Recognizing visual complaints in people with multiple sclerosis

van der Feen, Fleur; de Haan, Gera; van der Lijn, Iris; Huizinga, F.; Heersema, Thea; Meilof, Jan F.; Heutink, Joost

Published in:
Multiple Sclerosis and Related Disorders

DOI:
10.1016/j.msard.2021.103429

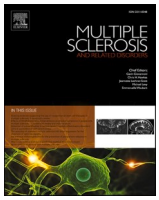
Publication date:
2022

Multiple Sclerosis and Related Disorders 57 (2022) 103429

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



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

F.E. van der Feen [a,b,*], G.A. de Haan [a,b], I. van der Lijn [a,b], F. Huizinga [c], J.F. Meilof [d], D. J. Heersema [e], J. Heutink [a,b]

[a] Clinical and Developmental Neuropsychology, University of Groningen, Grote Kruisstraat 1/2, 9712 TS, Groningen, The Netherlands
[b] Royal Dutch Visio, Center of Expertise for Blind and Partially Sighted People, PO box 1180, Huizen 1270 BD, The Netherlands
[c] Department of General Practice and Elderly Care Medicine, University Medical Center Groningen, University of Groningen, PO box 196, FA 21, Groningen 9700, The Netherlands
[d] Department of Neurology, Martini Hospital, PO box 30033, Groningen 9700 RM, The Netherlands
[e] Department of Neurology, University Medical Center Groningen, PO box 30001, Groningen 9700 RB, The Netherlands

ARTICLE INFO

Keywords:
Multiple sclerosis
Visual complaints
Rehabilitation
Vision
Prevalence

ABSTRACT

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.

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 (Colligris 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

* Corresponding author at: Clinical and Developmental Neuropsychology, University of Groningen, Grote Kruisstraat 1/2, 9712 TS, Groningen, The Netherland.
E-mail address: f.e.van.der.feen@rug.nl (F.E. van der Feen).

https://doi.org/10.1016/j.msard.2021.103429
Received 3 May 2021; Received in revised form 15 November 2021; Accepted 21 November 2021
Available online 24 November 2021

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 (Roodhooft, 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 SVCq (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 SVCq (Huizinga et al., 2020). Participants were excluded when they had any serious neurological, ophthalmological or psychiatric conditions. Healthy participants were recruited via *Panel Inzicht* 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 SVCq (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 SVCq 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 × 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 SVCq, 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 SVCq 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 SCVq 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 87, 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, (Supp 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',

Table 1
Demographics and disease characteristics of pwMS and healthy controls.

	MS total	HC	MS-ON	MS-NON
n	493	661	103	366
Sex (*n,%* female)	346 (70)	420 (64)	78 (76)	255 (70)
Age y (M ± SD)	50.66 (13.17)	50.66 (13.25)	48.96 (13.68)	51.11 (12.98)
Education (n,%)				
Low	56 (11.4)	135 (20.4)	44 (12.0)	9 (8.7)
Intermediate	229 (46.5)	168 (25.4)	164 (44.8)	54 (52.4)
High	208 (42.2)	358 (31.0)	158 (43.2)	40 (38.8)
Type of MS (n,%)				
RRMS	237 (48.1)	–	59 (57.3)	176 (48.1)
SPMS	175 (35.5)	–	33 (32.0)	139 (38.0)
PPMS	43 (8.7)	–	6 (5.8)	36 (9.8)
Other*	4 (0.8)	–	0 (0.0)	4 (1.1)
Unknown	34 (6.9))		5 (4.9)	11 (3.0)
EDSS (n,%)				
0–3	204 (41.4)	–	46 (44.7)	156 (42.6)
3.5–5.0	130 (26.4)	–	32 (31.1)	97 (26.5)
5.5–7.0	119 (24.1)	–	23 (22.3)	93 (25.4)
7+	22 (4.5)	–	2 (1.9)	20 (5.5)
Unknown	18 (3.7)	–	0 (0)	(0)
Duration (*M* ± SD)	14,01 (10.67)	–	13.74 (10.49)	14.05 (10.72)
Unknown (n)	19	–	0	2
VEP (n,%)	77 (15.6)	–	24 (23.3)	51 (13.9)
Aberrant	46 (59.7)	–	18 (75)	27 (52.9)
Unknown	18	–	0	0
Comorbidities (no)				
Ophthalmological**	15	–	6	7
Neurological***	24	–	8	15
Psychiatric****	2	–	0	2

M: mean; SD: standard deviation; EDSS: expanded disability status scale; VEP: visual evoked potential; no: number; TIA: transient ischemic attack; TBI: traumatic brain injury.

