Impairments in spatial navigation during walking in patients 70 years or younger with mild stroke

Charlotta Hamre[a-d]*, Brynjar Fure[e,f,g], Jorunn Lægdheim Helbostad[h], Torgeir Bruun Wyller[b,c], Hege Ihle-Hansen[b,d], Georgios Vlachos[d], Marie Helene Ursin[i] & Gro Gujord Tangen[b,j,k]

[a]Department of Physiotherapy, Oslo University Hospital (OUS), Norway; [b]Department of Geriatric Medicine, OUS, Norway; [c]Institute of Clinical Medicine, University of Oslo (UiO), Norway; [d]Department of Neurology, OUS, Norway; [e]Department of Internal Medicine, Central Hospital, Karlstad, Sweden; [f]Department of Neurology, Central Hospital, Karlstad and Örebro, Sweden; [g]School of Medical Sciences, Örebro University, Sweden; [h]Department of Neuromedicine and Movement Science, Norwegian University of Science and Technology, Norway; [i]Department of Geriatric Medicine, Bærum Hospital, Vestre Viken Trust, Norway; [j]Norwegian National Advisory Unit on Ageing and Health, Vestfold Hospital Trust, Norway; [k]Department of Interdisciplinary Health Sciences, UiO, Norway.

*corresponding author: charlotta.hamre@studmed.uio.no

Background: Spatial navigation, the ability to determine and maintain a route from one place to another, is needed for independence in everyday life. Knowledge about impairments in spatial navigation in people with mild stroke is scarce.

Objectives: To explore impairments in spatial navigation in patients ≤ 70 years after first-ever mild ischemic stroke (NIHSS≤3) and to explore which variables are associated with these impairments 12 months later.

Methods: Patients were examined in the acute phase, and after three and 12 months. To assess impairments in spatial navigation, we used the Floor Maze Test (FMT), with time and FMT-errors as outcomes. Patients' perceived navigational skills were collected using self-report. Logistic regression was used to explore which variables (sociodemographic data, stroke characteristics, cognition, and mobility) were associated with impaired navigation ability.

Results: 97 patients (20 female) were included. Mean (SD) age was 55.5 (11.4) years. Timed FMT improved significantly from the acute phase to 12 months (p=<.001). At 12 months, 24 (24.7 %) of the participants walked through the maze with errors, and 22 (22.7 %) reported spatial navigational problems. The Trail Making Test (TMT)-B was the only variable from the acute phase associated with FMT-errors at 12 months, and being female was the only variable associated with self-reported navigational problems at 12 months.

Conclusion: Nearly one in four patients experienced spatial navigation problems 12 months after a mild stroke. Executive function (TMT-B), measured in the acute phase, was associated with navigational impairments (FMT-errors) at 12 months, and being female was associated with self-reported navigational problems.

Keywords: Mild stroke, working age, spatial navigation, performance-based, self-report

Introduction

The number of people with only mild impairments after a stroke is increasing because of the positive effects of new treatments (e.g., prophylactic interventions, reperfusion therapy, stroke units).[1,2] Today, about two-thirds of patients experience only mild deficits in the acute phase.[3] Despite better outcomes, patients still report changes in both cognitive and physical function.[4,5] Furthermore, in the last two decades, the proportion of younger people affected by stroke has increased.[6-8] Thus, even mild impairments can reduce the ability to return to work,[9,10] affect everyday activity, and hinder participation in family and societal life.[11-13]

A common way to assess the severity of a stroke is using the National Institute of Health Stroke Scale (NIHSS).[14] There is no uniform definition of a mild stroke, but a NIHSS score from zero to three to five points have been described as indicative of a mild stroke.[15] It is also common to screen for cognitive impairments in persons with mild stroke, but navigational abilities are rarely addressed.[16] Spatial navigation is the ability to determine and maintain a route from one place to another.[17] Finding one's way is not a unitary cognitive function, but a complex interaction between multiple cognitive functions.[18,19]

