

Title:

The Mobility Assessment Course: a ready-to-use dynamic measure of visuospatial neglect

Short title: *A dynamic measure for neglect*

Katinka N. Nelemans¹, Tanja C.W. Nijboer^{1,2}, Antonia F. Ten Brink*¹,
KnowledgeBrokers Neglect Study Group

0000-0002-3900-5728

0000-0001-6683-0267

0000-0001-7634-0819

¹ Department of Experimental Psychology, Helmholtz Institute, Utrecht University, Utrecht, the Netherlands

² Centre of Excellence for Rehabilitation Medicine Utrecht, UMC Utrecht Brain Centre, University Medical Centre Utrecht, and De Hoogstraat Rehabilitation, Utrecht, the Netherlands

KnowledgeBrokers Neglect Study Group: Eugenie Brinkhof - physical therapist, Oscar Haver - rehabilitation physician, Marike Jansen - occupational therapist, Cindy van de Moosdijk – neuropsychologist, Anja Timmerarends - van Eck - nurse specialist

*Corresponding authors information: Antonia F. Ten Brink, Heidelberglaan 1 3584 CS Utrecht, The Netherlands, a.f.tenbrink@uu.nl

Abstract:

The Mobility Assessment Course (MAC) is a tool to measure visuospatial neglect in a dynamic fashion. Although the MAC has shown to dissociate between patients with and without neglect, it remains unclear whether it is applicable in clinical settings. We evaluated the MAC regarding its (1) feasibility as a diagnostic tool as part of standard care, (2) construct validity, and (3) underlying constructs and potential confounders. A consecutive sample of stroke patients (admitted to inpatient rehabilitation) completed the MAC, shape cancellation, line bisection, and/or Catherine Bergego Scale (CBS) as part of standard assessment. To assess feasibility, we computed the percentage of patients who completed the MAC. Construct validity was tested by evaluating MAC performance between patients with and without neglect, and controls. Finally, a regression analysis was conducted to assess underlying constructs and potential confounders of MAC performance (level of mobility, lesion side). The MAC was completed by 82% of patients ($N=182/223$; of whom 145 completed all tasks). Patients with neglect performed worse on the MAC (indicating more severe neglect) compared to patients without neglect and controls. The MAC had a lower sensitivity and higher specificity than paper-and-pencil tasks and the CBS. Performance on shape cancellation, line bisection, and CBS were predictors of MAC performance. Level of mobility and lesion side did not predict MAC scores, indicating that these factors do not confound its reliability. To conclude, the MAC is an easy-to-implement tool to evaluate neglect in a dynamic manner, which can be administered in addition to conventional paper-and-pencil tasks.

Keywords:

Stroke, Unilateral neglect, Mobility Assessment Course, Neuropsychological assessment, Catherine Bergego Scale

Data availability statement:

The data cannot be made publicly available because patients did not give explicit consent in which they agreed to share their data for public use. However, the anonymous data may be requested from the authors.

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Introduction

A common consequence of stroke is visuospatial neglect (VSN), defined as a failure to attend to the contralesional side of space (Azouvi et al, 2006; Buxbaum et al., 2004). VSN is heterogeneous and can differ regarding distance and frame of reference (Corbetta, 2014; Van der Stoep et al., 2013). In the acute and subacute phase post-stroke onset, approximately 30-70% of patients with right-hemisphere damage show VSN, against 20-60% of patients with left-hemisphere damage (Chen, Hreha, Goedert, & Barrett, 2015; Ringman et al., 2004; Ten Brink, Verwer, Biesbroek, Visser-Meily, & Nijboer, 2017). Most spontaneous neurological recovery (i.e. recovery of the impairment itself) takes place within the first three months post stroke (Kerkhoff & Schenk, 2012; Kwakkel & Kollen, 2007; Nijboer, Kollen & Kwakkel, 2013). After this initial period, recovery is thought to be mainly driven by the use of compensatory strategies (Kwakkel et al., 2004). Yet, not all patients fully recover from VSN. About 40% of patients with VSN still show VSN one year later (Nijboer, Kollen, & Kwakkel, 2013). Patients with VSN have a longer rehabilitation trajectory and worse functional outcome than patients without VSN (Chen, Hreha, Kong, & Barrett, 2015). It is, therefore, stressed that adequate and sensitive assessment of VSN is of utmost importance, so that patients can receive appropriate treatment. The goal of rehabilitation is to be able to execute daily life activities and reintegrate in society.

VSN is usually assessed with neuropsychological paper-and-pencil tasks, such as shape cancellation and line bisection. Performance in such static situations does, however, not always translate to behaviour in dynamic, daily life situations, in which stimuli are moving and multiple actions have to be performed simultaneously (e.g. walking and chatting). In paper-and-pencil tasks there are no moving stimuli, external distractions, or time-restrictions, which emphasizes the “static” nature. Therefore, using “dynamic” tasks in addition to static, paper-and-pencil tasks has been recommended in the assessment of VSN (Spreij et al., 2020; Azouvi, 2017). There is no strict distinction between static and dynamic tasks, instead, they could be considered to be two ends of a continuum. We consider tasks to be more “dynamic” when (1) stimuli

change as a patient moves through an environment, (2) when **time is limited to perform a task** due to for example the fleeting nature of information (e.g. sensory stimuli) or short-lived interactions with the environment, (3) and/or when a patient is required to multitask (Spreij et al., 2020). The more **these** aspects are met, the more we consider a task to be dynamic. Dynamic tasks can be more ecologically valid than static tasks but they do not have to be. For example, dual-computer tasks or temporal order judgement tasks (e.g. Bonato et al., 2010; 2015; Van der Stigchel & Nijboer, 2018) can be considered dynamic but do not show more resemblance with a daily life situation than static, paper-and-pencil tasks.

An example of a task in a dynamic setting is the Mobility Assessment Course (MAC), where a route of targets is displayed for the participants to find. The MAC was originally developed by Verlander and colleagues (2000), to measure the extent to which participants visually scan and identify hazards when walking. In first instance, the MAC was developed to measure general visual spatial disorders, including hemianopia and VSN. Verlander et al. (2000) found that the MAC was strongly related to the **clinical criteria** for neglect, and had acceptable levels of criterion validity with the Behavioural Inattention Test. This was mainly the case for the search performance, whereas the aspect of obstacle avoidance did not relate to measures of VSN. Based on these results, Verlander et al. (2000) suggested to, in the future, use a more structured version of the MAC to assess disorders in lateralized attention, such as VSN. Variations of the MAC have been described, in which for example multiple types of targets varying in shape and colour have been used (Cunningham, O'Rourke, Finlay, & Gallagher, 2017; Grech et al. 2017). Crucially, participants are moving through the corridor while searching for targets, using visual scanning and wayfinding. This makes it a dual-task, as participants are required to perform several operations at once (i.e. navigating and searching). This multitasking could lead to competition for cognitive resources and may negatively affect performance when the attentional abilities are limited (Spreij et al., 2020). Furthermore, because participants are not allowed to go back on the route, there is less room for compensatory strategies. The MAC has shown to dissociate between patients with and without VSN (Ten Brink, Visser-Meily and Nijboer, 2018) and is more intuitive in use than most digital tasks which require hardware, software, and some knowledge on how to compute and/or analyze the outcome measures. Yet, it is unclear whether the MAC is feasible to use as part of neuropsychological assessment in a standard clinical setting, which often takes place in the subacute phase post-stroke onset.