* Clinically Isolated Syndrome (2), MS with a benign course (1), Progressive Relapsing MS (1).

** Disorders of the optic nerve other than ON (12), phtitis bulbi (1), post enucleation socket syndrome (1), meibomian gland disease (1), Duane Syndrome (1).

*** Stroke/TIA (10), Epilepsy (7), TBI (5), Brain tumor (1), Spinal cord injury (1), Aneurysm (1), Spina bifida occulta (1), craniosynostosis (1).

**** Schizophrenia (1), psychosis (1).

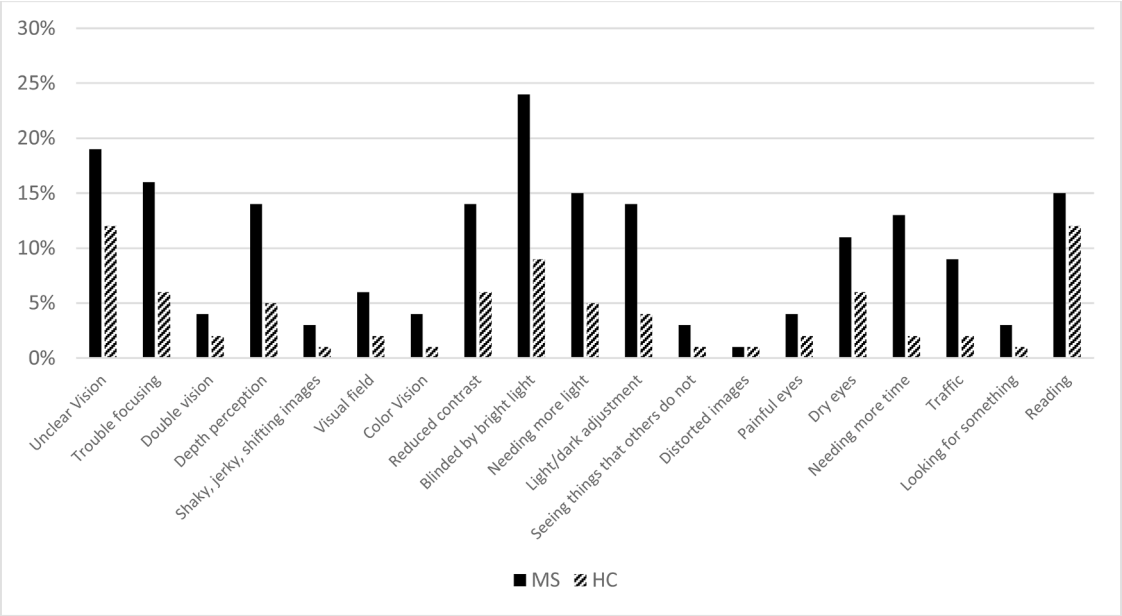


Fig. 1. Frequencies of complaints reported 'often/always' by pwMS (n = 493) and healthy controls (n = 661).

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.

