

## Het Verkennen van Associaties met Visuele Klachten in Mensen met Multiple Sclerosis

## Exploring Associations with Visual Complaints in People with Multiple Sclerosis

N.Z. van Dijk

Masterthese - Klinische Neuropsychologie

S3299171 Augustus 2022 Vakgroep Psychologie Rijksuniversiteit Groningen Thesebegeleider: Fleur van der Feen

Een masterthese is een proeve van bekwaamheid voor studenten. De goedkeuring van de masterthese is het bewijs dat de student over voldoende onderzoeks- en rapportagevaardigheden beschikt om af te studeren, maar biedt geen garantie voor de kwaliteit van het onderzoek en de resultaten van het onderzoek als zodanig, en de masterthese is dan ook niet zonder meer geschikt om als academische bron te worden gebruikt om naar te verwijzen. Indien u meer wilt weten over het in deze masterthese besproken onderzoek en eventueel daarop gebaseerde publicaties, waarnaar u zou kunnen verwijzen, kunt u contact opnemen met de genoemde begeleider.

#### Abstract

*Background:* Visual complaints are a common occurrence in multiple sclerosis (MS). Even though they decrease quality of life, few research has been done on the origins of the visual complaints. We therefore explored the associations with various functions that are commonly affected in people with MS; visual functions, visual perception, cognition and mood. *Methods:* We performed an exploratory cross-sectional study with a comparison group. People with MS with visual complaints (VC+; n = 68) and people with MS without visual complaints (VC+; n = 37) filled out the Screening Visual Complaints questionnaire (SVCq), and underwent a visual assessment and a neuropsychological assessment. Primary outcomes were the scores on the SVCq and its subscales, and the number of disorders per variable of interest. We also compared the number of disorders per test between the VC+ group and VC-group.

*Results:* The number of visual complaints showed a small correlation with the total number of disorders. The VC+ group generally suffered from more visual function disorders and more mood disorders than VC-. No significant correlations were found for visual perception and cognition in relation to the complaints.

*Conclusion:* People with MS who suffer visual complaints generally experience more disorders than those without visual complaints. This study emphasises the need for a more prominent role of mood in the care surrounding visual complaints in people with MS, and calls for in-depth research regarding fatigue.

#### **Exploring Associations with Visual Complaints in People with Multiple Sclerosis**

Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system (Banwell et al., 2016). The worldwide prevalence of MS is estimated to be 2.8 million people, and this number has been growing in every world region since 2013 (Walton et al., 2020). Though causes for the disease are undiscovered, the mechanisms of the disease are largely known; the inflammatory response to the central nervous system causes demyelination, which in turn can cause neurodegeneration. The more pronounced symptoms associated with MS include problems such as impaired movement of the limbs and difficulties in holding balance (McGinley et al., 2021). However, MS presents with disorders in other areas than balance and movement. 40-70% of MS patients suffer from cognitive impairment (Benedict et al., 2006; Langdon, 2011; Penner, 2017). The most common cognitive functions that are affected are speed of information processing and memory (Langdon, 2011). Mood disorders, such as depression and anxiety, are also known to occur in people with MS (Bruce & Arnett, 2009; Minden & Schiffer, 1990; Patten et al., 2017). The lifetime prevalence for major depressive disorder lies around 50% in the MS population (Arnett & Randolph, 2006; Giordano et al., 2011; Politte et al., 2008), while only 10-15% in the general population is affected (Politte et al., 2008). Anxiety disorders are also very common, the estimated prevalence in the MS population is 20-40% (Giordano et al., 2011). Lastly, people with MS also experience various disorders along the visual pathway. Visual problems occur in about 26% of the MS population (Barnes & McDonald, 1992; Vleugels et al., 2000). The cause of these problems are oftentimes visual disorders, such as optic neuritis, an inflammation of the optic nerve, or internuclear ophthalmoplegia (INO), an abnormality in eye movement (Balcer et al., 2015; Barnes & McDonald, 1992). These visual disorders oftentimes present alongside disorders in visual functions (Jasse et al., 2013). Visual functions are properties that are a staple of vision, such as acuity, contrast, or colour vision (Jasse et al., 2013). Visual function

disorders pertaining to afferent visual pathways can be found in 58.6% of people with MS (Bennett et al., 2019; Downey et al., 2002; Jasse et al., 2013). Visual perception is also known to be impaired in the MS population, even when there are no ophthalmological afflictions or psychiatric diagnoses present (Vleugels et al., 2000). Along with these disorders in vision, visual function and visual perception, MS patients also report various visual complaints (van der Feen et al., 2022). The most common visual complaints that were reported were blurred or fuzzy vision, difficulty with reading and diplopia (van der Feen et al., 2022). Previously, visual disorders, such as INO or optic neuritis, were seen as the leading cause for these visual complaints. However, there is not enough research done on visual complaints to confirm that visual complaints originate from visual disorders. Even more so, this idea has now been refuted by the fact that there are MS patients with visual complaints showing no history of these visual disorders (Jasse et al., 2013; van der Feen et al., 2022). We aim to investigate the possible associations between visual complaints of people with MS and visual function, visuoperceptual, cognitive and mood disorders.

There is a wide variety of visual function disorders people with MS experience, and they are also very prevalent in the population; 58.6% of the MS population has a deficit in their afferent visual pathway (Jasse et al., 2013). Visual functions are the first part of the visual pathway and they are a necessity in producing vision as we know. Therefore it may be possible that a disorder in visual function can affect visual complaints as well. Given the frequency of the visual function disorders and the fact that visual function is a staple of vision, we would like to propose a role of visual function disorders in visual complaints.

The second possible explanation for the visual complaints, is visual perception. It is estimated that 26% of people with MS have visuoperceptual impairments (Vleugels et al., 2000). Visual perception encompasses all the processes responsible for the interpretation and integration of visual information (Orloff-Schriber, 2004). It tells us what it is that we see, and

where an object is in relation to us (Cavanagh, 2011; Trobe, 2001; Zuidhoek, 2019). Visual perception lies higher along the visual pathway, but is just as important as visual functions are for producing the vision as we know. Next to the visual functions, visuoperceptual functioning could thus contribute to the experience of visual complaints.

Next, we would like to introduce the possible involvement of cognition in visual complaints. The most common cognitive impairments in people with MS are in speed of information processing and memory, but other cognitive domains are not excluded from impairment (Langdon, 2011). Various cognitive domains are involved in the processing of visual information, including speed of information processing and memory (Trobe, 2001). The impairments in these cognitive domains may thus affect the quality of vision, and may be related to visual complaints in people with MS.

Lastly, the experience of visual complaints may be influenced by mood. The lifetime prevalence of major depression for people with MS is estimated to be 50% (Feinstein, 2004), while for anxiety the numbers lie around 20 to 40% (Giordano et al., 2011). Complaints have a subjective nature, and are thus prone to changes in mood and psychological bias. Research shows a mood-congruency bias in attentional selection (Becker & Leinenger, 2011), meaning that attention is more easily directed to negative stimuli when a negative mood is present. Mood can thus alter where we direct our attention to, and could therefore influence the perception of the severity or frequency of visual complaints. Other than an attentional bias, mood could also influence visual complaints through a memory bias. Literature finds that there is a mood congruent-memory bias in subclinical depression (Del Valle & Mateos, 2018). Complaints may thus also be remembered in a way that corresponds to the mood at the time of reporting the complaints. One study showed that subjective memory complaints in depressed patients were reduced when mood improved (Antikainen et al., 2000), while another study even suggested that subjective memory complaints were a function of anxiety

and depression, and less so a measure of objective cognitive function (Yates et al., 2015). These studies highlight the subjective nature of complaints and their susceptibility to depression and anxiety. We hypothesise that people with MS who experience visual complaints may also suffer from higher levels of depression or anxiety than those without visual complaints.

#### The Current Study

In the current study we will be exploring whether the visual complaints have any relations with disorders in visual function, visual perception, cognition, and mood. To explore whether visual complaints are related to these variables the, we will be comparing the total number of disorders between people with MS with and without visual complaints. We will also make a comparison for the number of disorder per variable of interest. We hypothesise that, if there is a relation between the disorders and the visual complaints, the total number of disorders should be higher in patients with visual complaints.

#### Method

#### **Participants**

People with MS, all 18 years or older, were either referred to Visio by their neurologist at the University Medical Centre Groningen (UMCG) or Martini Hospital Groningen for their visual complaints, or invited to participate in the control group if they met certain criteria based on the Screening of Visual Complaints questionnaire (SVCq; Huizinga et al., 2020). People with MS with visual complaints were included if they had rated the frequency of one or more visual complaints as 'often/always' and/or if they rated the discomfort of the visual complaints with a 6 or higher. A person with MS could become part of the control group if they (a) had no more than five visual complaints; (b) rated the frequency of these complaints no higher than 'sometimes'; (c) rated the discomfort of the visual complaints no higher than 3. People with MS from another institution, but who were also referred to Visio for their visual complaints, were also included in the study. All participants who gave their consent were included, and the medical ethical committee approved of the research regarding the people with MS without visual complaints.