The feasibility of a task such as the MAC involves multiple aspects, relating to both practical and patient feasibility. A basic requirement for the MAC is the availability of a

corridor, preferably including several (i.e. 2 to 6) turns. Before the MAC can be used in a new setting, time needs to be invested. The route and target locations have to be selected, for which guidelines have been described (Ten Brink et al., 2018). Furthermore, staff needs to practice setting up and administering the MAC. Before each MAC administration, the examiner has to attach the targets at the appropriate locations, which will take about 4 minutes. The duration of the assessment itself ranged from 2.22 to 9.37 min in a previous study, with a median duration of 4.17 min (Ten Brink et al., 2018). Whether an assessment can be completed or not will depend on the available testing time, patient characteristics (e.g. their ability to move through the corridor, fatigue, motivation), and protocol violations (e.g. obstacles in the corridor, extreme distractions). In the current study, we implemented the MAC as part of a standard VSN assessment in an inpatient rehabilitation facility. All stroke patients who were admitted for inpatient rehabilitation participated in this assessment, independent of whether they showed signs of VSN or not. We focussed on the feasibility of administering the MAC by evaluating the percentage of patients who completed the task.

A second question regarded the construct validity of the MAC, that is, whether performance at the MAC reflects VSN, or is confounded by the level of mobility. Because there is no gold standard to assess VSN, the construct validity of the MAC cannot be directly tested. Nevertheless, evaluating independent relationships between performance at the MAC and VSN as measured with paper-and-pencil tasks, observations of VSN in daily life, and the level of mobility, will provide insight into the underlying construct of the MAC.

This study replicates and extends the study of Ten Brink, Visser-Meily, and Nijboer (2018). Crucially, a new, large convenient sample of stroke patients admitted to inpatient rehabilitation was included. The current aims were to evaluate the (1) feasibility of the MAC, (2) construct validity of the MAC, and (3) underlying constructs and potential confounders of the MAC. First, we assessed the feasibility of the MAC as part of standard care, by computing the percentage of patients who could complete the MAC during VSN assessment as usual care. Second, the construct validity was evaluated by first grouping stroke patients based on conventional VSN tasks (i.e. cancellation and bisection) and observations of neglect in daily life (as assessed with the Catherine Bergego Scale; CBS), and then by comparing MAC scores between patients with VSN, without VSN, and healthy controls. We expected patients with VSN as based on the conventional tasks to perform worse on the MAC (i.e. higher asymmetry scores) than patients without VSN. Third, we assessed whether the level of mobility predicted performance on the MAC, while controlling for performance at conventional VSN tasks and observations of neglect behaviour in daily life. Controlling for performance at conventional

VSN tasks is important because a relation is expected between the presence of VSN and motor impairments. Typically, patients with VSN are more severely affected in the motor domain compared to patients without VSN (Embrechts et al., 2020; Oh-Park, Hung, Chen, & Barrett, 2014; Spreij et al. 2020). If we would find a relation between the level of mobility and performance on the MAC, this could simply reflect the known relation between motor impairments and VSN. If there would be a relation between the level of mobility and performance on the MAC, while controlling for VSN as measured with conventional tasks, this might indicate that performance on the MAC is *confounded* by the level of mobility. We additionally assessed the relation between performance on the MAC, conventional VSN tasks and observations of neglect behaviour in daily life. Investigating which aspect of VSN is related most to performance at the MAC, provides insight into the construct that is measured. We expected that performance at the MAC would relate to all measures of VSN, since they all measure the construct of VSN. In addition, we expected that observations of neglect in daily life would show the strongest relation with performance at the MAC compared to performance at a shape cancellation and line bisection task, because the MAC and CBS are both administered in a dynamic setting **and may share common underlying mechanisms** (Spreij et al., 2020).

Methods

Patients

Stroke patients admitted for inpatient rehabilitation to the Hoogstraat Rehabilitation Centre, the Netherlands, were assessed for VSN as part of a standard procedure, within 2 weeks after admission. For the current study, data from September 2018 till October 2019 was used. Inclusion criteria to be scheduled for the VSN assessment were: (1) clinically diagnosed stroke; (2) no severe deficits in communication or comprehension of instructions and/or tasks; and (3) physically able to perform the VSN assessment (e.g. having enough energy to be tested, before being transferred to another location or home; this was evaluated by the rehabilitation physician, therapist, and/or psychologist). Patients with stroke who met these criteria were automatically scheduled for the VSN assessment as care as usual. Only in rare cases, stroke patients were not scheduled for a VSN assessment (e.g. due to early dismissal from the rehabilitation center or other logistic reasons). No data on the number of patients who were not scheduled was collected. We used data of healthy controls (i.e. volunteers without a history of neurological and/or psychiatric disorders) that were collected in a previous study, in which the MAC was administered in the same setting (Ten Brink et al., 2018).

Procedure and Stimuli

The VSN assessment started with the MAC, after which a shape cancellation and line bisection task were administered. The shape cancellation and line bisection task were performed on a desktop computer with a 68.8 x 33.8cm display screen, in a quiet room. The assessment took approximately 60 minutes. The VSN assessment could take place on a weekday, either in the morning or afternoon. Nurses filled out the CBS by observing the patient in the same week as the VSN assessment (i.e. no longer than 5 working days prior to, or after the VSN assessment). Demographic and clinical characteristics of the patients were retrieved from the electronic patient record.