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 NO. 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 RRMS. 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 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)	X^2	p	*Cramer's V*
Unclear Vision			15.48	<0.001*	0.12
Often/always	19% (0.7)	12% (−0.6)			
Sometimes	35% (−2.0)	45% (1.7)			
Never/hardly	46% (2.1)	43% (−1.8)			
Trouble focusing			30.76	<0.001*	0.16
Often/always	16% (5.4*)	6% (−5.4*)			
Sometimes	34% (−2.7*)	42% (2.7*)			
Never/hardly	50% (−0.7)	52% (0.7)			
Double vision			31.54	<0.001*	0.17
Often/always	4% (1.8)	2% (−1.8)			
Sometimes	22% (5.2*)	11% (−5.2*)			
Never/hardly	74% (−5.6*)	87% (5.6*)			
Depth perception			25.60	<0.001*	0.15
Often/always	14% (4.9*)	5% (−4.9*)			
Sometimes	21% (0.4)	21% (−0.4)			
Never/hardly	64% (−3.4*)	74% (3.4*)			
Shaky images			29.52	<0.001*	0.16
Often/always	3% (2.9*)	1% (−2.9*)			
Sometimes	18% (4.4*)	9% (−4.4*)			
Never/hardly	79% (−5.3*)	90% (5.3*)			
Visual field			33.78	<0.001*	0.17
Often/always	6% (4.3*)	2% (−4.3*)			
Sometimes	15% (3.6*)	8% (−3.6*)			
Never/hardly	79% (−5.4*)	90% (5.4*)			
Color vision			25.58	<0.001*	0.15
Often/always	4% (3.6*)	1% (−3.6*)			
Sometimes	12% (3.3*)	6% (−3.3*)			
Never/hardly	84% (−4.7*)	93% (4.7*)			
Reduced contrast			17.48	<0.001*	0.12
Often/always	14% (4.2*)	6% (−4.2*)			
Sometimes	29% (−1.3)	33% (1.3)			
Never/hardly	57% (−1.2)	61% (1.2)			
Blinded by bright light			52.45	<0.001*	0.21
Often/always	24% (7.2*)	9% (−7.2*)			
Sometimes	31% (−2.2)	37% (2.2)			
Never/hardly	45% (−3.1*)	54% (3.1*)			
Needing more light			46.82	<0.001*	0.20
Often/always	15% (6.0*)	5% (−6.0*)			
Sometimes	25% (2.2)	20% (−2.2)			
Never/hardly	60% (−5.7*)	76% (5.7*)			
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% (−0.3)	1% (0.3)			
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% (2.7*)	16% (−2.7*)			
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% (2.8*)	24% (−2.8*)			
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

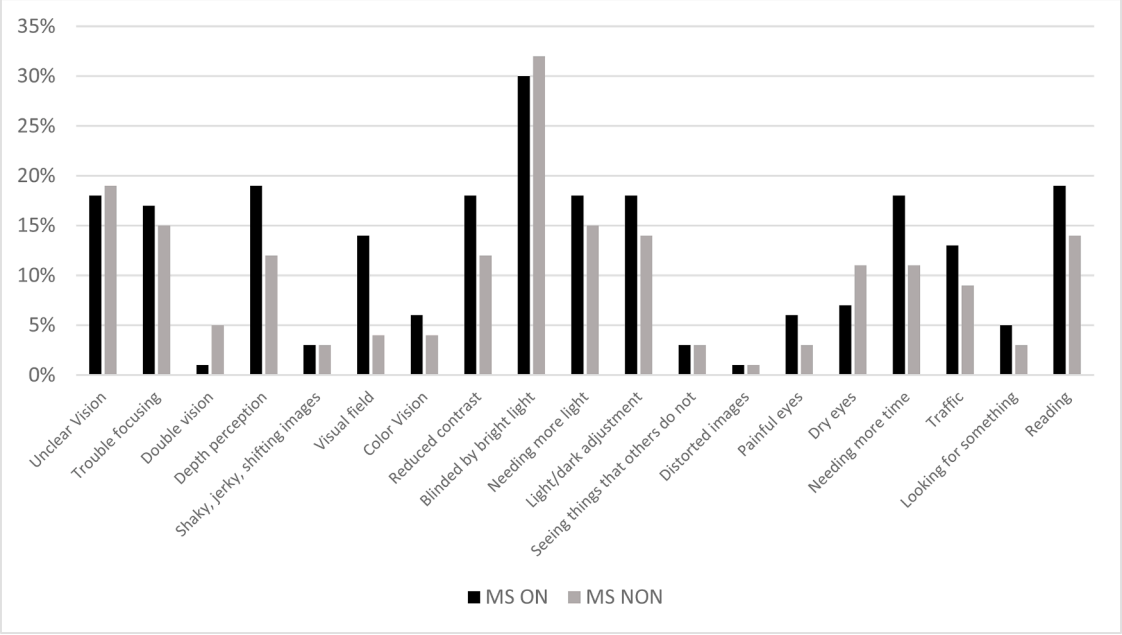


Fig. 2. Frequencies of complaints reported 'often/always' by pwMS with ($n = 103$) and without ($n = 366$) a history of ON.

