complaints may be underrecognized. If one would solely rely on objective measurement of visual functions, visual complaints may be missed. For example, while visual functions may be intact after a recovered optic neuritis (ON), pwMS do still report visual disturbances (Jasse et al., 2013; Cleary et al., 1997). Visual problems may also fluctuate from day to day or even hour to hour, which causes measurement of visual disturbances to be challenging (Roodhoft, 2012). Furthermore, visual complaints may be mistaken for more known symptoms that are easier to recognize, more predominant in MS, or more widely known. Moreover, research points out that it is difficult for patients to express their visual complaints, unless physicians ask about visual disturbances specifically. Visual complaints may be described as dizziness or as a headache, or generally as blurry vision (Hoff et al., 2019; Berthold-Lindstedt et al., 2017; Balcer et al., 2000). Worsened by time constraints, visual complaints may not be discussed at the doctor’s office and pwMS may not reach the appropriate care or rehabilitation, which may further reduce quality of life.

More knowledge and understanding of visual complaints reported by pwMS may improve recognition of visual complaints in MS and may facilitate access to appropriate care or rehabilitation. The purpose of our study is therefore to register prevalence, nature and associated discomfort of visual complaints in a cohort of pwMS. We also aim to compare the reported visual complaints of pwMS with (MS-ON) and without a history of ON (MS-NON). Furthermore, we aim to investigate associations with key characteristics of MS, such as type, disability in terms of EDSS (Cohen et al., 1993), disease duration, and with demographic variables.

2. Methods

2.1. Study population and design

This cohort study was performed at the MS Centrum Noord Nederland (MSCNN), a center specialized in care for pwMS. The patient cohort was invited to complete the SCVq (Huizinga et al., 2020). PwMS who did not speak Dutch or were, according to the neurologist, too severely disabled (cognitively or otherwise) were not invited to participate.

For a comparison group, healthy Dutch participants were invited to complete the SCVq (Huizinga et al., 2020). Participants were excluded when they had any serious neurological, ophthalmological or psychiatric conditions. Healthy participants were recruited via Panel Insicht and received a small financial reward. See Huizinga et al. (2020) for a detailed description of the methods. Of the total sample of healthy controls, a sample was selected to match the distribution of age and sex of the patient cohort.

2.2. Materials

The SCVq (Huizinga et al., 2020) was used to assess visual complaints as experienced in the last two weeks. Participants who used glasses or contact lenses were asked to answer the questions as if they were wearing them. First, participants reported any complaints regarding their sight. In the second part, participants rated 19 statements regarding visual complaints on frequency of occurrence (0—‘never/hardly’, 1—‘sometimes’ 2—‘often/always’). The total score of the SCVq is calculated by summing the score on all 19 complaints. At the end, participants rated their discomfort in daily life due to the visual complaints on a scale from 0 to 10.

2.3. Procedure

The invitations for the questionnaires were distributed among the pwMS either during the regular visits to the neurology departments (n = 409), or via postal mail (n = 198) between July 2017 and November 2019. The invitation contained a short information letter, the URL to a Qualtrics webpage in which the questionnaire was programmed, and a personal code for anonymization. The patients could complete the questionnaire anytime and anywhere, on a self-chosen device. After completion, an automatic e-mail with the results was sent to the neurologist. All patients who did not complete the questionnaire initially, received a follow-up telephone call. These patients either completed the questionnaire directly on the telephone in cooperation with a research assistant or filled out the questionnaire on their own until October 2020. Information concerning the type of MS, the year of the diagnosis, EDSS, history of ON, VEP, and comorbidities was extracted from the patients’ medical files.

2.4. Data analysis

2.4.1. Matching healthy controls to the patient group

The healthy controls were matched in terms of age and sex on group level to assure a comparable control group with respect to the patient group. For females and males separately, the distribution of age in the patient group was determined in 16 age groups (5-year range). The number of healthy controls needed in each age group was achieved by applying the same frequencies in each age group of the patient group to the healthy control group. The highest possible number of healthy controls in each age group was randomly selected from the healthy participants.

2.4.2. Assumptions

All variables were measured independently and were on the interval (total score, number of complaints, discomfort) or the ordinal level (individual complaints). Kolmogorov-Smirnov test of normality was used to assess normality for total score, number of complaints and the discomfort score. Since normality was violated for all of the variables, we performed non-parametric tests.