#### Materials

#### Visual Complaints

Firstly, we assessed the visual complaints with the Screening for Visual Complaints questionnaire (SVCq; Huizinga et al., 2020), which could be filled in digitally or on paper. This 21-item questionnaire (see Appendix A) inquired about a person's visual complaints over the past weeks. The first item asked whether the participant had experienced visual problems in their daily life, and if so, to rate the frequency 'no/hardly ever '(0), 'sometimes' (1), 'often/always' (2), and describe the complaints. The participant could indicate the frequency of these problems on a 3-point Likert scale 'no/hardly ever' (0), 'sometimes' (1) or 'often/always' (2). The next 19 items described various visual complaints, of which the participant could indicate the frequency on a 3-point Likert scale: 'no/hardly ever' (0), 'sometimes' (1) or 'often/always' (2). The last item asked the participant to rate the severity of the discomfort the experienced visual complaints posed on their daily life on a scale from 0 (no discomfort) to 10 (very severe discomfort). Three subscales were identified by Huizinga et al. (2020); diminished visual perception, altered visual perception and ocular discomfort (see Table 1). The total score of the SVCq was then calculated by summing the scores of the 19 items. The total score on the SVCq had a range from a minimal of 0 to a maximum of 38. Higher scores indicated a higher frequency or severity of the visual complaints. Scores on the subscales of the SVCq were also calculated.

#### Table 1

Overview of Items in Each Subscale of the SVCq

Subscale	Items	Maximum score
Diminished visual	Unclear vision (2)	22
perception	Trouble focusing (3)	
	Trouble seeing at reduced contrast (9)	
	Trouble reading (20)	
	More time needed (17)	
	More light needed (11)	
	Difficulty adjusting to light and dark (12)	
	Blinded by bright light (10)	
	Vision problems in traffic (18)	
	Trouble looking for objects (19)	
	Problems with depth perception or	
	estimating distances (5)	10
Altered visual perception	Altered perception of objects or faces (14)	12
perception	Seeing things that others do not (13)	
	Seeing shaky, jerky, or shifting images (6)	
	Double vision (4)	
	Missing part(s) of the visual field (7)	
	Altered colour experience (8)	
Ocular discomfort	Dry eyes (16)	4
	Painful eyes (15)	

*Note*. The item number is indicated between the brackets.

### Visual Functions

The visual functions were assessed using a Visual Basic Assessment (VBA; see Appendix B) as part of the DiaNAH protocol (de Vries et al., 2018). The standard VBA included tests for acuity, refraction, contrast sensitivity, visual field, eye movements and colour vision.

Acuity was measured participant monocularly and binocularly using the current refraction of the using the ETDRS 2000 chart (Precision Vision, 2020) from a distance of 4 m at 500 lux. Peak contrast sensitivity was measured monocularly using the Vistech contrast sensitivity chart (Pesudovs et al., 2004) or the Gecko test (Kooijman et al., 1994), both from a distance of 3 m at 500 lux. The monocular visual fields were measured using the Humphrey Field Analyzer, running the 24-2 SITA-Fast (ZEISS, 2021). Colour vision was tested monocularly using the Farnsworth D-15 (Good Lite, 2010) at 500 lux. If no disorder was found with the Farnsworth D-15, an additional, more sensitive test, was administered; the Lanthony D-15 (Good Lite, 2010).

An orthoptist assessed whether eye cooperation was normal. Eye alignment was determined with the cover/uncover test at a distance from far away and 30 cm. Convergence was determined using the near point of convergence test. Stereopsis was measured with either the Lang stereo test (LANG-STEREOTEST, 2021), the House Fly test (Stereo Optical, 2019) or the TNO test (Lameris, 2021). Eye motility was tested by letting the participant follow a light in eight directions. Smooth pursuit was tested by letting the participant follow an object both vertically and horizontally while keeping their head stationary. Saccades were assessed by letting the participant look at two objects 30 cm apart at an angle of 40°, both horizontally and vertically. The orthoptist determined whether the participant focus on a single object while moving their head. Optokinetic Nystagmus (OKN) could be discerned by letting the person follow a moving object while keeping their head stationary.

#### Visual Perception

The DiaNAH test battery (de Vries et al., 2018) was used to assess visuoperceptual disorders. The battery consisted of 11 tests and was specifically designed for individuals with acquired brain injury, such as MS (see Table 2 for an overview of all the tests). In this study, a new section regarding cognition was added. Participants took the tests on a drawing tablet, the Wacom Cintiq 24 Pro (Wacom, 2021), which was connected to a laptop running the software for the tests; Metrisquare (Metrisquare, 2021).

The Bells Test (Gauthier et al., 1989) aimed to asses lateralized attention and visuospatial cognition. The participant was presented with a full screen of 280 distractor objects and 35 target objects, the bells, randomly distributed over the screen. The task was to cross out all the bells the participant could find. The score was based on the total number of bells that were found and the amount of time the participant spent completing the task.

The Birthday Party Test (de Vries et al., 2020) assessed visual searching and lateralized attention. The participant was presented with a complex picture of a birthday party, and was asked to describe what they saw and what was happening. The score consisted of the total number of elements the participant mentioned in three categories: persons or animals (n = 9), objects (n = 18) and actions/relations (n = 13).

The Corsi Block Tapping Task (Richardson, 2007) assessed visuospatial working memory. The participant was presented with nine blocks on the screen which would light up in a particular sequence. The sequence would start with two blocks. After two sequences with the same number of blocks, one block would be added to the sequence, gradually increasing it. The participant was tasked to tap on the blocks in the same order as they originally lit up. The test stopped if the participant incorrectly repeated two sequences of the same length. The score was the Corsi Block Span, the longest sequence a participant was able to correctly repeat. There were three tests from the Leuven Perceptual Organization Screening Test (L-POST; Torfs et al., 2014) that assessed mid-level perception: Figure Ground Segmentation (figure ground segmentation), Global Motion Detection (motion perception) and Shape Ratio Discrimination (shape recognition). For every test, the participant was presented with a target picture and then had to choose out of three options which one was most similar to the target picture. For the Figure Ground Segmentation, a square with four curves cut out of it was the target. Two curves were formed by a differently coloured disk that sat on top of the square, the other two curves were cut out of the square and revealed a background in yet another colour. The participant then had to choose the square with the same shape. For the Global Motion Detection, the participant was presented with a target motion direction as illustrated by arrows moving in the direction of the arrows were pointing to. The participant had to choose the option where the majority of dots were moving in the target direction. For Shape Ratio Discrimination, the target was a rectangle. The participant then had to choose the rectangle with the same height-width ratio. For every test, the score was the number of correct answers the participant had given, with a maximum score of 5.

The Trail Making Test (Reitan, 1958) assessed visuomotor skills and cognitive flexibility, and consisted of two parts. In part A, the participant had to connect dots in a sequential order from 1 to 25 as quickly as possible. In part B, the participant had to connect 25 alternating numbers and letters, beginning with a number and then going on to the corresponding letter in the alphabet (1-A-2-B... etc.) as quickly as possible. The score on both parts was the time needed to complete the task. The B/A index was also calculated.

The Visual Object and Space Perception (VOSP) Dot Counting Task (Warrington & James, 1991) assessed visuospatial orientation. A random number of dots was shown on the screen for five seconds before vanishing. The participant was then asked how many dots they

had seen. The score was the number of correct answers the participant had given, with a maximum of 13.

The Taylor Complex Figure (Rey, 1983) assessed visuoconstructive skills. A complex figure was shown on the screen and the participant was asked to exactly copy the figure. The score was based on the number of components of the figure the participant was able to copy.

Crowding (Herzog et al., 2015) assessed crowding, or visual load. The participant was asked to fixate on a fixation cross, in the centre of the screen. Two groups of distractor letters on the right and left side of the cross were then flashed on the screen for 150 ms. One of those groups had a middle letter, the target letter. The participant was tasked to identify the target letter while keeping their gaze on the fixation cross. The score was the total number of correctly identified letters, with a maximum score of 10.

The VOSP Silhouettes (Warrington & James, 1991) measured object perception. Ten silhouettes were shown, five objects and five animals, which the participant had to identify. The score was the total number of correctly identified silhouettes.

#### Cognition

The Phonemic Fluency Test (Schmand et al., 2008) assessed the cognitive domains of language and executive functioning. The participant had to name as many words as possible starting with a specific letter within a one-minute time span. There were three rules for which words were not allowed; no proper names, no toponyms and no words with the same prefix in a row. The letters in question were D, A and T. The total score was the total amount of correct words beginning with a D, A and T (repetitions and variations on a word were excluded).