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

	MS ($n = 493$)			HC (661)					
	M (SD)	*Median*	*Range*	*M (SD)*	*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 ($n = 237$)		SPMS ($n = 175$)		PPMS ($n = 43$)				
	M (SD)	*Median*	*M (SD)*	*Median*	*M (SD)*	*Median*	*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			RRMS vs PPMS			SPMS vs PPMS		
	U	*p*	*r*	*U*	*p*	*r*	*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)				
	M (SD)	*Mdn*	*M (SD)*	*Mdn*	*M (SD)*	*Mdn*	*M (SD)*	*Mdn*	*H*	*df*	*p*
Total score	7.35 (6.43)	5.00	8.99 (7.46)	7.00	8.87 (7.59)	7.00	8.95 (7.72)	9.50	4.232	3	0.237
Discomfort	2.18 (2.17)	2.00	2.59 (2.32)	2.00	2.97 (2.65)	2.00	3.73 (2.66)	4.00	10.811	3	0.013*
No. of complaints	5.81 (4.45)	5.00	6.89 (4.98)	6.00	6.62 (4.96)	6.00	6.68 (5.04)	7.00	3.894	3	0.273
No. 'often/always'	1.54 (2.45)	0.00	2.10 (2.89)	1.00	2.25 (3.09)	1.00	2.27 (3.18)	1.00	5.139	3	0.162

Bold = significant p-value ($\alpha < 0.05$).

NO. Since visual problems decrease quality of life, it may be advisable to regularly assess self-reported visual complaints in clinical practice independent of occurrence of visual disorders such as ON. Assessing visual complaints may facilitate referral to further care in case of visual complaints, preventing unnecessary worsening of quality of life**.** PwMS with visual complaints may benefit from specific tools or training that may reduce difficulty with seeing, but also from general insights in making the world more accessible to the visual system, for example by applying extra contrast. Those tools, training or insights may facilitate seeing in general, possibly reducing multiple kinds of visual complaints.

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.

Funding

This work was supported by the Stichting Novum [Project NAH-Progress] Amsterdam, the Netherlands and ZonMW, program Expertisefunctie Zintuiglijk Gehandicapten [637,005,001].

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. Meilof:** 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.

Acknowledgments

The authors would like to thank all research assistants who contributed to the data collection for this study.

Supplementary materials

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

References

Armstrong, R.A., 2018. Visual problems associated with traumatic brain injury. Clin. Exp. Optom. 101 (6), 716–726. https://doi.org/10.1111/cxo.12670.

Balcer, L.J., Baier, M.L., Kunkle, A.M., Rudick, R.A., Weinstock-Guttman, B., Simonian, N., et al., 2000a. Self-reported visual dysfunction in multiple sclerosis: results from the 25-item national eye institute visual function questionnaire (VFQ-25). Mult. Scler. J. 6 (6), 382–385. https://doi.org/10.1177/135245850000600604.

Balcer, L.J., Baier, M.L., Kunkle, A.M., Rudick, R.A., Weinstock-Guttman, B., Simonian, N., et al., 2000b. Self-reported visual dysfunction in multiple sclerosis: results from the 25-item national eye institute visual function questionnaire (VFQ-25). Mult. Scler. 6 (6), 382–385.

Balcer, L.J., Miller, D.H., Reingold, S.C., Cohen, J.A., 2015. Vision and vision-related outcome measures in multiple sclerosis. Brain A J. Neurol. 138 (1), 11–27. https://doi.org/10.1093/brain/awu335.