2.4.3. Frequencies of complaints

For every complaint, the percentage of pwMS and healthy controls that experienced that complaint ‘never/hardly’, ‘sometimes’ or ‘often/always’ was calculated. The percentage of pwMS and healthy controls that reported the complaints ‘often/always’ was plotted in a combined bar graph. The same procedure was performed for MS-ON and MS-NON pwMS. Using 2 x 3 contingency tables and X^2 testing, the frequencies were compared between (1) pwMS and healthy controls and (2) MS-ON and MS-NON pwMS. Adjusted residuals (z-score of expected counts versus observed counts, taking sample size into account) were calculated. Applying Bonferroni’s correction, residuals of >2.64 were needed to reach a significance (0.05/6: p = 0.008) (MacDonald and Gardner, 2000). Cramer’s V was calculated for effect sizes (small: 0.07–0.21, medium: 0.21–0.35 and large: >0.35, df = 2 (Kim, 2017)).

2.4.4. SCVq scores

The total score on the SCVq, the discomfort score, the total number of complaints (number of complaints rated ‘often/always’, or ‘sometimes’), and the number of complaints that were reported ‘often/always’ were calculated and compared between (1) pwMS and healthy controls, (2) MS-ON and MS-NON pwMS, (3) pwMS with different types of MS (RRMS, SPMS and PPMS, (4) pwMS in different disability groups (mild, EDSS 0–3; moderate, EDSS 3.5–5; severe, EDSS 5.5–7 and very severe, EDSS >7), and (5) female and male pwMS. Kruskal-Wallis and Mann-Whitney-U tests were used for statistical testing. For effect sizes, coefficient r was calculated (small: 0.1–0.3, medium: 0.3–0.5 and large: 0.5–1.0 (Cohen, 1989)). Spearman’s correlations between the SCVq scores and disease duration and age were calculated.

3. Results

A total number of 607 SCVq’s were handed out. In total, 537 (89%)
SVCq’s were received back. After eliminating duplicates (in case a patient completed the SVCq multiple times during the study period), 507 unique pwMS remained. Of those, 493 (97%) patients gave consent to use the data. It took the patients approximately 10 min to complete the questionnaire. The patients that did not fill out the SVCq were either unwilling to do so, or could not be reached by telephone.

A total of 1402 healthy controls participated in the study. From the total healthy group, 661 age and sex matched controls were selected. The demographics, disease characteristics and comorbidities of the pwMS and the demographics of the controls are presented in Table 1. Seventy percent of the pwMS were female. Within the MS sub groups, this was 72% for RRMS, 74% for SPMS and 49% for PPMS.

3.1. Frequencies of complaints

3.1.1. PwMS and healthy controls

The frequencies of the complaints reported ‘often/always’ by pwMS and controls are presented in Fig. 1, a summary of the prevalence rates in pwMS is presented in Table 2 and test statistics are presented in Table 3. Within the cohort of pwMS, 90% of the pwMS experienced at least 1 complaint, 52% at least 5 and 23% at least 10 complaints. For the healthy controls this was respectively 67, 43 and 10%, indicating that visual complaints were prevalent in both pwMS and healthy controls.

The overall prevalence of the complaints was higher among pwMS than controls, except for having trouble focusing and experiencing distorted images. The effect sizes of the difference in frequencies of complaints reported either ‘often/always’ or ‘sometimes’ were regarded small, and in some cases medium size. However, the number of pwMS experiencing complaints ‘often or always’ was significantly higher than of healthy controls (adjusted residuals of >2.64) in the majority of the complaints (Tables 2 and 3), showing that pwMS experience visual complaints more frequently.

The prevalence of pwMS that rated double vision, seeing things that others do not and painful eyes as ‘often/always’ did not differ from controls, but more pwMS did report to experience these complaints ‘sometimes’ than controls.

Unclear vision and problems with reading were common among both pwMS (54 and 44%) and healthy controls (57 and 37%). PwMS reported these complaints more often, but the individual adjusted residuals did not show effects that were large enough (adjusted residuals of <2.64) to reach significance.

An analysis of the open question revealed similar complaints among the pwMS relative to the 19 statements of the SCVq. PwMS noted that complaints vary along the day and were influenced by temperature and the severity of their current fatigue.