The Digit Span (Wechsler, 2012) assessed working memory and executive functions and had three parts: the Digit Span Forward, Backward, and Sorting. The test instructor would read aloud a string of numbers, starting with a string of two numbers. After two strings of the same length, one number would be added to gradually elongate the strings of numbers. If the participant was unable to produce two strings of the same length, the test would stop. The participant was first given two practice strings to ensure that the task was understood correctly before commencing the real test. For the Digit Span Forward, the participant had to repeat the digits in the same order. For the Digit Span Backward, the participant had to repeat the digits backwards. The Digit Span Backward started out with four strings of two numbers, and then increased by one number after two strings of the same length. For the Digit Span Sorting, the participant had to sort the numbers from low to high. The score on every test was the number of strings the participant was able to successfully reproduce. The total score on the Digit Span was the sum of the scores on the Digit Span Forward, Backward and Sorting.

The 15 Words Test (Saan & Deelman, 1986) assessed verbal memory. The test instructor played an MP3 file where 15 words were read aloud. The participant had to reproduce as many of these 15 words; the sequence in which they recalled these words did not matter. This process would be repeated four more times, with the same words. The total score was the total number of words from all series the participant recalled correctly. After 20 to 25 minutes, the participant had to recall as many words as possible, this time only once. The total score for the delayed recall test was the total number of words correctly recalled.

#### Mood

The Hospital Anxiety and Depression Scale (HADS; Giordano et al., 2011) was used to measure symptoms of anxiety and depression. This questionnaire had 14 items, inquiring about the participant's experiences during the last 7 days regarding anxiety (7 items) and depression (7 items). The participant could indicate the frequency or severity of the problems on a 4-point Likert scale. The range of scores for the HADS anxiety (HADS-A) and HADS depression (HADS-D) laid between 0 (no symptoms) to 21 (most severe or frequent symptoms). The total score of the HADS was also calculated.

#### Table 2

## Overview of Tests Used

Test	Function/Domain/Symptoms	Range of Scores
	Visual Perception	
Bells Test	Lateralized attention/visuospatial	$0-35, 0-\infty$ sec
	cognition	
Birthday Party Test	Visual searching, lateralized	0-40
	attention	
Corsi Block Tapping Task	Visuospatial working memory	0-9
L-POST Figure Ground	Figure ground segmentation	0-5
Segmentation		
TMT-A, B, BA index	Visuomotor skills, processing speed,	$0-\infty$ sec
	cognitive flexibility	
VOSP Dot Counting Task	Visuospatial orientation	0-13
Taylor Complex Figure	Visuoconstructive skills	0-36, 0-∞ sec
L-POST Global Motion	Motor perception	0-5
Detection		
L-POST Shape Ratio	Shape recognition	0-5
Discrimination		
Crowding	Crowding/visual load	0-10
VOSP Silhouettes	Object perception	0-10
	Cognition	
Phonemic Fluency	Language/executive functioning	-
Digit Span Forward	Working memory	0-16
Digit Span Backward	Executive functioning/working	0-16
	memory	
Digit Span Sorting	Executive functioning	0-16
15 Words Test	Verbal memory	0-75, 0-15
	Mood	
HADS-A, HADS-D,	Anxiety and depression	21, 21, 42
HADS total		

*Note.* L-POST: Leuven perceptual organization screening test; TMT: trailmaking test; VOSP:

visual object and space perception.

#### Procedure

The participants were asked about their visual complaints by their neurologist at the UMCG or Martini Hospital using the SVCq. Participants in the group with visual complaints (VC+) were referred to Visio where the VBA and the NPA were carried out over the span of multiple days. Participants in the control group (VC-) underwent the same assessments all on the same day. Four days before the test day, the participants in the control group were called and asked if they still had no visual complaints.

#### **Data Analysis**

#### **Determining Normal and Abnormal Scores**

The tests measuring the visual functions, who were not performed by the orthoptist, used different systems to classify a test as being abnormal. For acuity, the log of the score on the ETDRS chart (Precision Vision, 2020) was taken; if this value was higher than 0.1, the score was classified as abnormal. Two tests were used to measure peak contrast sensitivity; the Gecko (Kooijman et al., 1994) and the Vistech (Pesudovs et al., 2004). If the log of the score on the Gecko was lower than 1.74, it was labelled as abnormal. If the Vistech was used, a norm sheet with unique values for each spatial frequency would indicate with colours whether a value was normal or abnormal; green would indicate normal, and everything else would be labelled as abnormal. The highest score from all the spatial frequencies was used for this process. The visual fields were classified as abnormal if they showed a mean pattern deviation of -3.0. The tests that measured colour vision would indicate directly if colour vision was abnormal.

For most tests on the NPA, the scores were labelled as abnormal if the score was below one standard deviation of the norm, or in other words, fell under the 17<sup>th</sup> percentile. For the other tests, different procedures were used to determine whether a function was abnormal. For the bulk of the visual perception tests, ranges were used, which did not always have a clear cut for the 17<sup>th</sup> percentile. This was true for the Dot Counting Task (Warrington & James, 1991); the maximum score (13) was equal to a range with its minimum value lower than the 17<sup>th</sup> percentile. We chose to classify the maximum score as normal, and everything below as abnormal. For Crowding (Herzog et al., 2015), the highest percentile for individuals over 50 with scores of 7 or higher was lower than 17. We classified every Crowding score below 8 as abnormal. Lastly, the HADS (Giordano et al., 2011) was scored according to the cut-off scores as proposed by Stern (2014). For each scale, a score of 7 or lower was classified as a non-case, therefore we classified scores of 8 or higher as abnormal.

#### Frequency Analysis

SPSS Statistics version 26 (IBM Corp, 2019) was used for the frequency analysis and the correlational analyses. A frequency analysis was carried out on the binary variables that indicated whether a function was disordered or not. We did this for all tests and split our results by group. We followed up with a Chi-square test to determine whether these frequencies differed between the two groups. Cramer's V was used to determine the strength of this relation (small: 0.07-0.21, medium: 0.21-0.35 and large: >0.35, df = 1 (Kim, 2017)).

#### Correlations Between the Dependent Variables and Scores on the SVCq

Firstly, we checked the assumption of normality for all variables using the Shapiro-Wilk Test of Normality with the addition of multiple Q-Q plots. Outliers were identified via visual examination of boxplots. First, Spearman's correlations were calculated for the total number of disorders and the scores of the SVCq scale and the subscales (small: 0.1–0.3, medium: 0.3–0.5 and large: 0.5–1.0 (Cohen et al., 1993)). The analysis for the total number of disorders was only carried out on the participants who completed both the VBA and the NPA. To evaluate whether the number of disorders in visual function, visual perception, cognition and mood had a relation to the scores on the SVCq and the subscales, multiple non-parametric Spearman's correlations were calculated. For the number of visual function and perception tests a partial correlation was calculated since not all participants had done all tests. We calculated Spearman's correlations between the raw scores of the HADS with the scores of the SVCq and the subscales.

#### Results

#### **Participants**

There were 68 participants in the VC+ group and 37 participants in the VC- group. In the VC+ group, 76.5% was female, this percentage was 67.6% for the VC- group. The mean age in years in the VC+ group was 52.41 and 51.51 in the VC- group. Demographics, and the scores on the HADS and the SVCq are provided in Table 3.

#### Table 3

Demographics, Means and Standard Deviations of HADS and SVCq scores per Group

		V	VC+				VC-	
		Demogr	aphics					
Sex (n, % female)		68	(76.5)			37	(67.7)	
Age y $(M \pm SD)$		52.4	1 (1.41)	)		51.5	51 (2.23	5)
-		Test So	cores					
	n	М	SD	Range	n	М	SD	Range
HADS-A	63	5.83	3.36	0-14	36	4.08	2.34	0-8
HADS-D	63	4.68	3.25	0-16	36	2.72	1.99	0-7
HADS total	63	10.51	5.97	1-27	36	6.81	3.70	1-15
Diminished visual perception	65	11.20	3.68	3-19	37	1.57	1.50	0-5
Altered visual perception	65	2.63	2.06	0-8	37	.38	.68	0-3
Ocular discomfort	65	1.35	1.14	0-4	37	.19	.40	0-1
SVCq total score	65	15.18	5.45	4-27	37	2.14	1.77	0-5

*Note*. M: mean; SD: standard deviation; HADS: hospital anxiety and depression scale; SVCq: screening visual complaints questionnaire.

**Frequencies of Abnormal Functions Across Groups** 

The frequencies of abnormal functions split by group are displayed in Table 4, as well as the test statistics. The prevalence of abnormal tests was higher among the individuals in the VC+ group than those in VC- for 12 of the 35 measured tests. From the tests of the VBA, acuity, visual fields, OKN, peak contrast sensitivity, stereopsis and smooth pursuit were significantly higher in the VC+ group than the VC- group. The tests within the NPA that were different across groups were the TMT-B, the Digit Span Sorting, the HADS-D and A, Dot Counting Task and the VOSP Silhouettes. The effect sizes of the difference in prevalence of abnormal tests were regarded as small to medium. The prevalence of abnormal tests for both the HADS-A and HADS-D appeared to be significantly higher for VC+ than for VC-.