Navigational abilities are needed in everyday life, and the consequences of impairments can be illuminated by using the International Classification of Functioning, Disability and Health framework (ICF).[20] The ICF framework has three domains i.e. body structure and function, activity, and participation. Spatial navigation belongs to the body function domain. By causing impairments in spatial navigation, the stroke may limit activities and participation. We use our navigational abilities both while walking in familiar locations (e.g., going to the local grocery store) and when visiting unfamiliar places (e.g., being a tourist in a new place).[21] Thus, navigation ability is crucial for maintaining participation in both formal and informal activities in the society.[13,22] In a prevalence study of patients with mild stroke in the chronic phase (n=62), self-reported navigation problems were present in around one-third of the participants.[23] The same study also showed that the self-reported navigational problems were associated with reductions in autonomy and quality of life. In addition, persons with stroke have more difficulties in performance-based navigation tasks than controls.[18,24,25]

A review of topographical studies has shown the medial temporal lobes, especially the hippocampus, to be of importance in wayfinding.[26] After a stroke, topographical studies about lateralization of spatial navigation have attributed an important functional role to the right

hemisphere,[27] while others have pointed out that the left hemisphere as well is crucial for such tasks.[28]

There is limited research on all three domains of the ICF regarding the consequences of impairments in spatial navigation caused by a mild stroke. Also, there is a lack of information about long-term navigation problems and whether there are factors associated with impairments after 12 months. In addition, the knowledge of the patients' self-reported spatial navigation problems is scarce.

This study aimed to describe impairments in spatial navigation during walking in the acute phase and after three and 12 months in patients 70 years or younger after a first-ever mild ischemic stroke defined by a NIHSS score of ≤ 3. In addition, we wanted to explore which variables in the acute phase were associated with impairments in performance-based (FMT-errors)[19] and self-reported spatial navigation at 12 months.

Materials and methods

Study design and participants

This observational, longitudinal cohort study recruited patients from a larger study entitled "Hidden impairments after stroke." The main study consecutively included patients hospitalized in the acute stroke units of Oslo University Hospital, Ullevål Clinic, or Vestre Viken Hospital Trust, Bærum Hospital, from November 2014 to December 2016. The sample size was determined by the available number of cases at these two units during the study period. For the current study, the inclusion criteria were age 18-70 years ("working age") and having a first-ever unilateral mild ischemic stroke. Mild stroke was defined as a NIHSS score from zero to three.[14] The diagnosis was based on the history of symptoms and findings on the neurological examination, and all patients underwent magnetic resonance (MRI) for verification.[29] If patients had no acute infarction on MRI, but neurological deficits compatible with cerebrovascular disease lasting more than 24 hours, they were considered to have ischemic stroke. Patients were not included if they had a cognitive decline prior to the stroke, indicated as a mean score on the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[30] > 3.2.[31] If the patients suffered a new stroke during the 12 months, they were withdrawn from further follow-up. All patients gave their written, informed consent before inclusion. The study was approved by the Regional Committee for Medical and Health

Research Ethics in the Southeast of Norway (reference 2014/1268). The manuscript of this study conforms to the STROBE statements.[32]

Participants

Information regarding age, gender, and years of education were collected in the acute ward by interviews and patients' record. Patients were examined in the acute phase and after three and 12 months. The examination in the acute phase and at three months were part of the clinical routine, while the assessment at 12 months follow-up was added for study purposes. All three times at the hospital. Physiotherapists working at the stroke units and trained in assessing patients with the Floor Maze Test (FMT)[19] conducted the assessments. At the 12-month assessment, the patients were also asked about their self-perceived navigation skills.