3.1.2. PwMS with and without a history of ON

Fig. 2 shows the frequencies of the complaints reported ‘often/always’ by MS-ON pwMS and MS-NON pwMS, test statistics are presented in the Supplementary materials, (Suppl 1). Most complaints were equally prevalent in the MS-ON and MS-NON groups. With a medium effect size, the MS-ON pwMS reported to experience color vision ‘sometimes’ more frequently (29 vs 7%). The prevalence of complaints regarding visual field was higher in MS-ON pwMS, with a small effect size. MS-ON pwMS reported to experience this complaint ‘often/always’ (14 vs 4%). Depth perception and needing more time were also reported by more MS-ON than MS-NON pwMS (48 vs 31% and 54 vs 40%).

3.2. Total SVCq score, number of complaints and discomfort

Table 4 and the Supplementary materials (Suppl 2) present the total scores on the SVCq, the experienced discomfort and the number of complaints (total and ‘often/always’) of pwMS and controls. Compared to the healthy controls, pwMS had a higher total score and higher number of complaints, with small effect sizes. The experienced discomfort did not differ between pwMS and controls. MS-ON pwMS showed a higher total score, more discomfort in daily life and a higher total number of complaints compared to MS-NON pwMS. Effect sizes were small.

3.3. Type of MS, EDSS and disease duration

Tables 5–7 show the total scores, the experienced discomfort and the number of complaints for type of MS and disability score. PwMS with SPMS showed the highest total score and reported more complaints than pwMS with RRMS or PPMS, with small effect sizes. PwMS with RRMS and PPMS did not differ from each other. PwMS with a higher disability score experienced more discomfort from visual complaints, with a significant difference between pwMS with mild disability and severe or very severe disability (Suppl 3). The total score and number of complaints slightly increased with disability, but not significantly. With small effect sizes, discomfort and number of complaints ‘often/always’ increased with disease duration (Suppl 4). The nature of complaints was hardly influenced type by of MS or disability (Suppl 5 and 6).

3.4. Demographics

Female pwMS had on average a higher total score, reported more complaints and, though not significantly, experienced more discomfort from these complaints than male pwMS. All effect sizes were small. Older pwMS reported significantly more complaints as ‘often/always’,...
However, most other complaints were known to be characteristic of ON (Salter et al., 2013; Shams and Plant, with color vision and visual field more often, which are complaints a history of ON. PwMS with a history of ON reported to have problems and sex. While the prevalence of visual complaints has a high baseline in healthy controls, pwMS do report to experience visual complaints more often. This is in accordance with previous studies among pwMS, but the correlation was only small (Suppl 7).

4. Discussion

The aim of the present study was to investigate the prevalence, nature and discomfort of visual complaints in pwMS, and the association of visual complaints with ON, type of MS, disability, disease duration, age and sex. While the prevalence of visual complaints has a high baseline in healthy controls, pwMS do report to experience visual complaints more often. This is in accordance with previous studies among pwMS, but the prevalence rate of visual complaints in our study was higher than previously reported (Ma et al., 2002; Noble et al., 2006; Balcer et al., 2000). These studies used the NEI-VFQ-25 (Mangione et al., 2001), targeting difficulties with visual activities and assessing only a small number of functional complaints, whereas the SVCq assesses primarily functional complaints. While the overall effect sizes between pwMS and controls were small to medium, especially a larger proportion than expected of the pwMS reported the complaints as ‘often/always’.

In addition, our study shows that not only the prevalence of visual complaints is high, pwMS also experience a wide array of different visual complaints. Only some visual complaints have been mentioned in earlier research in association with visual disorders known to occur in MS, such as ON or eye movement abnormalities. In our study, pwMS with a history of ON did report a higher number of complaints than pwMS without a history of ON. PwMS with a history of ON reported to have problems with color vision and visual field more often, which are complaints known to be characteristic of ON (Salter et al., 2013; Shams and Plant, 2009; Bermel and Balcer, 2013). However, most other complaints were equally prevalent in pwMS with and without a history of ON. This indicates that ON may only explain some of the visual complaints, and that pwMS may be more susceptible to many kinds of visual complaints, regardless of a history of ON. MS-ON pwMS in our study with an aberrant VEP-result only experienced altered color vision more often than the MS-NON pwMS in our study with an aberrant VEP-result. This may indicate that some pwMS in the MS-NON group might have had an (sub clinical) ON, leading to an aberrant VEP, but not to altered color vision.