#### Table 4

Frequency Analysis Abnormal Functions per Group, Sorted by Effect Size

		VC+		VC-			
	n	Abnormal	n	Abnormal	χ2	р	Cramer's
		(%)		(%)			V
Acuity	15	23.4	0	0	9.926	.002**	.315
TMT-B	26	42.6	4	12.1	9.169	.002**	.312
Nystagmus	14	20.9	0	0	8.934	.003**	.293
Visual fields	18	41.9	4	12.1	8.029	.005**	.325
Digit Span Sorting	18	29.0	2	5.6	7.728	.005**	.281
OKN	10	17.2	0	0	7.13	.008**	.274
Peak contrast sensitivity	11	21.6	1	2.8	6.267	.012*	.268
TMT BA index	19	31.1	3	9.1	5.812	.016*	.249
Stereopsis	9	13.8	0	0	5.619	.018*	.235
HADS-D	9	14.3	0	0	5.567	.017*	.239
HADS-A	20	31.7	4	11.1	5.311	.021*	.232
VOSP Dot Counting	17	27.0	3	8.8	4.45	.035*	.214
Task							
Smooth pursuit	31	47.7	10	27.0	4.189	.041*	.203
VOSP Silhouettes	13	21.3	2	5.9	3.909	.048*	.203
Colour vision	13	31.0	4	12.1	3.739	.053	.223

		VC+		VC-			
	n	Abnormal	n	Abnormal	χ2	р	Cramer's
		(%)		(%)			V
Digit Span Total	11	17.7	2	5.6	2.94	.086	.173
Eye motility	8	12.7	1	2.7	2.844	.092	.169
Eye alignment	10	15.2	2	5.4	2.188	.139	.146
Bells time	22	25.5	7	21.2	2.068	.15	.148
Convergence	3	5.3	0	0	1.743	.187	.14
Digit Span Forward	5	8.1	6	16.7	1.691	.193	.131
VOR	5	8.5	1	2.7	1.293	.256	.116
Birthday Party Test	5	7.9	5	14.7	1.094	.296	.106
L-POST Shape Ratio	9	14.5	8	22.9	1.077	.299	.105
Discrimination							
TMT-A	23	37.1	9	27.3	0.931	.335	.099
Bells Test	7	11.5	6	18.8	0.924	.336	.1
15 Words Test	22	35.5	16	44.4	0.77	.38	.089
Phonemic Fluency	28	45.2	13	36.1	0.767	.381	.088
L-POST Global Motion	7	11.3	6	17.1	0.66	.416	.083
Detection							
L-POST Figure Ground	11	17.5	4	11.4	0.631	.427	.08
Segmentation							
15 Words Test recall	9	14.5	7	19.4	0.405	.525	.064
Corsi Block Span	8	12.7	3	9.1	0.278	.598	.054
Digit Span Backward	13	21.0	6	16.7	0.27	.604	.052
Crowding	27	62.8	19	59.4	0.09	.764	.035
Taylor Complex Figure	8	13.6	4	12.1	0.039	.844	.02
Saccades	30	45.5	17	45.9	0.002	.962	.005

*Note*. The dotted line divides between significant and non-significant  $\chi^2$  values. TMT: trailmaking test; OKN: optokinetic nystagmus; HADS: hospital anxiety and depression scale; VOSP: visual object and space perception; VOR: vestibulo-ocular reflex; L-POST; Leuven perceptual organization screening test.

\**p* < .05. \*\**p* < .01.

## Relationship between SVCq scores and Number of Abnormal Visual Function and **Perception Tests**

Table 5 presents the correlations between the scores on the SVCq scales, the total number of abnormal tests, the number of abnormal tests in visual function and perception. The total number of abnormal tests correlated with the total score of the SVCq and the subscale regarding diminished visual perception. The number of abnormal functions in visual function increases significantly with higher scores on the SVCq and the subscale regarding diminished visual perception. These correlations have a small to moderate effect size. The number of abnormal tests in visual perception hardly related to scores on the SVCq.

#### Table 5

Partial Spearman Correlations of Total Number of Abnormal Tests, Abnormal Visual

		SVCq	Diminished visual	Altered visual	Ocular
		total	perception	perception	discomfort
Total	$r_s$	.216*	.255*	.158	045
abnormal	р	.038	.014	.130	.669
	n	91	91	91	91
Abnormal	rs	.293**	.311**	.196	.073
visual	р	.003	.002	.051	.472
function	n	98	98	98	98
Abnormal	rs	.121	.149	.104	051
visual	р	.242	.149	.315	.621
perception	n	93	93	93	93

Function and Visual Perception, and SVCq Scores

Note. SVCq: screening visual complaints questionnaire

\*p < .05. \*\*p < .01.

#### Relationship Between SVCq Scores and Number of Abnormal Cognition Tests and

#### **HADS Scores**

Table 6 shows the correlations between SVCq scores, the number of abnormal tests in cognition, and the scores on the HADS scales. The scores on the HADS-D and the total score on the HADS correlated significantly with the total score on the SVCq and its subscales regarding diminished and altered visual perception. The effect sizes for these correlations were small to moderate. The score on the HADS-A also correlated with the total SVCq score and diminished visual perception, but not with altered visual perception. These effect sizes are small. The number of abnormal tests in cognition hardly seems to influence scores on the scales of the SVCq. There also was a significant correlation between the HADS-D and the number of abnormal tests in cognition (r = .235, p = .02).

#### Table 6

		SVCq	Diminished visual	Altered visual	Ocular
		total	perception	perception	discomfort
Abnormal	$r_s$	.035	0.74	.006	096
cognition	р	.737	.475	.954	.352
	n	96	96	96	96
HADS-A	$r_s$	.235*	.236*	.184	.087
	р	.020	.020	.070	.394
	n	97	97	97	97
HADS-D	$r_s$	.325**	.367**	.229*	.017
	p	.001	.000	.024	.869
	n	97	97	97	97
HADS total	$r_s$	.303**	.324**	.230*	.056
	p	.003	.001	.023	.584
	n	97	97	97	97

Spearman Correlations of Abnormal Cognition, HADS Scores, and SVCq Scores

Note. SVCq: screening visual complaints questionnaire; HADS: hospital anxiety and

depression scale.

p < .05. \*\* p < .01.

#### Discussion

The aim of this study was to explore associations between visual complaints and the number of visual functions, visual perception, cognition, and mood. The results confirmed our hypothesis; people with visual complaints generally experienced more disorders.

Overall, participants who had more visual complaints also experienced more disorders in visual function. A higher association was found for the complaints regarding diminished visual perception. For the visual function tests, disorders were found for every visual function that was measured, but only in the groups with visual complaints. Most notably, for acuity, nystagmus, OKN and stereopsis, no cases of dysfunction were found in the VC- group. This could imply that dysfunction of these visual functions are more important in relation to the visual complaints than other visual functions. Vice versa, disordered saccadic movements have been found in roughly half of the participants in both groups, a prevalence which is in accordance with previous studies (Downey et al., 2002; Jasse et al., 2013). This could mean that a disorder in saccadic movements does not play a big role in the production of visual complaints. However, prevalences in our study for nystagmus, colour vision, contrast sensitivity, acuity and visual fields are lower than earlier studies found (Downey et al., 2002; Jasse et al., 2013; Reulen et al., 1983). The low prevalences are against expectations, seeing that we handled lenient cut-offs (1 standard deviation below the norm), when compared to most literature (2 standard deviations below the norm). We did find higher prevalences than existing literature dictated for smooth pursuit and saccades. Jasse et al. (2013) has found that ophthalmological afflictions are more common in males than females with persistent visual complaints. The aforementioned studies had either an approximate male to female distribution or more males, whereas our study is a good approximation of the distribution within the MS population, and included more females. Therefore, an effect of sex in the studies of Downey et al. (2002) and Jasse et al. (2013) could have influenced these prevalences.

For visual perception, disorders were found for every test in both groups. There were more disorders for the TMT-B, TMT BA index, the VOSP Dot Counting Task and the VOSP Silhouettes in the VC+ group than in the VC- group. These tests measure visuomotor skills, mental flexibility, visuospatial orientation and object perception, respectively. Literature does not report prevalences for specific visuoperceptual functions, making comparison with our sample impossible. Furthermore, a crowding disorder was common in both groups. This is in line with an earlier finding that crowding is more prevalent in people with neurodegenerative disorders than in healthy controls (Yong et al., 2014), and it has been connected to a slowed processing speed in people with MS (Langdon, 2011; Pitteri et al., 2020). Even with these group differences, the number of visual perception disorders not seem to play a role in the production of visual complaints. Remarkable was the group difference for TMT-B, which was only second most significant to acuity. The TMT-B is a versatile test, measuring a myriad of cognitive functions, such as processing speed and cognitive flexibility (MacPherson et al., 2017; Tombaugh, 2004). It is therefore possible that the group difference stems from cognitive dysfunctions.