Mobility Assessment Course

Participants were instructed to walk or drive (i.e. with a wheelchair or walker/rollator) a predefined route in the rehabilitation centre, without stopping or turning back. Whether patients used a wheelchair or walking aid was based upon their individual capacity (i.e. patients could move through the hallway as how they would normally do). In other words, only patients who normally used a wheelchair could complete the MAC in a wheelchair. Patients who did not come to the testing room in a wheelchair, were not offered to use a wheelchair. If patients were not able to move independently with their wheelchair, the examiner slowly pushed the wheelchair. Pushing the wheelchair removes the dual-aspect of the task and was therefore only chosen if the patient otherwise could not do the task at all, to make the task as inclusive as possible. We evaluated potential confounding effects of pushing the wheelchair (see “Statistical analyses”). There was no reception or main entrance present at the route. However, therapists, patients, and visitors could move through the corridors. The targets used were 24 yellow laminated cards, each 10 x 10cm. The targets were positioned on each side (12 left, 12 right) in a corridor of ~1.5 meters wide and ~2 meters high. Per side of the route, four targets were placed at low positions (40-85 cm), four at medium high positions (85-125 cm), and four at high positions (125-165 cm). If the patient used a wheelchair, ‘medium high’ positions were used instead of ‘high’ positions. At every turn, an arrow was presented, so participants could proceed their route independently (Figure 1). The targets were placed with a minimum of 1.5 meters apart from each other, a minimum of 10 cm away from a corner or door, and a minimum of 21 cm after a fire extinguisher, painting, or handle. Targets were never placed on a window, moving object, or hidden behind objects such as coffee machines or plant containers.

One examiner administered the MAC. Setting up the route took approximately 4 minutes. Sample targets and arrows were shown to the participant while providing the task

instructions. While walking/driving the route, participants had to indicate that they had seen the target, either verbal or non-verbal (i.e. pointing). When the participant indicated they had seen a target, the examiner confirmed by a simple ‘‘yes’’ or ‘‘correct’’ and noted the response on an evaluation form. The examiner observed and scored the following: whether the patient used a wheelchair or walking aid, the number of omissions left, the number of omissions right, and qualitative observations about the search strategy (e.g. looking forward or moving from target to target). The qualitative notes were included in the clinical report, but not used in the current study.

When a target location was not visible during the task—for example, due to obstruction by a person or object—this target was not included in the computation of the total amount of omissions. To control for the number of invisible targets, the number of omissions was divided by the number of visible targets and was multiplied by the maximum amount of targets [e.g., $(4/11) \times 12$], giving the corrected number of omissions. Next, the asymmetry score was computed as the absolute difference between the corrected number of omissions on the left and right sides. Since we wanted to combine data of patients with left-sided and patients with right-sided VSN, we used the absolute asymmetry score (i.e. the absolute difference between the corrected number of omissions left and right). An asymmetry score of 2.3 or more was considered an indication for VSN (Ten Brink et al., 2018). The manual of the MAC can be retrieved upon request with the authors.



Figure 1. Example of a part of the route with a target (yellow square; left-hand side of the figure) and arrow pointing to the left (center of the figure) used in the Mobility Assessment Course.

Shape cancellation

The computerized shape cancellation task consisted of 56 small targets including 2 example targets ($0.6^{\circ} \times 0.6^{\circ}$), 52 large distractors ($0.95^{\circ} \times 0.95^{\circ}$), 13 letters, and 10 words (widths ranging from 0.95° to 2.1° and heights ranging from 0.45° to 0.95°). Patients were seated at 90 cm distance from the screen. They were instructed to click all targets and tell the examiner when they had completed the task. No time limit was given. If patients were not able to use the computer mouse due to motor impairments, a paper-and-pencil version of the shape cancellation task was administered. We used the absolute omission difference score, computed as the difference in the number of omissions at the left versus right side of the screen. The threshold for VSN was based on the average omission difference score of 28 healthy controls in the study of Van der Stoep et al. (2013), which was 1.05. In line with Van der Stoep et al. (2013), the threshold for VSN was set at ≥ 2 .

Line bisection

The line bisection task was based on the task of McIntosh et al. (2005). Patients had to bisect the subjective midpoint of 32 black horizontal lines, which were presented one by one on a white background. There were eight repetitions of four unique lines, created by crossing two left endpoint positions (far: -120mm and -240mm; near: -30mm and -60mm from the horizontal midline of the screen) with two right endpoint positions (far: 120mm and 240mm; near: 30mm and 60mm from the horizontal midline of the screen). Patients were seated at 30 cm from the screen in the near condition and at 120 cm of the screen in the far condition. When patients were not able to use the computer mouse due to motor impairments, a paper-and-pencil version of the line bisection was administered. In this case only the “near” condition and only three lines could be observed. Per line type, we computed the absolute average deviation from the actual midpoint. The normal range of deviations was based on the performance of 30 healthy controls. A deviation above threshold (i.e. outside normal range) on ≥ 2 lines was used as a threshold for VSN.

Catherine Bergego Scale

The CBS is an observation scale for neglect in activities in daily life (Azouvi et al., 2003; Ten Brink et al., 2013). It measures performance in personal (body parts, body surface), peripersonal (within reaching distance), and extrapersonal space (beyond reaching distance), as well as in perceptual, representational, and motor domains. For 10 items, presence and severity of neglect

were scored by the nurse, resulting in a total score of 0 (never/no neglect) to 30 (always/severe neglect). In the week of the VSN assessment, the nursing staff filled out the CBS based on observations that were made on a day-to-day basis. Nursing staff was trained beforehand to only score behavioural observations within the framework of neglect and no other deficits (e.g. motor and/or sensory deficits or memory impairment). A score of ≥ 6 was used as a threshold for neglect (Ten Brink et al., 2013).

Demographic and clinical characteristics

For each patient, the medical record was reviewed to capture the following data: age, sex, time post-stroke onset, stroke type, lesion side, cognitive impairments as measured with the Montreal Cognitive Assessment (MoCA; Nasreddine, et al., 2005), motor strength of the paretic arm and leg as measured with the Motricity Index Arm and Leg, respectively (Kwakkel & Kollen, 2007), and independence in activities of daily living as measured with the Barthel Index (Quinn, Langhorne, & Stott, 2011).

Statistical analyses

Patients were labelled as having VSN (VSN+) when they obtained abnormal scores on two or more VSN assessment tasks (i.e. cancellation task, line bisection task near, line bisection task far, and/or CBS) and labelled as not having VSN (VSN-) when this was not the case. The MAC was – given the aims of the research – not used to define the VSN+ and VSN- groups. The level of significance was set at an alpha of 0.05. Effect sizes were computed with the Pearson correlation coefficient using the following formula: $r = Z/\sqrt{N}$ (Rosenthal, 1994). For Chi-square tests, Cramer's V was reported. Effect sizes of $>.10$ were considered to reflect a small, $>.30$ a medium, and $>.50$ a large effect (Field, 2013). Statistical analyses were performed using SPSS version 26.

Demographic and clinical characteristics

We compared the VSN+, VSN-, and healthy control groups regarding age and sex using a Kruskal-Wallis test and Chi-square test. The VSN+ and VSN- groups were compared regarding time post-stroke, lesion side, Barthel Index, Motricity Index arm and leg, MoCA, CBS, line bisection near and far (deviation), shape cancellation (asymmetry score), and level of mobility on the MAC, using Mann Whitney tests and Chi-square tests.