Discomfort did not differ between the pwMS and controls, while pwMS reported visual complaints more often. This may be counterintuitive. However, pwMS generally suffer from multiple symptoms, which may make it more difficult to distinguish the impact on well-being of vision-related problems from other symptoms, since vision-related problems may be only one of the many factors contributing to discomfort in daily life (Barin et al., 2018). Research also points out that visual disturbances negatively impact quality of life more than several chronic diseases, but not MS (Langelaan et al., 2007). Moreover, pwMS are constantly adapting to their progressing disease while continuing to use coping strategies (Jean et al., 1997).

With regard to other MS-related variables, pwMS with a longer disease duration experience more complaints often, with more discomfort than pwMS with a shorter disease duration. This indicates that complaints that are experienced more often may lead to more discomfort. Disability was only associated with the experienced discomfort, but not with the number of complaints. This is in accordance with Collins et al. (2016) who suggested that the EDSS score does not correlate well with patient-reported disability in general. This is largely explained by the limited number of items related to visual functioning in the EDSS (Collins et al., 2016). Visual disturbances will not increase the EDSS score. Regarding type of MS, people with SPMS reported more complaints than people with PPMS. People with SPMS also seem to report more complaints than people with PPMS. However, since females reported more complaints than males, the difference in the number of visual complaints between PPMS and SPMS may be explained by the difference in male-female distribution, since the predominance of females in SPMS (72 vs 49% in PPMS) may account for the higher number of complaints (Miller and Leary, 2007).

It has to be noted that healthy participants with severe ophthalmological, neurological and psychiatric disorders were excluded from the study, while pwMS with these disorders were not excluded from the

| Table 2 |
|----------|
| Prevalence of the individual complaints in pwMS. |
| Complaints | % in pwMS |
| Unclear vision, trouble focusing, blinded by bright light | 50-55% |
| Reading, needing more time, light/dark adjustment, reduced contrast, needing more light | 40-45% |
| Dry eyes, depth perception, traffic, seeing things that other do not | 30-36% |
| Painful eyes, double vision, shaky images, visual field | 21-27% |
| Color vision, looking for something, distorted images | 11-14% |

Italic: reported ‘often/always’ by significantly more pwMS than controls.

Fig. 1. Frequencies of complaints reported ‘often/always’ by pwMS (n = 493) and healthy controls (n = 661).
Table 3
Percentage of pwMS and HC that experienced the complaint, standardized residuals and results of chi square tests on frequencies of complaints in MS vs HC.