Cognitive disorders were found in both groups. There were more disorders for the Digit Span Sorting, the TMT-B and the TMT BA index in the group of people with MS with visual complaints. Our findings suggest that executive functioning, but especially processing speed may relate to visual complaints, as opposed to the overall number of cognitive disorders. Yet, literature finds that overall cognitive deterioration in people with MS is related to motor function, specifically upper body motor function and dexterity, a crucial component of the TMT-B (Benedict et al., 2011; Costa et al., 2017; Mistri et al., 2022). Furthermore, overall cognition deterioration has been connected to poorer low contrast visual acuity in people with MS (Wieder et al., 2013), which can be related to the group difference in acuity. These findings support the idea that an overall cognitive deterioration may be connected to visual complaints in people with MS.

Additionally, indications for mild depression were found only in our group of people with MS with visual complaints. Anxiety symptoms were found in both groups, though significantly more in the VC+ group. We found that people who scored higher on the HADS also scored higher on the SVCq, and the subscales of diminished and altered visual perception. Mood has been show to induce attentional and memory biases (Becker & Leinenger, 2011; Del Valle & Mateos, 2018), which could have affected the experience of visual complaints. Specifically depression could indirectly affect visual complaints through its negative influence on cognition (Marazziti et al., 2010), including psychomotor speed and executive functioning (Stordal et al., 2004; Tsourtos et al., 2002), which were more disordered in the VC+ group. This supports the idea that depression may be indirectly involved in the production of visual complaints. However, it can also be argued that the visual complaints precede mood disorders. Vision-specific distress was found to be the strongest predictor of depressive symptoms in people with visual impairment (Rees et al., 2010), proposing the emotional reaction to the visual impairment to be the biggest contributor to depressive symptoms. Visual complaints could trigger similar negative emotional reactions as they also lessen the quality of vision and quality of life (Langelaan et al., 2007). Lastly, people with MS reported that their visual complaints were influenced by their current level of fatigue (van der Feen et al., 2022). Though mechanisms are still unknown, fatigue may have influenced the complaints through cognition, as research shows that fatigue is associated with cognitive impairment (Cameron et al., 2014; Parmenter et al., 2003).

#### **Strengths and Limitations**

**Different Test Days** 

The performance on the VBA and NPA in the VC+ group may be less reliable than the VC- group, as external factors that may influence performance on these assessments were inconsistent due to different test days. The external factors were consistent between the two assessments in the VC- group, as these were carried out on the same day. However, people in the VC- group could have experienced effects of fatigue from the VBA on performance of the NPA, unlike the VC+ group. Therefore, the number of disorders may have been underestimated or overestimated in both groups, making our results less reliable.

#### The Limited Participant Pool

Next, our sample size was rather small. Since the study was carried out in a healthcare setting, there was little control over the number of people that could participate in the study. It proved difficult to find enough people with MS for the VC- group from this limited participant pool, who also fulfilled the three criteria for participating in the control group. As seen in van der Feen et al. (2022), 52% of people with MS experienced at least 5 visual complaints, and 90% at least 1. However, the healthcare setting has benefitted this study, as it allowed for inclusion of people who exactly matched the target population; those who want to receive care for their visual complaints. Additionally, our sample, is a good reflection of the MS population; it follows the same male to female distribution and has a varied range of ages.

#### The Large Number of Tests

Lastly, we would like address the matter of chance capitalisation, or an increase in Type I errors due to the large number of tests we ran. We opted not to apply a Bonferroni correction, seeing that our study is of the explorative type and takes a broader perspective; a Bonferroni correction would have been too conservative and could have caused Type II errors, possibly causing some of the smaller correlations we found to be overlooked.

#### **Implications for Future Research**

This study has provided valuable insights that have addressed the gap in knowledge whilst contributing to existing literature, and builds toward a better understanding of visual complaints in people with MS. More research is needed to further explore the individual relations of our variables with visual complaints. An important topic for follow-up research, is the role of sex in visual functions. Better understanding of the effects of sex could lead to a more refined approach to prevention, diagnosis and treatment of visual dysfunction. Though our study found no relation with cognition as a whole to visual complaints, our findings imply that executive functioning and processing speed in particular do seem to correlate. Future studies could study the different facets of executive functions and processing speed, in relation to visual complaints in more depth. Another topic of interest regarding cognition, would be the relation between fatigue and visual complaints in people with MS. In addition, the relation with mood needs to be clarified, as it is unclear whether improved mood improves visual complaints, whether a reduction of visual complaints causes an improved mood, or that the variables are part of a vicious circle. Regardless of the direction of this relation, the findings hold clear implications that mood should get a more prominent role in the care surrounding visual complaints, hopefully lessening the impact they have on daily life and improving the overall quality of life in people with MS.

#### References

- Arnett, P., & Randolph, J. J. (2006). Longitudinal course of depression symptoms in multiple sclerosis. *Journal of Neurology, Neurosurgery and Psychiatry*, 77(5), 606–610. https://doi.org/10.1136/jnnp.2004.047712
- Balcer, L. J., Miller, D. H., Reingold, S. C., & Cohen, J. A. (2015). Vision and vision-related outcome measures in multiple sclerosis. *Brain*, 138(1), 11–27. https://doi.org/10.1093/brain/awu335
- Banwell, B., Giovannoni, G., Hawkes, C., & Lublind, F. (2016). Multiple sclerosis and related disorders. In *Multiple Sclerosis and Related Disorders* (Vol. 5, Issue 2, p. A1). Elsevier, https://doi.org/10.1016/j.msard.2016.01.002
- Barnes, D., & McDonald, W. I. (1992). The ocular manifestations of multiple sclerosis. 2:
  Abnormalities of eye movements. In *Journal of Neurology, Neurosurgery and Psychiatry* (Vol. 55, Issue 10, pp. 863–868). https://doi.org/10.1136/jnnp.55.10.863
- Becker, M. W., & Leinenger, M. (2011). Attentional selection is biased toward moodcongruent stimuli. *Emotion*, *11*(5), 1248–1254. https://doi.org/10.1037/a0023524
- Benedict, R. H. B., Cookfair, D., Gavett, R., Gunther, M., Munschauer, F., Garg, N., &
  Weinstock-Guttman, B. (2006). Validity of the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). *Journal of the International Neuropsychological Society*, *12*(4), 549–558. https://doi.org/10.1017/S1355617706060723
- Benedict, R. H. B., Holtzer, R., Motl, R. W., Foley, F. W., Kaur, S., Hojnacki, D., &
  Weinstock-Guttman, B. (2011). Upper and lower extremity motor function and cognitive impairment in multiple sclerosis. *Journal of the International Neuropsychological Society*, *17*(4), 643–653. https://doi.org/10.1017/S1355617711000403
- Bennett, C. R., Bex, P. J., Bauer, C. M., & Merabet, L. B. (2019). The Assessment of Visual Function and Functional Vision. *Seminars in Pediatric Neurology*, *31*, 30–40.

https://doi.org/10.1016/j.spen.2019.05.006

- Bruce, J. M., & Arnett, P. (2009). Clinical correlates of generalized worry in multiple sclerosis. *Journal of Clinical and Experimental Neuropsychology*, *31*(6), 698–705. https://doi.org/10.1080/13803390802484789
- Cameron, M. H., Peterson, V., Boudreau, E. A., Downs, A., Lovera, J., Kim, E., McMillan,
  G. P., Turner, A. P., Haselkorn, J. K., & Bourdette, D. (2014). Fatigue Is Associated with
  Poor Sleep in People with Multiple Sclerosis and Cognitive Impairment. *Multiple Sclerosis International*, 2014, 1–5. https://doi.org/10.1155/2014/872732
- Cavanagh, P. (2011). Visual cognition. In *Vision Research* (Vol. 51, Issue 13, pp. 1538– 1551). NIH Public Access. https://doi.org/10.1016/j.visres.2011.01.015
- 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. *Journal of the Neurological Sciences*, *115*(2), 132–135. https://doi.org/10.1016/0022-510X(93)90215-K
- Costa, S. L., Genova, H. M., Deluca, J., & Chiaravalloti, N. D. (2017). Information processing speed in multiple sclerosis: Past, present, and future. In *Multiple Sclerosis* (Vol. 23, Issue 6, pp. 772–789). SAGE Publications Ltd. https://doi.org/10.1177/1352458516645869
- de Vries, S. M., Heutink, J., Melis-Dankers, B. J. M., Vrijling, A. C. L., Cornelissen, F. W., & Tucha, O. (2018). Screening of visual perceptual disorders following acquired brain injury: A Delphi study. *Applied Neuropsychology:Adult*, 25(3), 197–209. https://doi.org/10.1080/23279095.2016.1275636
- de Vries, S. M., Tucha, O., Melis-Dankers, B. J. M., Vrijling, A. C. L., Ribbers, S., Cornelissen, F. W., & Heutink, J. (2020). The Birthday Party Test (BPT); A new picture description test to support the assessment of simultanagnosia in patients with acquired brain injury. *Applied Neuropsychology:Adult*.