Feasibility

The feasibility of the MAC was evaluated by providing descriptive data on the percentage of patients who were and were not able to complete the MAC, and what the reasons were for not completing the MAC. These could be target obstructions in the hallway or the lack of physical and/or cognitive capabilities of the patient at the moment of testing.

Construct validity

The asymmetry score on the MAC was compared between the three groups (i.e. VSN-, VSN+, controls) with a Kruskal-Wallis test. All stroke patients who completed the MAC were included. Post-hoc Mann Whitney tests were used. Additionally, the percentages of the patients who scored above and below the cut-off of the MAC were provided per stroke group (i.e. VSN-, VSN+). To gain more insight into the sensitivity and specificity of the individual tests, percentages of patients who scored above and below the cut-off of the MAC were provided per test (i.e. VSN groups based on the shape cancellation, line bisection near and far, and CBS) and for patients with VSN on both the line bisection near and shape cancellation task.

Potential confounders

We performed a multiple linear regression analysis with the absolute MAC asymmetry score as the dependent variable. Independent variables were age, sex, shape cancellation (absolute asymmetry score), line bisection near and far (absolute deviation), CBS, and level of mobility. For the level of mobility, we created three dummy variables in which ‘walking with aid’ (i.e. the patient used an aid to walk the route), ‘wheelchair independent’ (i.e. the patient could drive the wheelchair independently), and ‘wheelchair dependent’ (i.e. the patient needed help to drive the wheelchair and was pushed by the examiner) were compared with ‘walking’. The potential predictors were checked for collinearity, but none were strongly correlated with each other (all Variance Inflation Factors; $VIF \leq 5.00$). All potential predictors were included at once (enter method) to restrict the risk of capitalizing on chance features of the data. All stroke patients who completed the MAC were included.

Results

Demographic and clinical characteristics

Of 224 stroke patients who were assessed for VSN within the specified time period, one was excluded because no data was available. A group of 223 stroke patients were included in the study, of whom 54 (24.2%) showed VSN. From a previous study, all 47 healthy controls were

included (Ten Brink et al., 2018). An overview of demographic and clinical characteristics is provided in Table 1.

The age was comparable between the VSN+ group, VSN- group, and the healthy controls. The distribution of sex differed between groups, with fewer men in the control group (42%) than in the VSN- group (63%) and VSN+ group (59%), this was a small effect. The VSN+ and VSN- groups were comparable regarding stroke type and time post-stroke. There were more patients with right hemispherical lesions in the VSN+ group than the VSN- group, this was a small effect. The VSN+ group obtained lower scores on the Barthel Index and MoCA than the VSN- group, indicating that the VSN+ group showed lower functional independence and lower overall cognitive functioning compared to the VSN- group, these were small effects. The VSN+ and VSN- groups were comparable regarding Motricity Index Arm and Motricity Index Leg.

Scores on the VSN measures (i.e. shape cancellation, line bisection, and CBS) were, as expected, higher in the VSN+ group than in the VSN- group, these were large effects. The VSN+ group differed from the VSN- group regarding the level of mobility during the MAC, with more patients who were dependent in a wheelchair (i.e. pushed by examiner) in the VSN+ group (45.5%) than the VSN- group (18.2%).

Table 1. Demographic and clinical characteristics of stroke patients with visuospatial neglect (VSN+), without VSN (VSN-), and healthy controls. Values depict medians (IQR) or frequencies (%).

Outcome	N	VSN+	N	VSN-	N	Healthy controls	Statistical comparison between groups
Age (years)	54	60.5 (54-67)	169	58 (49-67)	47	56.99 (49.99-63.99)	$\chi^2(2) = 3.20, p = .202, V = .13$
Sex, % male	54	32 (59.26%)	169	106 (62.72%)	47	20 (42.55%)	$\chi^2(1) = 6.18, p = .046, V = .15^*$
Time post-stroke onset (days)	36	25.5 (12.5-38.5)	93	22 (14-30)			$U = 1370.0, p = .110, r = -.14$
Lesion side, % right	34	29 (53.70%)	95	42 (24.85%)			$\chi^2(1) = 17.15, p < .001, V = .37^{**}$
Stroke type	33		93				$\chi^2(1) = 2.76, p = .251, V = .15$
- % Ischemic		23 (42.59%)		76 (44.97%)			
- % Intracerebral haemorrhage		7 (12.96%)		14 (8.28%)			
- % Subarachnoid haemorrhage		3 (5.56%)		3 (1.78%)			
MoCA (0-30)	18	21 (17.75-24.25)	54	23 (18.75-27.25)			$U = 315.0, p = .039, r = -.25^*$
Barthel Index (0-20)	18	10.5 (6.87-14.13)	59	16 (12.5-19.5)			$U = 361.0, p = .040, r = -.23^*$
Motricity Index arm (0-100)	16	55.5 (-6.38-104.13)	54	84 (66-102)			$U = 306.0, p = .074, r = -.21$
Motricity Index leg (0-100)	16	79 (45.25-112.75)	54	91 (78.25-103.75)			$U = 351.5, p = .242, r = -.14$
Shape cancellation (asymmetry, 0-27)	51	2 (-1.5-5.5)	165	0 (0)			$U = 1390.5, p < .001, r = -.57^{**}$
Line bisection near (deviation in mm)	44	3.94 (1.75-6.14)	151	1.41 (0.71-2.12)			$U = 1082.0, p < .001, r = -.49^{**}$
Line bisection far (deviation in mm)	43	17.63 (6.44-28.83)	153	5.03 (2.95-7.12)			$U = 909.0, p < .001, r = -.52^{**}$
Catherine Bergego Scale (0-30)	53	11.4 (5.28-17.53)	146	1 (-0.5-2.5)			$U = 1023.0, p < .001, r = -.57^{**}$
MAC, level of mobility	44		137		47		$\chi^2(3) = 14.53, p = .002, V = .28^*$
- Walking		12 (27.3%)		58 (42.3%)		47 (100%)	
- Walking with aid		4 (9.1%)		29 (21.2%)		0	
- Wheelchair independent		8 (18.2%)		25 (18.2%)		0	
- Wheelchair dependent		20 (45.5%)		25 (18.2%)		0	

Note. MoCA = Montreal Cognitive Assessment, MAC = Mobility Assessment Course, VSN = visuospatial neglect. Not for all patients data was available for all variables (e.g. not all tasks were administered in all patients), therefore the sample sizes differ per outcome variable. Note that 138 patients in the VSN- group completed the MAC, but for 1 patient no data was available on the level of mobility during the MAC. Asterisks indicate statistical significance with $p < .05^*$, and with $p < .001^{**}$.