| Complaint                  | MS (n = 493) Frequencies (adjusted residuals) | HC (n = 661) Frequencies (adjusted residuals) | $\chi^2$ | p     | Cramer's $\phi$ |
|----------------------------|-----------------------------------------------|-----------------------------------------------|----------|-------|-----------------|
| Unclear Vision             |                                               |                                               |          |       |                 |
| Often/always               | 19% (0.7)                                    | 12% (-0.6)                                    | 15.48    | <0.001 | 0.12            |
| Sometimes                  | 35% (1.7)                                    | 45% (-2.0)                                    |          |       |                 |
| Never/hardly               | 46% (2.1)                                    | 43% (-1.8)                                    |          |       |                 |
| Trouble focusing           |                                               |                                               |          |       |                 |
| Often/always               | 16% (5.4)                                    | 6% (-5.4)                                     | 30.76    | <0.001 | 0.16            |
| Sometimes                  | 34% (2.7)                                    | 42% (-2.7)                                    |          |       |                 |
| Never/hardly               | 50% (0.7)                                    | 52% (2.7)                                     |          |       |                 |
| Double vision              |                                               |                                               |          |       |                 |
| Often/always               | 4% (1.8)                                     | 2% (-1.8)                                     | 31.54    | <0.001 | 0.17            |
| Sometimes                  | 22% (5.2)                                    | 11% (-5.2)                                    |          |       |                 |
| Never/hardly               | 74% (5.6)                                    | 87% (5.6)                                     |          |       |                 |
| Depth perception           |                                               |                                               |          |       |                 |
| Often/always               | 14% (4.9)                                    | 5% (-4.9)                                     | 25.60    | <0.001 | 0.15            |
| Sometimes                  | 21% (0.4)                                    | 21% (-0.4)                                    |          |       |                 |
| Never/hardly               | 64% (3.4)                                    | 74% (3.4)                                     |          |       |                 |
| Shaky images               |                                               |                                               |          |       |                 |
| Often/always               | 3% (2.9)                                     | 1% (-2.9)                                     | 29.52    | <0.001 | 0.16            |
| Sometimes                  | 18% (4.4)                                    | 9% (-4.4)                                     |          |       |                 |
| Never/hardly               | 79% (5.3)                                    | 90% (5.3)                                     |          |       |                 |
| Visual field               |                                               |                                               |          |       |                 |
| Often/always               | 6% (4.3)                                     | 2% (-4.3)                                     | 33.78    | <0.001 | 0.17            |
| Sometimes                  | 15% (3.6)                                    | 8% (-3.6)                                     |          |       |                 |
| Never/hardly               | 79% (5.4)                                    | 90% (5.4)                                     |          |       |                 |
| Color vision               |                                               |                                               |          |       |                 |
| Often/always               | 4% (3.6)                                     | 1% (-3.6)                                     | 25.58    | <0.001 | 0.15            |
| Sometimes                  | 12% (3.3)                                    | 6% (-3.3)                                     |          |       |                 |
| Never/hardly               | 84% (4.7)                                    | 93% (4.7)                                     |          |       |                 |
| Reduced contrast           |                                               |                                               |          |       |                 |
| Often/always               | 14% (4.2)                                    | 6% (-4.2)                                     | 17.48    | <0.001 | 0.12            |
| Sometimes                  | 29% (1.3)                                    | 33% (1.3)                                     |          |       |                 |
| Never/hardly               | 57% (1.2)                                    | 61% (1.2)                                     |          |       |                 |
| Blinded by bright light    |                                               |                                               |          |       |                 |
| Often/always               | 24% (7.2)                                    | 9% (-7.2)                                     | 52.45    | <0.001 | 0.21            |
| Sometimes                  | 31% (2.2)                                    | 37% (2.2)                                     |          |       |                 |
| Never/hardly               | 45% (3.1)                                    | 54% (3.1)                                     |          |       |                 |
| Needing more light         |                                               |                                               |          |       |                 |
| Often/always               | 15% (6.0)                                    | 5% (-6.0)                                     | 46.82    | <0.001 | 0.20            |
| Sometimes                  | 25% (2.2)                                    | 20% (-2.2)                                    |          |       |                 |

Table 3 (continued)