https://doi.org/10.1080/23279095.2020.1763998

- Del Valle, C. H. C., & Mateos, P. M. (2018). Implicit Mood Congruent Memory Bias in Subclinical Depression. *International Journal of Cognitive Therapy*, 11(3), 287–298. https://doi.org/10.1007/s41811-018-0030-0
- Downey, D. L., Stahl, J. S., Bhidayasiri, R., Derwenskus, J., Adams, N. L., Ruff, R. L., & Leigh, R. J. (2002). Saccadic and vestibular abnormalities in multiple sclerosis: Sensitive clinical signs of brainstem and cerebellar involvement. *Annals of the New York Academy* of Sciences, 956, 438–440. https://doi.org/10.1111/j.1749-6632.2002.tb02849.x
- Feinstein, A. (2004). The Neuropsychiatry of Multiple Sclerosis. In *Canadian Journal of Psychiatry* (Vol. 49, Issue 3, pp. 157–163). Canadian Psychiatric Association. https://doi.org/10.1177/070674370404900302
- Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The Bells Test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology*, *11*(2), 49–54.
- Giordano, A., Granella, F., Lugaresi, A., Martinelli, V., Trojano, M., Confalonieri, P., Radice, D., & Solari, A. (2011). Anxiety and depression in multiple sclerosis patients around diagnosis. *Journal of the Neurological Sciences*, 307(1–2), 86–91. https://doi.org/10.1016/j.jns.2011.05.008
- Good Lite. (2010). *Farnsworth D-15 Color Test. Illuminant C*, 1–4. www.goodlite.com%7C1.800.362.3860%7C1.888.362.2576fax
- Herzog, M. H., Sayim, B., Chicherov, V., & Manassi, M. (2015). Crowding, grouping, and object recognition: A matter of appearance. *Journal of Vision*, 15(6), 1–18. https://doi.org/10.1167/15.6.5
- Huizinga, F., Heutink, J., de Haan, G. A., van der Lijn, I., van der Feen, F. E., Vrijling, A. C.L., Melis-Dankers, B. J. M., de Vries, S. M., Tucha, O., & Koerts, J. (2020). Thedevelopment of the Screening of Visual Complaints questionnaire for patients with

neurodegenerative disorders: Evaluation of psychometric features in a community sample. *PLoS ONE*, *15*(4), 1–24. https://doi.org/10.1371/journal.pone.0232232

IBM Corp. (2019). SPSS Statistics for Window, Version 26.0 (Version 26.0). IBM Corp.

Jasse, L., Vukusic, S., Durand-Dubief, F., Vartin, C., Piras, C., Bernard, M., Pélisson, D., Confavreux, C., Vighetto, A., & Tilikete, C. (2013). Persistent visual impairment in multiple sclerosis: Prevalence, mechanisms and resulting disability. *Multiple Sclerosis Journal*, 19(12), 1618–1626. https://doi.org/10.1177/1352458513479840

Kim, H.-Y. (2017). Statistical notes for clinical researchers: Chi-squared test and Fisher's exact test. *Restorative Dentistry & Endodontics*, 42(2), 152. https://doi.org/10.5395/rde.2017.42.2.152

Kooijman, A. C., Looijestijn, J. A., Welling, J. A., & van der Wildt, G. J. (1994). Groningen
Edge Contrast Chart (GECKO) and Glare measurements. In *Studies in Health Technology and Informatics* (pp. 101–110).

Lameris. (2021). TNO Stereotest. https://www.lameris-group.nl/product/tno-stereotest/

LANG-STEREOTEST. (2021). MAIN CHARACTERISTCS OF LANG-STEREOTESTS, SCIENTIFIC PAPERS. https://www.lang-stereotest.com/pages/video

- Langdon, D. W. (2011). Cognition in multiple sclerosis. *Current Opinion in Neurology*, 24(3), 244–249. https://doi.org/10.1097/WCO.0b013e328346a43b
- 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 Epidemiology*, 14(3), 119–126. https://doi.org/10.1080/09286580601139212
- MacPherson, S. E., Cox, S. R., Dickie, D. A., Karama, S., Starr, J. M., Evans, A. C., Bastin,M. E., Wardlaw, J. M., & Deary, I. J. (2017). Processing speed and the relationshipbetween Trail Making Test-B performance, cortical thinning and white matter

microstructure in older adults. *Cortex*, 95, 92–103. https://doi.org/10.1016/j.cortex.2017.07.021

- Marazziti, D., Consoli, G., Picchetti, M., Carlini, M., & Faravelli, L. (2010). Cognitive impairment in major depression. In *European Journal of Pharmacology* (Vol. 626, Issue 1, pp. 83–86). https://doi.org/10.1016/j.ejphar.2009.08.046
- McGinley, M. P., Goldschmidt, C. H., & Rae-Grant, A. D. (2021). Diagnosis and Treatment of Multiple Sclerosis: A Review. In *JAMA Journal of the American Medical Association* (Vol. 325, Issue 8, pp. 765–779). American Medical Association. https://doi.org/10.1001/jama.2020.26858
- Metrisquare. (2021). *Neuropsychologische tests*. https://www.metrisquare.nl/neuropsychologische-tests/
- Minden, S. L., & Schiffer, R. B. (1990). Affective Disorders in Multiple Sclerosis Review and Recommendations for Clinical Research. Archives of Neurology, 47(1), 98–104. https://doi.org/10.1001/archneur.1990.00530010124031
- Mistri, D., Cacciaguerra, L., Storelli, L., Meani, A., Cordani, C., Rocca, M. A., & Filippi, M. (2022). The association between cognition and motor performance is beyond structural damage in relapsing–remitting multiple sclerosis. *Journal of Neurology*, *1*, 3. https://doi.org/10.1007/s00415-022-11044-8
- Orloff-Schriber, S. (2004). Learning Disability in Plain English. In S. N. S. B. T.-L. R. (Second E. ORLOFF (Ed.), *Learning Re-enabled* (pp. 5–17). Elsevier. https://doi.org/10.1016/B978-0-323-02772-4.50007-X
- Parmenter, B. A., Denney, D. R., & Lynch, S. G. (2003). The cognitive performance of patients with multiple sclerosis during periods of high and low fatigue. *Multiple Sclerosis*, 9(2), 111–118. https://doi.org/10.1191/1352458503ms859oa

Patten, S. B., Marrie, R. A., & Carta, M. G. (2017). Depression in multiple sclerosis. In

*International Review of Psychiatry* (Vol. 29, Issue 5, pp. 463–472). https://doi.org/10.1080/09540261.2017.1322555

Penner, I. K. (2017). Cognition in multiple sclerosis. *Neurodegenerative Disease Management*, 7(6), 19–21. https://doi.org/10.2217/nmt-2017-0036

Pesudovs, K., Hazel, C. A., Doran, R. M. L., & Elliott, D. B. (2004). The usefulness of Vistech and FACT contrast sensitivity charts for cataract and refractive surgery outcomes research. *British Journal of Ophthalmology*, 88(1), 11–16. https://doi.org/10.1136/bjo.88.1.11

- Pitteri, M., Dapor, C., Ziccardi, S., Guandalini, M., Meggiato, R., & Calabrese, M. (2020).
  Visual-attentional load unveils slowed processing speed in multiple sclerosis patients: A pilot study with a tablet-based videogame. *Brain Sciences*, *10*(11), 1–12.
  https://doi.org/10.3390/brainsci10110871
- Politte, L. C., Huffman, J. C., & Stern, T. A. (2008). Neuropsychiatric manifestations of multiple sclerosis. *Primary Care Companion to the Journal of Clinical Psychiatry*, 10(4), 318–324. https://doi.org/10.4088/PCC.v10n0408

Precision Vision. (2020). ETDRS Charts.

- Rees, G., Tee, H. W., Marella, M., Fenwick, E., Dirani, M., & Lamoureux, E. L. (2010).
  Vision-specific distress and depressive symptoms in people with vision impairment. *Investigative Ophthalmology and Visual Science*, *51*(6), 2891–2896.
  https://doi.org/10.1167/iovs.09-5080
- Reitan, R. M. (1958). Validity of the Trail Making Test as an Indicator of Organic Brain Damage. *Perceptual and Motor Skills*, 8(3), 271–276. https://doi.org/10.2466/pms.1958.8.3.271
- Reulen, J. P. H., Sanders, E. A. C. M., & Hogenhuis, L. A. H. (1983). Eye movement disorders in multiple sclerosis and optic neuritis. *Brain*, 106(1), 121–140.

https://doi.org/10.1093/brain/106.1.121

Rey, A. (1983). Reativo delle figure complesse A e B.

- Richardson, J. T. E. (2007). Measures of short-term memory: A historical review. *Cortex*, *43*(5), 635–650. https://doi.org/10.1016/S0010-9452(08)70493-3
- Saan, R. J., & Deelman, B. G. (1986). *De 15-Woordentests A en B. Een voorlopige handleiding (Intern Rapport)*. AZG, afdeling Neuropsychologie, Groningen.
- Schmand, B., Groenink, S. C., & Dungen, M. van den. (2008). Letterfluency: psychometrische eigenschappen en Nederlandse normen. *Tijdschrift Voor Gerontologie En Geriatrie*, 39(2), 64–74.