Feasibility

Of 223 stroke patients, 182 (81.6%) completed the MAC. In 9 of 182 assessments (4.95%), 1 up to 3 targets were obstructed and the asymmetry score was corrected for those obstructed targets as described in the method section. In 16 of 182 assessments (7.2%), the task was aborted due to unexpected situations hampering further testing on the route. For example, one assessment was withheld because of cycling training for children crossing the route of the MAC. In 26 of 182 assessments (11.6%), the task was aborted or not administered at all, due to a patients lack of physical or motivational capabilities, or fatigue. Of these 26 patients, 11 could not complete the MAC due to limited physical capabilities, 6 due to fatigue, and 9 due to a combination of limited physical and motivational capabilities. For example, one patient had no wheelchair, and was too tired to complete the MAC walking. Only the data of the 182 patients who completed the MAC were used in the remaining analyses.

Construct validity

VSN+ patients obtained higher MAC asymmetry scores ($Mdn = 2.0$, $IQR = 5.87$) than VSN- patients ($Mdn = 0$, $IQR = 1.0$; $U = 1417.5$, $Z = -5.82$, $p < .001$, $r = -.43$), which was a medium effect (Figure 2). Furthermore, VSN+ patients obtained higher MAC asymmetry scores compared to healthy controls ($Mdn = 0$, $IQR = 1.0$, $U = 256$, $Z = -3.59$, $p < .001$, $r = -.44$), which was a medium effect. There was no difference between VSN- patients and healthy controls regarding the MAC asymmetry score ($U = 1552$, $Z = -0.56$, $p = .573$, $r = -.04$). In the VSN+ group, 20 of 44 patients (45.5%) obtained a MAC asymmetry score above the cut-off score (i.e. 2.3 or higher), which was the case for 7 of 138 patients (5.1%) in the VSN- group.

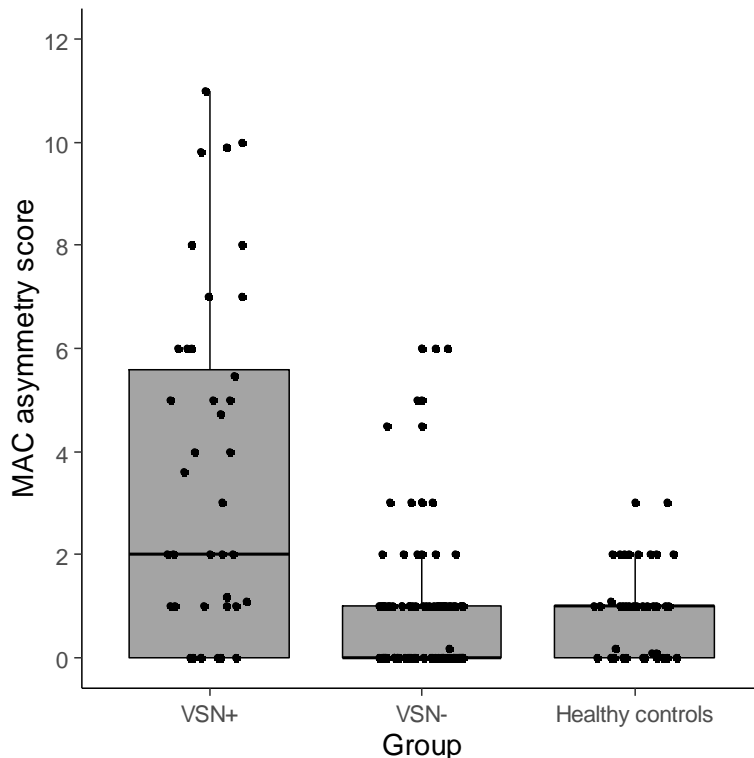


Figure 2. Boxplots depicting the asymmetry score on the Mobility Assessment Course (MAC), split for patients with visuospatial neglect (VSN+; $N = 44$), without VSN (VSN-; $N = 138$), and healthy controls ($N = 47$). The thick line in the middle is the median. The top and bottom box lines show the first and third quartiles. The whiskers show the maximum and minimum values, with the exceptions of outliers. Black dots depict scores of individual participants. In the VSN+ group, 45.5% of patients scored above the cut-off score (2.3) against 5.1% in the VSN- group.

Percentages of patients with VSN based on individual tasks and the MAC are depicted in Table 2. Based on the shape cancellation task, 30.3% of patients with, and 10.3% of patients without VSN based on the shape cancellation task showed VSN on the MAC. When patients were grouped based on the line bisection near, 29.4% of patients with, and 8.5% of patients without VSN showed VSN on the MAC. When patients were grouped based on the line bisection far, 23.9% of patients with, and 9.0% of patients without VSN based on the line bisection far showed VSN on the MAC. Regarding the CBS, 39.2% of patients with, and 5.4% without VSN based on the CBS showed VSN on the MAC. Finally, we defined VSN based upon abnormal performance on both the shape cancellation and line bisection near, which could be considered a conventional and more conservative way of defining VSN. In this comparison, 50.0% of patients who showed VSN on both shape cancellation and line bisection near also showed VSN on the MAC, which was 10.6% of patients without VSN on both tasks.

Table 2. Percentages of patients with visuospatial neglect (VSN) on the Mobility Assessment Course (MAC), split for patients with and without VSN based on four different tasks.

	Shape cancellation (<i>N</i> =178)		Line bisection near (<i>N</i> =168)		Line bisection far (<i>N</i> =168)		CBS (<i>N</i> =163)		Shape cancellation <i>and</i> line bisection near (<i>N</i> =143)	
	VSN	No VSN	VSN	No VSN	VSN	No VSN	VSN	No VSN	VSN	No VSN
<i>N</i>	33	145	51	117	46	122	51	112	16	135
MAC VSN										
VSN (%)	30.3%	10.3%	29.4%	8.5%	23.9%	9.0%	39.2%	5.4%	50.0%	10.6%
No VSN (%)	69.7%	89.7%	70.6%	91.5%	76.1%	91.0%	60.8%	94.6%	50.0%	89.4%

Abbreviations: CBS = Catherine Bergego scale, MAC = Mobility Assessment Course, VSN = visuospatial neglect.

Underlying constructs and potential confounders

A total of 145 patients completed the MAC, shape cancellation task, line bisection near and far, and CBS, and were included in the regression model. The regression model was significant, $F(9) = 14.22$, $p < .001$, and explained 49% (R^2) of the variance in MAC asymmetry score (Table 3). MAC asymmetry scores were independently predicted by the deviations at the line bisection near and far, the asymmetry score at the shape cancellation, and the CBS score. The CBS score was the strongest predictor with 19% explained variance, followed by the shape cancellation asymmetry score with 9% explained variance. The level of mobility (i.e. whether patients walked with or without aid, or used a wheelchair dependent or independent) did not predict the asymmetry score on the MAC.