Outcome measures

The NIHSS was used to evaluate stroke severity and whether the patient met the inclusion criteria.[14] The NIHSS rates impairments in 11 functional domains commonly affected in patients with stroke, such as level of consciousness and orientation, facial palsy, motor function in arm and leg, language, and inattention. It ranges from zero to 42 points, where a higher score indicates a more severe impairment. To assess pre-stroke cognitive status, the IQCODE was used.[30] The IQCODE is a 16-item questionnaire scored on a one- to five-point ordinal scale by a relative or next of kin, and it has shown sensitivity to screen for cognitive decline in stroke population.[33] Stroke location was categorized into right or left hemisphere, cerebellum or multiple brain regions and dichotomized into lesion in the right hemisphere versus the others to highlight any impact of the right hemisphere on spatial navigation. Patients with infarctions in multiple brain regions that included right hemisphere were dichotomized into the right hemisphere category.

The Mini-Mental State Examination (MMSE) was used to assess cognitive status.[34] The MMSE is scored from zero to 30 points based on tasks targeting orientation, attention, calculation, recall, and complex commands, and a higher score indicates better cognitive functioning. It has shown good validity when used in patients with stroke.[35] In addition, the Trail Making Test (TMT) parts A and B were applied, where TMT-A measures focused attention, visual search, and motor function, and TMT-B measures executive functioning, divided attention, visual search, and motor function.[36] Both the MMSE and the TMTs are common tools for assessment of cognition after stroke.[37]

For gait speed, patients walked six meters, starting from a stand-still position, and were instructed to walk at their normal speed. Time in seconds with one decimal was measured by a hand-held stopwatch, and then the speed in meters per second (m/s) was calculated.

Dependent variables

To assess spatial navigation, we used the FMT.[19] The FMT is a two-dimensional maze task created on a 7 × 10-foot solid dark blue wax cloth with white tape indicating the lines of the maze (Figure 1) and requires navigation during walking. The FMT was performed as described in the original paper by Sanders et al. 2008. It has shown good validity and test-retest reliability when used in a sample of community-dwelling older people.[19] The patients were positioned at the entry of the maze and then given instructions. Two components of the FMT were timed: (1) planning time (PT), the time from finishing the instructions until the patient starts to walk; (2) immediate maze time (IMT), the time spent walking through the maze from entry to exit, and then summarized to a Total Maze Time (TotalMT). Time in seconds was measured using a handheld stopwatch. While walking through the maze, participants were permitted to correct any wrong turns. These wrong turns were counted as FMT-errors. If a patient asked for advice during the walk, the initial instructions were repeated. The FMT were operationalized into two different outcomes: Timed performance (PT, IMT, and TotalMT) in seconds, and to a dichotomous score of error-free performance (error-free = 0) versus performance with errors or discontinuation of the TotalMT (FMT-error > 1).

We used the newly developed Spatial Orientation Screening (SOS) to assess self-reported navigational impairments. The SOS is a screening tool consisting of four questions targeting impairments in orientation in familiar and unfamiliar surroundings, recognizing familiar places, and whether any impairments have led to reduced participation in society. Each question is scored from zero (no problems) to two (frequent/pronounced problems). The total score ranges from zero to eight, where high scores indicate more severe impairments. To describe self-reported spatial navigation problems at 12 months, the SOS was dichotomized into experiencing no problem (SOS=0) or having problems (SOS ≥1). The SOS is currently under validation. The MMSE, TMT A and B, FMT and gait speed were assessed at all three time point, while the SOS was only conducted at the 12 months follow-up.

Statistical analyses

Data are presented as means and standard deviation (SD) for normally distributed variables, as median and interquartile ranges (IQR) for variables with skewed distribution, and as proportions and percentage for categorical variables. Changes over the three testing time points (i.e., acute phase, three, and 12 months) were explored by using the Friedman's test since the data had a skewed distribution, and also McNemar test for dichotomous outcome. If the overall change was statistically significant, we proceeded with pairwise comparisons between each of the test points (i.e., acute phase to three months, three to 12 months, and acute phase to 12 months) using the Wilcoxon signed-rank test. To allow for multiple comparisons, we applied the Bonferroni correction to these analyses using a significance level at p=.017.