Stereo Optical. (2019). Original Stereo Fly Stereoset.

https://www.stereooptical.com/products/stereotests-color-tests/original-stereo-fly/

- Stern, A. F. (2014). The Hospital Anxiety and Depression Scale. Occupational Medicine, 64(5), 393–394. https://doi.org/10.1093/occmed/kqu024
- Stordal, K. I., Lundervold, A. J., Egeland, J., Mykletun, A., Asbjørnsen, A., Landrø, N. I., Roness, A., Rund, B. R., Sundet, K., Oedegaard, K. J., & Lund, A. (2004). Impairment across executive functions in recurrent major depression. *Nordic Journal of Psychiatry*, 58(1), 41–47. https://doi.org/10.1080/08039480310000789
- Tombaugh, T. N. (2004). Trail Making Test A and B: Normative data stratified by age and education. Archives of Clinical Neuropsychology, 19(2), 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8
- Torfs, K., Vancleef, K., Lafosse, C., Wagemans, J., & De-Wit, L. (2014). The Leuven Perceptual Organization Screening Test (L-POST), an online test to assess mid-level visual perception. *Behavior Research Methods*, 46(2), 472–487. https://doi.org/10.3758/s13428-013-0382-6

Trobe, J. D. (2001). How the Human Visual System Works. In The Neurology of Vision (pp.

3–42). Oxford University Press.

- Tsourtos, G., Thompson, J. C., & Stough, C. (2002). Evidence of an early information processing speed deficit in unipolar major depression. *Psychological Medicine*, 32(2), 259–265. https://doi.org/10.1017/S0033291701005001
- van der Feen, F. E., de Haan, G. A., van der Lijn, I., Huizinga, F., Meilof, J. F., Heersema, D. J., & Heutink, J. (2022). Recognizing visual complaints in people with multiple sclerosis: Prevalence, nature and associations with key characteristics of MS. *Multiple Sclerosis and Related Disorders*, *57*, 103429.

https://doi.org/10.1016/j.msard.2021.103429

- Vleugels, L., Lafosse, C., Van Nunen, A., Nachtergaele, S., Ketelaer, P., Charlier, M., & Vandenbussche, E. (2000). Visuoperceptual impairment in multiple sclerosis patients diagnosed with neuropsychological tasks. *Multiple Sclerosis*, 6(4), 241–254. https://doi.org/10.1191/135245800678827879
- Wacom. (2021). Wacom Cintiq Pro. https://www.wacom.com/en-es/products/pendisplays/wacom-cintiq-pro-24
- Walton, C., King, R., Rechtman, L., Kaye, W., Leray, E., Marrie, R. A., Robertson, N., La Rocca, N., Uitdehaag, B., van der Mei, I., Wallin, M., Helme, A., Angood Napier, C., Rijke, N., & Baneke, P. (2020). Rising prevalence of multiple sclerosis worldwide:
  Insights from the Atlas of MS, third edition. *Multiple Sclerosis Journal*, 26(14), 1816–1821. https://doi.org/10.1177/1352458520970841
- Warrington, E. K., & James, M. (1991). The Visual Object and Space Perception Battery. In *Thames Valley Test Company*. Thames Valley Test Company.
- Wechsler, D. (2012). WAIS-IV-NL Nederlandstalige bewerking, afname- en scoringshandleiding [The Dutch language version of the WAIS-IV: Administration and scoring manual]. Pearson Assessment and Information B.V.

- Wieder, L., G\u00e4de, G., Pech, L. M., Zimmermann, H., Wernecke, K. D., D\u00f6rr, J. M., Bellmann-Strobl, J., Paul, F., & Brandt, A. U. (2013). Low contrast visual acuity testing is associated with cognitive performance in multiple sclerosis: A cross-sectional pilot study. *BMC Neurology*, *13*. https://doi.org/10.1186/1471-2377-13-167
- Yong, K. X. X., Shakespeare, T. J., Cash, D., Henley, S. M. D., Nicholas, J. M., Ridgway, G. R., Golden, H. L., Warrington, E. K., Carton, A. M., Kaski, D., Schott, J. M., Warren, J. D., & Crutch, S. J. (2014). Prominent effects and neural correlates of visual crowding in a neurodegenerative disease population. *Brain*, *137*(12), 3284–3299. https://doi.org/10.1093/brain/awu293

ZEISS. (2021). ZEISS Humphrey Field Analyzer 3.

https://www.zeiss.com/meditec/us/product-portfolio/perimetry/humphrey-visual-fieldanalyzer-3-with-sita-faster.html

Zuidhoek, S. (2019). CVI in beeld. Als de hersenen de oorzaak zijn van slechtziendheid bij kinderen.





## SCREENING VISUELE KLACHTEN (SVK)

Datum:	
Naam:	
Geslacht:	
Wat is uw hoogst afgeronde opleiding?	

Dit is een vragenlijst met uitspraken over problemen die met uw zicht te maken hebben. Als u een bril of contactlenzen heeft, ga er dan bij de beantwoording van de vragen vanuit dat u deze draagt.

Elke vraag heeft meerdere antwoordmogelijkheden. Kies het antwoord dat het meest op u van toepassing is. Het gaat daarbij steeds om de <u>afgelopen weken</u>.

Als u niet zeker weet welk antwoord u moet kiezen, geef dan het best passende antwoord. Kruis bij alle volgende vragen s.v.p. 1 antwoord aan. Er zijn in totaal 3 pagina's.

	Ja	Nee
Bent u bekend bij een oogarts?		
Indien 'Ja':		
Bij welke oogarts (of welk ziekenhuis) bent u bekend?		

Voor welke oogheelkundige aandoening(en) bent u bekend bij de oogarts?

		Nee/nauwelijks	Soms	Vaak/ altijd
1	Ervaart u in het dagelijks leven problemen met uw			
zicht?				

Indien 'Soms' of 'Vaak/altijd': Kunt u aangeven welke problemen of klachten u heeft met uw zicht?

a.

- b. c.
- ••
- d.

		Nee/ nauwelijks	Soms	Vaak/ altijd
2	Heeft u de indruk dat u minder scherp bent gaan zien?			
3	Heeft u moeite met scherpstellen of duurt het langer voordat u een scherp beeld heeft?			
4	Heeft u last van dubbelzien of dubbelbeelden?	•		
5	Heeft u moeite met dieptezien of afstanden inschatten?			
6	Heeft u last van trillende, schokkerige of bewegende beelden?			
7	Heeft u het idee dat u delen mist in het gezichtsveld?			
8	Ervaart u kleuren anders dan vroeger?			
9	Heeft u moeite met het zien bij verminderd contrast (bijv. wanneer letters niet zijn afgedrukt op een witte, maar op een grijze achtergrond)?			
10	Wordt u, meer dan vroeger, verblind door fel licht?			

11	Heeft u de indruk dat alles donkerder lijkt of heeft u meer behoefte aan licht dan vroeger?		
12	Heeft u moeite met het wennen aan licht of donker?		
13	Ziet u wel eens dingen die anderen niet zien (denk bijv. aan flitsen, patronen, voorwerpen of dieren)?		
14	Heeft u de indruk dat u voorwerpen of gezichten anders waarneemt, bijvoorbeeld vervormd of met nabeelden?		
15	Heeft u pijn aan uw ogen?		
16	Heeft u last van droge ogen?		
17	Heeft u het idee dat u meer tijd nodig hebt om dingen te zien?		
18	Heeft u moeite met zien of waarnemen bij deelname aan het verkeer (lopen, fietsen en autorijden)?		
19	Heeft u, <u>vanwege uw zicht</u> , moeite met het zoeken en vinden van dingen?		
20	Heeft u, vanwege uw zicht, moeite met lezen?		

21	In hoeverre wordt u in het dagelijks leven gehindere door bovenstaande klachten met betrekking tot het zien?	Geef een cijfer van 0 tot 10 (omcirkel het juiste antwoord)		
_	0 = geen hinder 10 = zeer ernstige hinder	0 1 2	2345678	9 10
			Ja	Nee
	Stelt u advies, onderzoek en/of revalidatie voor de hierboven genoemde klachten op prijs?			

Wilt u controleren of u alle vragen heeft beantwoord? Bij elke vraag dient 1 antwoord aangekruist te zijn.

## Dank u wel. Dit is het einde van de vragenlijst.

#### Appendix B

#### **Protocol VBO NAH-Progress**

# Doelgroep: cliënten met de <u>ziekte van Parkinson</u> of <u>Multiple Sclerose (MS)</u> met visuele klachten

#### Doel:

Met dit protocol proberen we de best mogelijke zorg te bieden aan cliënten met visuele klachten ten gevolge van de ziekte van Parkinson of Multiple Sclerose (MS). Met onderstaande testen denken we dat het mogelijk moet zijn om aan te tonen of juist uit te sluiten dat de klachten het gevolg zijn van lagere orde (sensorische en oculomotorische) visuele functiestoornissen. Dit protocol is gebaseerd op het 'Protocol VBO DiaNAH' en zal in verband met een nieuwe doelgroep met regelmaat geëvalueerd worden.