Supplementary analysis were conducted with ‘lesion side’ as additional predictor (Supplementary Table 1). Results showed that lesion side did not independently predict the asymmetry score on the MAC.

Table 3. Linear regression results predicting asymmetry score on the Mobility Assessment Course, including all stroke patients without missing data on any of the variables ($N = 145$).

	<i>b</i> (95% CI)	SE	<i>p</i>	R^2
Age (years)	-0.01 (-0.27 to 0.13)	0.01	.490	.00
Sex = male (vs female)	0.17 (-0.39 to 0.73)	2.83	.539	.00
Catherine Bergego Scale	0.13** (0.08 to 0.17)	0.02	< .001	.19
Shape cancellation (asymmetry)	0.15** (0.07 to 0.24)	0.04	< .001	.09
Line bisection near (deviation in mm)	0.26** (0.12 to 0.39)	0.07	< .001	.01
Line bisection far (deviation in mm)	-0.03* (-0.06 to -0.01)	0.01	.025	.04
Walking vs. walking with aid	-0.32 (-1.02 to 0.39)	0.36	.374	.01
Walking vs. wheelchair independent	-0.17 (-0.89 to 0.55)	0.37	.643	.00
Walking vs. wheelchair dependent	-0.08 (-0.63 to 0.78)	0.36	.834	.00

Abbreviations: SE, standard error; CI, confidence interval.

Asterisks indicate statistical significance with $\alpha < .05^*$, and with $\alpha < .001^{**}$.

Discussion

The aim of the current study was to investigate the feasibility, construct validity, underlying constructs, and potential confounders of the MAC in a convenient sample of stroke patients. Of 223 stroke patients, 81.6% completed the MAC. In 6.3% of patients, the MAC could not be

administered reliably due to practical issues, such as disruptions in the corridor in which the MAC was assessed. In 11.6% of patients, the task could not be completed due to patient-related characteristic, such as fatigue. In the study of Ten Brink et al. (2018), only 1 out of 113 patients (0.88%) could not complete the MAC. Importantly, in the study of Ten Brink et al. (2018), patients participated in the context of scientific research, leading to a biased sample excluding patients with high levels of fatigue. Nevertheless, the number of completed MAC assessments (81.6%) is lower than those for paper-and-pencil tasks, which can be completed by most patients. The relatively low completion rate for the MAC is partly due to the use of a real-life setting (i.e. a corridor), which is used by others as well and, therefore, not always suitable for administration of the MAC. This can be solved to some extent by making sure no other activities take place when the MAC is administered, or administer the MAC at a different moment, which both have not been done in the current study. However, in a clinical setting, this will not always be possible logistically and results are, therefore, realistic. Furthermore, not all patients were physically able to complete the MAC, especially those patients without a wheelchair but with severely affected motor function (e.g. walking slowly with a walking aid). This could be solved by either using a shorter route with less targets, which should be validated first, and/or by offering patients the possibility to use a wheelchair during the MAC. There are some drawbacks with this latter approach, as not all patients might want to use a wheelchair for this aim, and using a wheelchair deviates from their usual way of moving which makes the situation less comparable to daily life. Notably, the completion rate in the current study is conservative due to the study design. The MAC was sometimes administered at the end of a fully scheduled rehabilitation day, at which point patients did not always have energy left to complete the MAC. Taking all considerations into account, our results show the MAC can be systematically administered in a clinical setting to some extent. Within the current set-up, the MAC is feasible to administer as part of standard care in 4 out of 5 stroke patients admitted to inpatient rehabilitation, in the subacute phase post-stroke onset. The reported completion rates are, considering the nature of the task, not fully generalizable to other settings.

Our second aim was to study the construct validity of the MAC by comparing MAC performance between patients with and without VSN, and healthy controls. The goal of the comparison between groups was to test whether the patients with VSN (i.e. based on shape cancellation, line bisection, and Catherine Bergego Scale) would show worse performance on the MAC compared to patients without VSN. Stroke patients with VSN based on conventional tasks and/or observations of neglect in daily life obtained higher MAC asymmetry scores (i.e. worse performance, indicating a asymmetry in lateralized attention) compared to patients

without VSN and healthy controls. There were no differences on group level between stroke patients without VSN and healthy controls regarding the MAC asymmetry scores. This replicated the known group differences as seen in previous studies (Cunningham, O'Rourke, Finlay, & Gallagher, 2017; Grech et al., 2017; Ten Brink, Visser-Meily and Nijboer, 2018; Verlander et al., 2000).

In addition to these group comparisons, we **computed** percentages of patients who showed VSN as measured with the MAC, separately for patients with and without VSN based on two or more existing tasks (i.e. shape cancellation, line bisection near and far, and/or CBS) and separately for patients with and without VSN based on two conventional paper-and-pencil tasks (i.e. line bisection near and shape cancellation). Of the patients who showed VSN on two or more of the existing tasks, 45% also showed VSN on the MAC, which was 50% for patients who showed VSN on both paper-and-pencil tasks. This suggests that the MAC is less sensitive than the *combination* of line bisection, shape cancellation, and/or CBS. Yet, the MAC seems to be highly specific, as 95% of the patients who did not show VSN on two or more of the assessment tasks also did not show VSN at the MAC. Similarly, of patients who did not show VSN on both paper-and-pencil tasks, 89.4% did not show VSN at the MAC. Grech et al. (2017) also compared performance at the MAC with performance at two paper-and-pencil tasks (i.e. shape cancellation and line bisection). Compared to the paper-and-pencil tasks, the MAC total score had a higher sensitivity (74.2% versus 20.0%-43.3%) and a lower specificity (69.4% versus 94.4%-100%; Grech et al., 2017). Since there is no gold standard for the assessment of VSN, the groups do not perfectly reflect presence/absence of VSN, which might explain the discrepancy between studies. Interestingly, in the study of Grech et al. (2017), a clinical diagnosis of VSN was used as the gold standard, which overlapped more with MAC performance than performance at shape cancellation and line bisection.