Barin, L., Salmen, A., Disanto, G., Babačić, H., Calabrese, P., Chan, A., et al., 2018. The disease burden of multiple sclerosis from the individual and population perspective: which symptoms matter most? Mult. Scler. Relat. Disord. 25, 112–121. https://doi.org/10.1016/j.msard.2018.07.013.

Bermel, R.A., Balcer, L.J., 2013. Optic neuritis and the evaluation of visual impairment in multiple sclerosis. Contin. Lifelong Learn. Neurol. 19 (4), 1074–1086. https://doi.org/10.1212/01.CON.0000433282.00221.7e.

Berthold-Lindstedt, M., Ygge, J., Borg, K, 2017. Visual dysfunction is underestimated in patients with acquired brain injury. J. Rehabil. Med. 49 (4), 327–332. https://doi.org/10.2340/16501977-2218.

Cleary, P.A., Beck, R.W., Bourque, L.B., Backlund, J.C., Miskala, P.H., 1997. Visual symptoms after optic neuritis. Results from the optic neuritis treatment trial. J. Neuroophthalmol. 17 (1), 18–23. https://doi.org/10.1016/S0002-9394(14)70814-1 quiz 24–8.

Cohen, R.A., Kessler, H.R., Fischer, M., 1993. The extended disability status scale (EDSS) as a predictor of impairments of functional activities of daily living in multiple sclerosis. J. Neurol. Sci. 115 (2), 132–135. https://doi.org/10.1016/0022-510X(93)90215-K.

Cohen, J., 1989. Statistical Power Analysis for the Behavioral Sciences. Routledge, New York, pp. 77–82.

Colligris, P., Perez De Lara, M.J., Colligris, B., Pintor, J., 2018. Ocular manifestations of Alzheimer's and other neurodegenerative diseases: the prospect of the eye as a tool for the early diagnosis of Alzheimer's disease. J. Ophthalmol. 2018 https://doi.org/10.1155/2018/8538573.

Collins, C.D.E., Ivry, B., Bowen, J.D., Cheng, E.M., Dobson, R., Goodin, D.S., et al., 2016. A comparative analysis of patient-reported expanded disability status scale tools. Mult. Scler. 22 (10), 1349–1358. https://doi.org/10.1177/1352458515616205.

Costello, F., 2016. Vision disturbances in multiple sclerosis. Semin. Neurol. 36 (2), 185–195. https://doi.org/10.1055/s-0036-1579692.

Davidsdottir, S., Cronin-Golomb, A., Lee, A., 2005. Visual and spatial symptoms in Parkinson's disease. Vis. Res. 45 (10), 1285–1296. https://doi.org/10.1016/j.visres.2004.11.006, 2005.

Francis, C.E., 2013. Visual issues in multiple sclerosis. Phys. Med. Rehabil. Clin. N. Am. 24 (4), 687–702. https://doi.org/10.1016/j.pmr.2013.06.002.

Heesen, C., Böhm, J., Reich, C., Kasper, J., Goebel, M., Gold, S.M., 2008. Patient perception of bodily functions in multiple sclerosis: gait and visual function are the most valuable. Mult. Scler. 14 (7), 988–991. https://doi.org/10.1177/1352458508088916.

Hepworth, L., Rowe, F., Walker, M., Rockliffe, J., Noonan, C., Howard, C., et al., 2016. Post-stroke visual impairment: a systematic literature review of types and recovery of visual conditions. Ophthalmol. Res. An. Int. J. 5 (1), 1–43. https://doi.org/10.9734/OR/2016/21767, 2016 Jan 10.

Hickman, S.J., Raoof, N., McLean, R.J., Gottlob, I., 2014. Vision and multiple sclerosis. Mult. Scler. Relat. Disord. 3 (1), 3–16. https://doi.org/10.1016/j.msard.2013.04.004, 2014 Jan.

Hoff, J.M., Dhayalan, M., Midelfart, A., Tharaldsen, A.R., Bø, L., 2019. Synsproblemer ved multippel sklerose. Tidsskr. Den Nor. Legeforen. 139 (11) https://doi.org/10.4045/tidsskr.18.0786.