In onderstaand protocol is een testbatterij opgenomen. Het is de bedoeling dat al deze testen worden afgenomen. Soms kan aanvullend onderzoek zinvol zijn. Voorbeelden van testen waarbij een aanvullend onderzoek raadzaam kan zijn, staan aangegeven met \*. Uitleg over gemaakte keuzes is weergegeven in het document 'FAQ VBO DiaNAH'. Als er een Frequently Asked Question is, staat dit achter de test aangegeven met '(FAQ)'.

Als je merkt dat je niet (meer) in staat bent één of meer van de testen af te nemen, neem dan contact op met je regionale klinisch fysicus. Oorzaken kunnen zijn dat apparatuur ontbreekt, je niet in staat bent de apparatuur te bedienen of niet (meer) de vaardigheden beheerst om de test af te nemen. Meldt zo'n situatie bij jouw regionale klinisch fysicus zodat in onderling overleg gekeken kan worden hoe de situatie verholpen kan worden.

NB. De tijdsduur van het VBO is 120 minuten. In zijn algemeenheid zal dat volstaan. Uiteraard is het mogelijk aanvullende testen uit te voeren indien de hulpvragen van de cliënt hierom vragen.

### Testbatterij:

#### - Gezichtsscherpte met eigen correctie:

Monoculair en binoculair
 Testmethode: ETDRS 2000 letterkaart, bij voorkeur
 Afstand: 4 meter
 Verlichting op testkaart: 500 lux
 Gebruikte correctie van cliënt noteren

#### - **Refractie** (regulier):

Indien briladvies, vermeld dit in het verslag. NB. Bij voorkeur correctieglaasjes gebruiken met smalle ringetjes

#### - Gezichtsscherpte met optimale refractie:

o Monoculair

Testmethode: ETDRS 2000 letterkaart, bij voorkeur

Afstand: 4 meter

Verlichting op testkaart: 500 lux

Binoculair
 Testmethode: ETDRS 2000 letterkaart, bij voorkeur
 Afstand: 4 meter
 Verlichting op testkaart: 500 lux

NB. Indien de binoculaire gezichtsscherpte lager (>=5 letters) is dan de monoculaire gezichtsscherpte; indicatie voor vervolgonderzoek (grijsfilters, lichtlab).

Vink aan in scoreformulier of je de testen met optimale refractie of met eigen correctie hebt uitgevoerd.

#### - Contrastgevoeligheid:

Monoculair\*

Testmethode: Vistech Afstand: 3 meter Verlichting op testkaart: 500 lux Noteer het antwoord per spatiële frequentie (A, B, C, D en E) waarbij het laatste correcte antwoord werd gegeven (bijv. A5, B6, C5, D4, E1).

\*Indicatie aanvullend onderzoek:

- 1. Indien monoculair afwijkend, dan meting binoculair (500 lux)
- 2. Indien de piekcontrastgevoeligheid gedaald is bij 500 lux

#### - Leesvisus en leestempo

- o Binoculair
  - Testkaart: LEO-leeskaart
  - Verlichting op testkaart: 2000 lux.

Gebruikte additie, afstand, M-waarde en leestempo (woorden/minuut) noteren.

NB. Bepaal wat de kleinste letters zijn waarbij de tekst nog <u>vlot en foutloos</u> gelezen kan worden. De lettergrootte van deze tekst bepaalt de leesvisus.

\*Indicatie aanvullend onderzoek:

Indien leesvisus en/of leestempo aanleiding geeft tot nader onderzoek gericht op leesvraag: inzet LVA

#### - Gezichtsvelden (FAQ)\*

- $\circ$  Binoculair
  - Testmethode: Goldmann
  - Isopter: V-4e

Laten fixeren met het dominante oog.

Goed plotten. Noteren van horizontale diameter in graden; Verticale diameter in graden; Subjectieve betrouwbaarheid.

• Monoculair (OD en OS)\*

Testmethode: Humphrey Field Analyzer (of gelijkwaardig, FAQ):

Programma: 24-2, Sita fast.

Let goed op centrale fixatie. Noteren Mean deviation in dB; Pattern deviation in dB; False positives; False negatives; Subjectieve betrouwbaarheid \* Indien afwijkende monoculaire gezichtsvelden: zie aanvullend onderzoek.

#### - **Oogbewegingen** (FAQ):

- Bepalen oogstand (cover/uncover test veraf en 30 cm), alternerend
- Bepalen convergentie (voorwerp)
- Bepalen binoculair zien (Lang stereo, evt TNO of housefly)
- Oogbewegingen: lampje laten volgen vanaf midden naar re, midden naar li, midden -boven, midden-beneden. Daarna mid- re boven, mid li boven, mid li onder, mid re onder. Evt eindstandnystagmus.
- Volgbewegingen: voorwerp laten volgen van rechts naar links, 40 graden heen en weer. En van boven naar beneden. Enkele keren herhalen en op kijken naar neusbrug client om verschillen OD en OS te beoordelen.
- Saccades: twee voorwerpen op 30 cm afstand, 40 graden uit elkaar houden, eerst horizontaal dan verticaal. Naar voorwerpen laten kijken op commando. Naar neusbrug kijken.

- Beoordelen nystagmus (FAQ)
- o VOR
- OKN
- Indien diplopie\*: uitgebreide anamnese en specificeren diplopie
- Observeren knipperfrequentie: normaal (ongeveer eens per 10 seconden), hoog of laag (primair van toepassing bij PD).
- Observeren pupilreactie\*.

Verslag (KVS):

- Motiliteit: 'Binoculair zien → Onderzoek naar oogmobiliteit'
- Oogstand: 'Binoculair zien  $\rightarrow$  Covertest'
- Convergentie: 'Binoculair zien  $\rightarrow$  Convergentie'
- Nystagmus: 'Binoculair zien  $\rightarrow$  Cornea lichtreflex'
- **Kleurenzien**\* (MS monoculair, PD binoculair)
  - Testmethode: Farnsworth D-15 (15 Hue saturé)
  - Verlichting op testkaart: 500 lux

\* Indien er geen stoornis is vastgesteld, afnemen Lanthony D-15 (15 Hue desaturé, zie aanvullend onderzoek)

- **OCT** 
  - Macula (glaucoomprotocol)
  - Papil (glaucoomprotocol)

Meting zonder correctie

#### - EMC-test (Tobii eyetracker)

- Sferisch equivalent berekenen van dominante oog met toepassing van additie voor leeftijd (zie tabel).
- Meting uitvoeren met standaard bril met sferische brillenglazen (<u>niet</u> eigen correctie) in verduisterde ruimte.

Leeftijd (jaar)	Afstand 50 cm
Alle leeftijden	-
< 40	-
40-55	+ 1.0 Dpt
> 55	+ 1.75 Dpt

#### Mogelijk aanvullend onderzoek (\*):

- Anamnese: dubbelziensklachten uitvragen en specificeren (onder welke omstandigheden, monoculair / binoculair)

#### - **Pupilreacties** + beoordeling grootte pupillen

Subjectieve beoordeling directe en indirecte lichtreactie
 Testmethode: Swinging light test
 NB. Op indicatie meten van absolute diameter pupil OD en OS (bij 10 en 500 lux)

#### - Oogdruk

Indien cliënt niet bij oogarts bekend is, en er aanleiding is op basis van (monoculaire) gezichtsvelduitval en/of 1 of meer gebieden die niet als groen of grijs worden aangegeven op de papil OCT, dan meting van oogdruk met Non Contact tonometer. Indien oogdruk >25: meting met Eyecare

#### - Kleurenzien

Indien er geen afwijking gevonden wordt met de 15 Hue saturé, dan afname 15 Hue desaturé. Met de 15 Hue saturé kan geen milde kleurzienstoornis worden vastgesteld, met de 15 Hue desaturé kan dat wel:

Testmethode: Lanthony D-15 (15 Hue desaturé)
 Verlichting op testkaart: 500 lux
 MS: monoculair; PD: binoculair

#### Mogelijk vervolgonderzoek:

#### - Oogheelkundig Onderzoek:

Indien aanleiding op basis van observatie en/of bevindingen onderzoek overleggen met de oogarts waarna mogelijk inzet OHO

#### - LVA:

Indien leesvisus en/of leestempo aanleiding geeft tot nader onderzoek gericht op leesvraag

#### - Lichtlabonderzoek en adaptatieonderzoek:

Indien op basis van de uitkomsten van het VBO licht een belangrijke rol speelt, er klachten mbt licht in de CVS en SVK gerapporteerd worden, en/of de (piek)contrastgevoeligheid kijkend met 2 ogen lager is dan de contrastgevoeligheid van het beste oog en/of de binoculaire gezichtsscherpte lager (>=5 letters) is dan de monoculaire gezichtsscherpte, vermeld in het MD-2 als bespreekverzoek 'inzet van een lichtlabonderzoek en adaptatieonderzoek'.