Administering the MAC in addition to *individual* static tasks increases the possibility to adequately assess and subsequently treat VSN, as reflected by the double dissociation in the study of Ten Brink and colleagues (2018). **Similarly**, in the current study, 8.5% to 10.3% of patients who did not show VSN on one of the paper-and-pencil tasks, showed VSN on the MAC and would otherwise have been missed. However, the individual paper-and-pencil tasks and the CBS seemed to be more sensitive than the MAC, as 60.8% to 76.1% of patients who showed VSN on one of these individual tests did not show VSN on the MAC. One important difference between the study of Ten Brink et al. (2018) and the current one regards the nature of the patient sample. In the study of Ten Brink et al. (2018), the VSN patients were recruited as part of a larger RCT, whereas in the current study we included a convenient sample of stroke patients

admitted to inpatient rehabilitation. Potentially, the preselected patients for the RCT showed more clear-cut VSN in observations (hence, rehabilitation physicians and therapists recommended patients to be included in the study) and also showed moderate to severe VSN on the conventional tests. The aim of the current study was essentially to test the feasibility and applicability of the MAC as part of care as usual, instead of an instrument to be used in scientific research. As it turns out, the associations between the MAC and conventional tests are much weaker in a representative sample of stroke patients receiving inpatient rehabilitation. Although still feasible, the added value of the MAC as a diagnostic instrument next to the conventional pen-and-paper tests seems much lower than suggested in previous studies. In about 10% of patients however, the MAC was still able to detect VSN compared to conventional tests.

A third question regarded whether the level of mobility would affect performance at the MAC. As expected, the level of mobility differed between patients with and without VSN. Compared to the non-VSN group, patients with VSN more frequently used a wheelchair and were more often dependent on the examiner for moving through the corridors. This is in line with previous research: stroke patients with lower levels of mobility are more severely affected, which is related to the presence and severity of VSN (Embrechts et al., 2020; Oh-Park, Hung, Chen, & Barrett, 2014; Spreij et al. 2020). Since the MAC is a task in which participants are moving, a reduced level of mobility could potentially affect performance in two different ways. At one hand, difficulties with moving (e.g. resulting in the need of using an aid while moving) could increase mental load, resulting in worse search performance (Hara, 2015). On the other hand, if patients are pushed in their wheelchair by the examiner this removes the dual-task aspect of the MAC, which might result in better search performance. Since we did not have within-subject data on the level of mobility, and the level of mobility was linked to the condition of the patient, we could not dissociate between these different factors that were likely to contribute to MAC performance. To gain insight into the constructs and potential confounders that are measured with the MAC, we assessed the independent relationships between MAC performance, level of mobility, and different measures of VSN. All VSN measures were significant predictors of MAC performance, whereas this was not the case for the level of mobility. These results confirm that the MAC is a specific measure for VSN, and performance is not affected by different levels of mobility. In an exploratory analysis, we found that lesion side was not independently related with MAC performance. Thus, even though more patients with right than left brain damage showed VSN, lesion side did not explain any variance of MAC performance in addition to the conventional measures for VSN or observations of neglect in

daily life as measured with the CBS. This shows that the MAC can be administered both in patients with left or right brain damage.

Observations of VSN in daily life (i.e. measured with the CBS) predicted 19% of the variance in performance at the MAC, versus 9% for the shape cancellation, 1% for the line bisections in near space, and 4% for the line bisection in far space. The high prediction rate of the CBS was in line with our hypothesis, since the CBS is used to observe VSN behaviour in real-life situations similar to the MAC. The MAC and the CBS are both administered in a dynamic setting and leave less room for the use of compensation strategies, as opposed to conventional tasks such as shape cancellation, for which slowed search at one side or looking back is not incorporated in the final score. The dynamic aspect and the dual-task aspect of the MAC might assess the presence and genuine severity of VSN that patients may show in real life scenarios, which are also observed and scored with the CBS (Azouvi et al., 2003; Ten Brink, Visser-Meily, & Nijboer, 2018).

Both the CBS and the MAC have their own advantages and disadvantages, and both are a valuable addition to the assessment of VSN. A disadvantage of the CBS is that it is not always possible to observe a patient in all 10 daily life situations. Nurses might not always have time to fill out the CBS, or a patient might not be admitted to inpatient rehabilitation. In addition, the daily life situations that are observed with the CBS are less controlled than the setting of the MAC and, therefore, differ more between patients. The MAC allows to get a quick impression of VSN behaviour in a setting that is both measuring aspects of daily life settings and is relatively controlled. Because the MAC has a clear scoring system (i.e. counting the number of omissions), this is more standardized than the scoring of the CBS (i.e. rating the degree of “neglect behaviour”). Furthermore, the MAC can be administered at one moment, whereas multiple moments of observation are needed for the CBS. A disadvantage of the MAC is that the route differs between centers. This requires to obtain cut-off scores (norms) per corridor/route. Additionally, the specific test conditions can differ per assessment, for example, due to people walking through the corridors.

Strengths and limitations

The main strength of the study is the large number of included patients ($N = 223$, of whom 182 completed the MAC), which improves the reliability of our findings. In addition, the MAC was administered as part of standard care with inpatients, which shows that the MAC can be implemented in a clinical setting. There are also several limitations. First, the data on lesion side was available only for a small group of patients, resulting in a small sample in the

supplementary regression analysis. Nevertheless, effect sizes were calculated and the small sample most likely did not affect the conclusions drawn.

Second, our analysis on the underlying constructs and potential confounders of MAC performance was an exploratory analysis and results should be carefully interpreted, as explained in the introduction and methods.

Third, the effect of level of mobility on MAC performance was studied regarding the capacity of individual patients. Therefore, performance on the MAC **might** still differ within one person when using a wheelchair versus when walking. Future studies could include a between-subject condition with different levels of mobility (e.g. asking participants to perform the task once while in a wheelchair, and once while walking), which would yield additional insights into the constructs measured with the MAC.

Fourth, we did not have information on the presence or absence of hemianopia. Possibly, hemianopia could have negatively affected performance at the MAC.

Fifth, we did not systematically investigate how much time, training, and experience is necessary for examiners to adequately administer the MAC. To minimize differences in task administration, a manual with detailed instructions is available. In addition, examiners will have clinical experience in guiding their patients through the corridors, ensuring patient's safety. Nevertheless, differences in implementation of the task might affect results. In our study we compared the data between examiners on a broad level and concluded that we did not find reasons to assume an effect on our current data. In clinical practice we would like to emphasize the adherence to protocol for clinicians is vital. Future studies could evaluate the training of examiners. In addition, studies on using the MAC in other settings, such as outpatient treatment or follow-up clinical care, could be of value.

Finally, as mentioned before, the MAC was not administered in a controlled environment, since we aimed to study the MAC in a realistic setting (i.e. a setting in which the task will eventually be implemented). People could freely use the corridors during assessment. When setting up the route for the first time, preferably, **no main** entrance should be part of the route, because of possible hinder by too many bystanders. Having a shorter route, with less than 24 targets, will potentially ease the selection of suitable corridors. It is, therefore, worth investigating the influence of route length on the sensitivity and specificity of the MAC.