| Complaint                  | MS (n = 493) Frequencies (adjusted residuals) | HC (n = 661) Frequencies (adjusted residuals) | $\chi^2$ | p     | Cramer's $\phi$ |
|----------------------------|-----------------------------------------------|-----------------------------------------------|----------|-------|-----------------|
| Light/dark adjustment      |                                               |                                               | 42.62    | <0.001 | 0.19            |
| Often/always               | 14% (6.5)                                    | 4% (-6.5)                                     |          |       |                 |
| Sometimes                  | 29% (0.3)                                    | 30% (0.3)                                     |          |       |                 |
| Never/hardly               | 57% (3.4)                                    | 67% (3.4)                                     |          |       |                 |
| Seeing things that others do not |                                             |                                               | 18.59    | <0.001 | 0.13            |
| Often/always               | 3% (1.8)                                     | 1% (-1.8)                                     |          |       |                 |
| Sometimes                  | 27% (3.8)                                    | 18% (3.8)                                     |          |       |                 |
| Never/hardly               | 70% (4.3)                                    | 81% (4.3)                                     |          |       |                 |
| Distorted images           |                                               |                                               | 4.51     | 0.105 | 0.06            |
| Often/always               | 1% (1.2)                                     | 1% (1.2)                                      |          |       |                 |
| Sometimes                  | 10% (2.1)                                    | 6% (2.1)                                      |          |       |                 |
| Never/hardly               | 90% (1.9)                                    | 93% (1.9)                                     |          |       |                 |
| Painful eyes               |                                               |                                               | 13.96    | <0.001 | 0.11            |
| Often/always               | 4% (2.3)                                     | 2% (-2.3)                                     |          |       |                 |
| Sometimes                  | 23% (3.0)                                    | 16% (3.0)                                     |          |       |                 |
| Never/hardly               | 74% (3.5)                                    | 82% (3.5)                                     |          |       |                 |
| Dry eyes                   |                                               |                                               | 15.73    | <0.001 | 0.12            |
| Often/always               | 11% (3.0)                                    | 6% (3.0)                                      |          |       |                 |
| Sometimes                  | 25% (3.0)                                    | 33% (3.0)                                     |          |       |                 |
| Never/hardly               | 64% (1.2)                                    | 61% (1.2)                                     |          |       |                 |
| Needing more time          |                                               |                                               | 66.45    | <0.001 | 0.24            |
| Often/always               | 13% (7.1)                                    | 2% (7.1)                                      |          |       |                 |
| Sometimes                  | 31% (3.3)                                    | 24% (3.3)                                     |          |       |                 |
| Never/hardly               | 56% (6.4)                                    | 74% (6.4)                                     |          |       |                 |
| Traffic                    |                                               |                                               | 49.34    | <0.001 | 0.21            |
| Often/always               | 9% (5.8)                                     | 2% (5.8)                                      |          |       |                 |
| Sometimes                  | 23% (3.3)                                    | 16% (3.3)                                     |          |       |                 |
| Never/hardly               | 67% (6.0)                                    | 83% (6.0)                                     |          |       |                 |
| Looking for something      |                                               |                                               | 9.69     | 0.008 | 0.09            |
| Often/always               | 3% (2.7)                                     | 1% (2.7)                                      |          |       |                 |
| Sometimes                  | 10% (1.5)                                    | 8% (1.5)                                      |          |       |                 |
| Never/hardly               | 87% (2.5)                                    | 91% (2.5)                                     |          |       |                 |
| Reading                    |                                               |                                               | 6.86     | 0.032 | 0.08            |
| Often/always               | 15% (1.8)                                    | 12% (1.8)                                     |          |       |                 |
| Sometimes                  | 29% (1.5)                                    | 25% (1.5)                                     |          |       |                 |
| Never/hardly               | 56% (2.5)                                    | 63% (2.5)                                     |          |       |                 |

* = significant adjusted residuals (>2.64) and a significant $p$-value ($\alpha < 0.05$).
analysis. However, the number of pwMS with any of these severe disorders was small and excluding them from analysis did not alter the results. Apart from pwMS that were too severely disabled to complete the SVCq, we did not exclude any other participants to optimally approach a full inception cohort of pwMS. Another potential limitation to our study is that the cohort pwMS described in our paper may differ from clinical populations elsewhere. The results could therefore be either an underestimation or an overestimation of the prevalence of visual complaints in other cohorts of pwMS.

In conclusion, the SVCq brings to light that the prevalence of visual complaints among pwMS is relatively high compared to people without MS and the nature of these complaints shows great variety and variability. Visual complaints may occur in people with all types of MS, anytime along the disease course, and both in people with and without

Fig. 2. Frequencies of complaints reported 'often/always' by pwMS with (n = 103) and without (n = 366) a history of ON.

Table 4
Mean and median of SVCq-scores of the pwMS and the healthy controls, with Mann Whitney U test results.

|                      | MS (n = 493) | Median | Range       | HC (n=661) | Median | Range       | U     | p        | r   |
|----------------------|-------------|--------|-------------|------------|--------|-------------|-------|----------|-----|
| Total score          | 8.32 (7.11) | 7.00   | 0–32        | 5.65 (5.42) | 4.00   | 0–38        | 128,832.00 | <0.001* | 0.18 |
| Discomfort           | 2.60 (2.40) | 2.00   | 0–10        | 2.72 (2.54) | 2.00   | 0–10        | 159,932.50 | 0.587   | 0.02 |
| No. of complaints    | 6.41 (4.80) | 6.00   | 0–19        | 4.86 (4.18) | 0.00   | 0–19        | 132,390.50 | <0.001* | 0.22 |
| No. ‘often/always’   | 1.92 (2.79) | 1.00   | 0–13        | 0.79 (1.80) | 4.00   | 0–19        | 125,813.00 | <0.001* | 0.16 |

* = significant p-value (α<0.05).