Huizinga, F., Heutink, J., de Haan, G.A., van der Lijn, I., van der Feen, F.E., Vrijling, A.C. L., et al., 2020. The development of the screening of visual complaints questionnaire for patients with neurodegenerative disorders: evaluation of psychometric features in a community sample. PLoS ONE 15 (4), e0232232. https://doi.org/10.1371/journal.pone.0232232.

Jasse, L., Vukusic, S., Durand-Dubief, F., Vartin, C., Piras, C., Bernard, M., et al., 2013. Persistent visual impairment in multiple sclerosis: prevalence, mechanisms and resulting disability. Mult. Scler. J. 19 (12), 1618–1626. https://doi.org/10.1177/1352458513479840.

Jean, V.M., Beatty, W.W., Paul, R.H., Mullins, L., 1997. Coping with general and disease-related stressors by patients with multiple sclerosis: relationships to psychological distress. Mult. Scler. 3 (3), 191–196. https://doi.org/10.1177/135245859700300304.

Kim, H.Y., 2017. Statistical notes for clinical researchers: chi-squared test and Fisher's exact test. Restor. Dent. Endod. 42 (2), 152. https://doi.org/10.5395/rde.2017.42.2.152.

Langelaan, M., de Boer, M.R., van Nispen, R.M.A., Wouters, B., Moll, A.C., van Rens, G.H. M.B., 2007. Impact of visual impairment on quality of life: a Comparison with quality of life in the general population and with other chronic conditions. Ophthalmic Epidemiol. 14 (3), 119–126. https://doi.org/10.1080/09286580601139212.

Ma, S.L., Shea, J.A., Galetta, S.L., Jacobs, D.A., Markowitz, C.E., Maguire, M.G., et al., 2002. Self-reported visual dysfunction in multiple sclerosis: new data from the VFQ-25 and development of an MS-specific vision questionnaire. Am. J. Ophthalmol. 133 (5), 686–692. https://doi.org/10.1016/S0002-9394(02)01337-5.

MacDonald, P.L., Gardner, R.C., 2000. Type I error rate comparisons of post hoc procedures for I j chi-square tables. Educ. Psychol. Meas. 60 (5), 735–754. https://doi.org/10.1177/00131640021970871.

Mangione, C.M., Lee, P.P., Gutierrez, P.R., Spritzer, K., Berry, S., Hays, R.D., 2001. Development of the 25-item national eye institute visual function questionnaire. Arch. Ophthalmol. 119 (7), 1050–1058. https://doi.org/10.1001/archopht.119.7.1050. Available from:

Miller, D.H., Leary, S.M., 2007. Primary-progressive multiple sclerosis. Lancet Neurol. 6 (10), 903–912. https://doi.org/10.1016/S1474-4422(07)70243-0.

Noble, J., Forooghian, F., Sproule, M., Westall, C., O'Connor, P., 2006. Utility of the national eye institute VFQ-25 questionnaire in a heterogeneous group of multiple sclerosis patients. Am. J. Ophthalmol. 142 (3), 464–468. https://doi.org/10.1016/j.ajo.2006.04.051.

Roodhooft, J.M., 2012. Summary of eye examinations of 284 patients with multiple sclerosis. Int. J. MS Care 14 (1), 31–38. https://doi.org/10.7224/1537-2073-14.1.31.

Salter, A.R., Tyry, T., Vollmer, T., Cutter, G.R., Marrie, R.A., 2013. Seeing" in NARCOMS: a look at vision-related quality of life in the NARCOMS registry. Mult. Scler. J. 19 (7), 953–960. https://doi.org/10.1177/1352458512469694.

Shams, P.N., Plant, G.T., 2009. Optic neuritis: a review. Int. MS J. 16 (3), 82–90.

Vleugels, L., Lafosse, C., van Nunen, A.N., Nachtergaele, S., Ketelaer, P., Charlier, M., et al., 2000. Visuoperceptual impairment in multiple sclerosis patients diagnosed with neuropsychological tasks. Mult. Scler. J. 6 (4), 241–254. https://doi.org/10.1177/135245850000600406.