Clinical implementation and conclusion

The MAC is a useful addition to the assessment of VSN, as it provides information about VSN in a more dynamic situation as compared to paper-and-pencil tasks. Before implementing the

MAC in a new setting, it should be evaluated whether there is a suitable route, enough time to train the staff, and enough time to prepare and administer the MAC. A drawback of the MAC is that time is needed to prepare the task before it can be administered. If it turns out not to be possible to administer the MAC in all stroke patients, however, it could still be of value to administer the MAC in specific cases. Furthermore, administering the MAC within the first month post-stroke can be a challenge as patients are still recovering from severe brain damage, leading to fatigue and a range of physical and mental impairments. Indeed, we found that in 11.6% of the patients, the MAC could not be completed due to physical disabilities, such as fatigue. This raises the question **of** in which phase post-stroke onset the MAC should be administered. A reason to administer the MAC in the subacute phase (i.e. the first month post stroke-onset) is the importance to assess VSN as quickly as possible to select the appropriate treatment. Rehabilitation of VSN should take place quickly following stroke (Chen, Hreha, Kong, & Barrett, 2015). In addition, better insight in the specific construct of VSN can help to offer a more personal and suitable rehabilitation trajectory for each patient (Kimura et al., 2018). However, the MAC could also be a useful instrument at the end of a rehabilitation program to assess whether there **still** is VSN. In addition to the quantitative outcome (i.e. the asymmetry score), the MAC allows to observe behaviour qualitatively in a setting that mimics the dynamics of daily life. Such information is useful for psycho-education, as patients and their loved ones will easily see the similarities between performance at the MAC and situations they encounter in their own life, such as crossing a street, or for advice regarding their own home environment or additional therapies.

To conclude, the MAC can be used to assess VSN in a dynamic setting. The MAC is feasible to administer in four out of five patients as part of a standard assessment for VSN in the first month post-stroke onset. With the cut-offs used in the current study, the MAC has a lower sensitivity and a higher specificity as compared to conventional paper-and-pencil tasks and observations of neglect in daily life (CBS). Importantly, about 8.5% to 10.3% of patients who did not show VSN at shape cancellation and line bisection tasks, did show VSN at the MAC and would have been missed if only the conventional paper-and-pencil tasks were administered. This percentage is much lower when compared to the CBS (5.4%), which is not surprising since both MAC and CBS are tasks with dynamic aspects. Therefore, we recommend to administer at least one dynamic task (e.g. either the MAC or CBS) in addition to paper-and-pencil tasks in the assessment of VSN. There is evidence for a good construct validity of the MAC, and performance is not confounded by the level of mobility or lesion side. The MAC

does not require specific hardware and is easy to administer, and could be implemented in the subacute or a later phase post-stroke onset.

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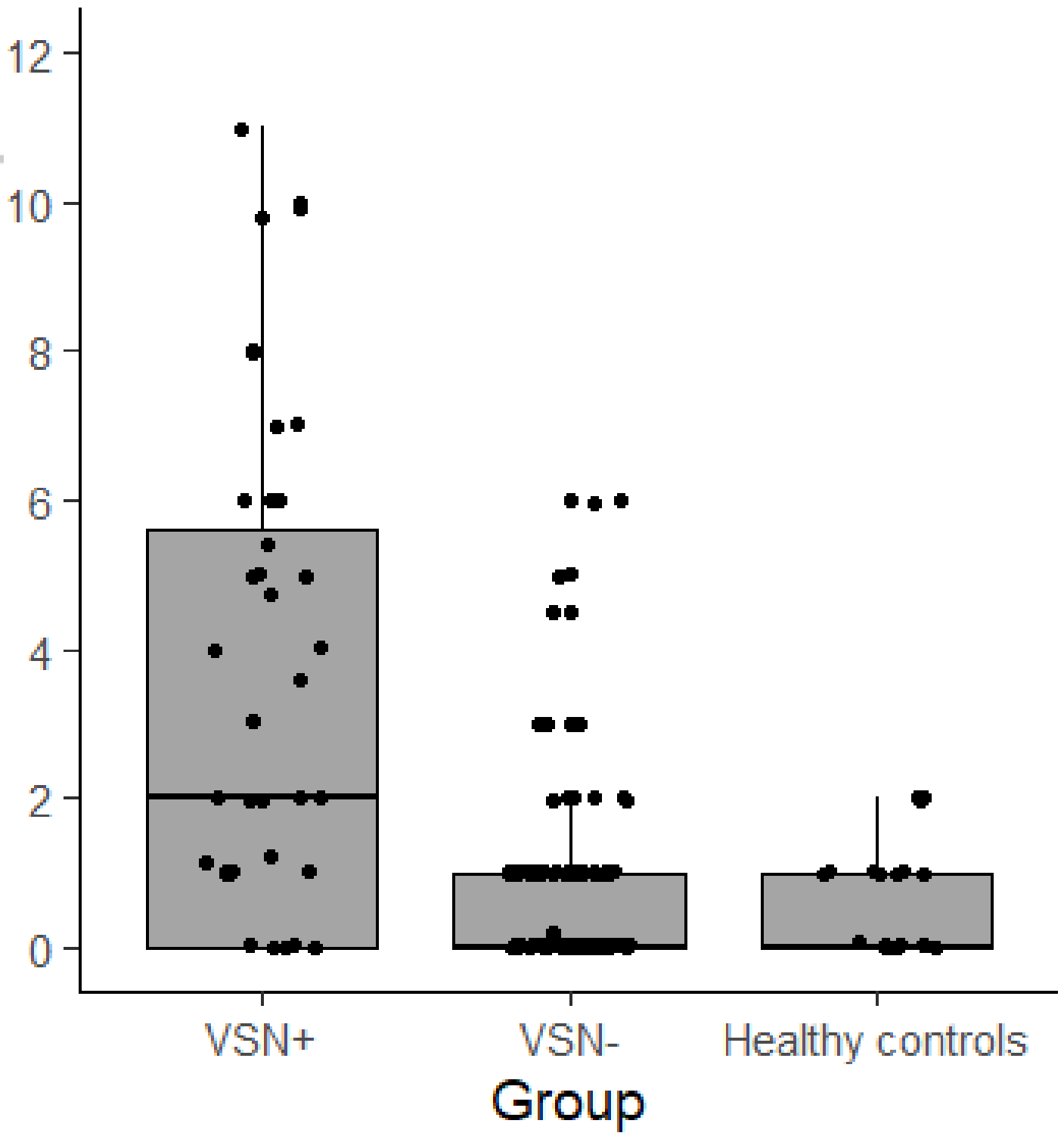
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