Table 5
Mean and median of SCVq-scores of people with different types of MS, with Kruskal-Wallis test results.

|                      | RRMS (n = 237) | Median | Range       | SPMS (n = 175) | Median | Range       | PPMS (n = 43) | Median | Range       | H     | df | p    |
|----------------------|----------------|--------|-------------|----------------|--------|-------------|---------------|--------|-------------|-------|-----|------|
| Total score          | 7.68 (6.62)    | 6.00   | 9.37 (7.52) | 8.00           | 6.14   | 6.05        | 4.00          | 9.236  | 2           | 0.010* |     |      |
| Discomfort           | 2.33 (2.25)    | 2.00   | 2.82 (2.40) | 2.00           | 2.65   | 2.80        | 1.00          | 4.015  | 2           | 0.134 |     |      |
| No. of complaints    | 6.03 (4.54)    | 5.00   | 7.10 (4.96) | 7.00           | 4.74   | 4.04        | 3.00          | 9.707  | 2           | 0.008* |     |      |
| No. ‘often/always’   | 1.65 (2.56)    | 0.00   | 2.27 (3.00) | 1.00           | 1.40   | 2.37        | 0.00          | 6.385  | 2           | 0.041* |     |      |

* = significant p-value (α<0.05).

Table 6
Pairwise comparison of types of MS with Mann-Whitney U test results.

|                      | RRMS vs SPMS | U     | p    | r    | RRMS vs PPMS | U     | p    | r    | SPMS vs PPMS | U     | p    | r    |
|----------------------|--------------|-------|------|-----|-------------|-------|------|-----|-------------|-------|------|-----|
| Total score          | 18,131.00    | 0.029*| 0.11 | 4520.50 | 0.112       | 0.10 | 2784.50 | 0.008* | 0.11 |
| No. of complaints    | 18,210.50    | 0.034*| 0.10 | 4255.50 | 0.085       | 0.10 | 2722.00 | 0.005* | 0.12 |
| No. ‘often/always’   | 18,485.50    | 0.045*| 0.10 | 4625.00 | 0.295       | 0.06 | 3049.50 | 0.041* | 0.07 |

* = significant p-value (α<0.05).
Table 7 Mean and median SCVq-scores of pwMS with different disease severity.

|              | Mild (n = 204) | Moderate (n = 130) | Severe (n = 119) | Very severe (n = 22) |
|--------------|---------------|-------------------|------------------|---------------------|
| **Total score** | 7.35 (6.43) | 5.00              | 8.09 (7.46)      | 7.00                |
| **Discomfort** | 2.18 (2.17) | 2.00              | 2.59 (2.32)      | 2.00                |
| **No. of complaints** | 5.81 (4.45) | 5.00              | 6.89 (4.98)      | 4.00                |
| **No. ‘often/always’** | 1.54 (2.45) | 0.00              | 2.10 (2.89)      | 1.00                |

Bold = significant p-value (α < 0.05).

NO. Since visual problems decrease quality of life, it may be advisable to regularly assess reported visual complaints in clinical practice in accordance with the 1964 Declaration of Helsinki. Consent was obtained from all participants.

Future research should focus on explaining the variety and variability of the visual complaints of pwMS, and on determining which patients are most in need of rehabilitation or may benefit most from additional care to reduce the impact of visual problems in daily life.

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**Ethical statement**

The study was approved by the Medical Ethics Review Board (Medisch Ethische toetsingscommissie; METc; NL62728.042.17) of the University Medical centre Groningen and has been performed in accordance with the 1964 Declaration of Helsinki. Consent was obtained from all participants.

**CRediT authorship contribution statement**

F.E. van der Feen: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization. G.A. de Haan: Conceptualization, Methodology, Writing – review & editing, Supervision. I. van der Lijn: Conceptualization, Methodology, Writing – review & editing. F. Huizinga: Investigation, Writing – review & editing. J.F. Meillof: Conceptualization, Methodology, Resources, Writing – review & editing, Funding acquisition. D.J. Heersema: Conceptualization, Methodology, Resources, Writing – review & editing, Funding acquisition. J. Heutink: Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

**Declaration of Competing Interest**

The authors declare that they have no conflict of interest.

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**Supplementary materials**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2021.103429.

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