To explore which variables in the acute phase were associated with having navigational problems in either errors in performance-based navigation (FMT-errors, dichotomized to present yes/no) or in self-reported navigational complaints (dichotomized to present yes/no) at 12 months follow-up, we performed two multiple logistic regression analyses. Independent variables in these models were chosen based on previous studies and clinical reasoning, and included sociodemographic data (age, sex, and education) as they are commonly known as factors affecting function after stroke, stroke characteristics including stroke severity (NIHSS) and lesion side (right/left) as earlier studies have produced conflicting results,[27,28] the cognitive domains of memory and executive function (MMSE, TMT-B)[19,38], and as the task contained walking, we included gait speed. Patients with multiple infarctions that involved the right hemisphere were categorized into the reference category of right hemisphere.

Correlation analyses were made to determine if there were collinearity issues between the independent variables (rs $\geq$0.7). We used univariate binary logistic regression analyses to determine which of the independent variables we should include in the multivariate model ($p<0.5$). We used odds ratios with 95% confidence intervals to compare the strengths of the association between the independent variables and the main outcome of performance-based or self-reported navigational problems. The Hosmer-Lemeshow Goodness-of-Fit Test for logistic data was used to verify that the models supported the data.

Data were analyzed using the Statistical Package for Social Science (SPSS) version 25 (IBM Corporation, Armonk, NY). P-values <0.05 were considered as indicators of statistical significance, and all tests were two-sided.

Results

The inclusion process and study flow are shown in Figure 2. In total, 97 patients attended the 12-months' follow-up. Table 1 shows the sociodemographic and clinical characteristics of the patients. The mean (SD) age was 55.5 (11.4) years, total rang 30 – 70 years, and 20 (20.6%) were women. Patients were included and examined at median (Q_1, Q_3) day 4 (2,5) after arriving at the hospital, and length of stay was median (Q_1, Q_3) 6.0 (5.0, 8.0) days. NIHSS mean (SD) at inclusion was 0.6 (0.9) points, where the majority (68%) had a score of zero, indicating no measurable neurological impairments detected by the NIHSS. None of the patients used a walking device.

We found a statistically significant improvement in the Floor Maze Test timed performance on PT, IMT and TotalMT from the acute phase to 12 months (Table 2). When looking for differences between each time point (the acute phase to three months, and between three and 12 months), only the TotalMT showed a statistically significant difference from three to 12 months (Table 2). The correlation between the PT and IMT was r_s= 0.24, p=0.02 in the acute phase, and r_s=0.17, p=0.09 at 12 months. All participants managed to find their way through the maze. In the acute phase, 31 (32.0%) of the participants walked the maze with errors compared to 24 (24.7%) at 12 months (p=0.28). Self-perceived navigation problems were reported from 22 (22.7%) of the participants at 12 months.

Table 3 shows the results from the multiple logistic regression analyses. In the adjusted model, the only variable from the acute phase associated with FMT-errors at 12 months was the TMT-B, with an odds ratio (95% CI) of 1.00 (1.00-1.03) (p=0.02). For self-reported navigation problems, female gender was the only significant variable, odds ratio (95% CI) 3.68 (1.11-12.18) (p=0.03).

Discussion

We aimed to explore impairments in spatial navigation after mild stroke. Our findings indicate that although most of the patients with mild stroke performed well on the FMT, patients' timed performance on the FMT from the acute phase to 12 months significantly improved. Further, more than one in five patients either had FMT-errors or self-reported problems in spatial navigation 12 months post stroke. The only variable measured in the acute phase that was independently associated with having navigational impairments (FMT-errors) at 12 months was TMT-B, and for self-reported navigational problems at 12 months, female gender was the only associated independent variable. To our knowledge, this is the first

longitudinal study exploring impairments in spatial navigation in a large number of participants with mild stroke.

For persons with stroke, the knowledge of spatial navigation during walking is sparse.[23] Our results indicate that although all the participants were able to find their way through the maze, still approximately 25% walked with errors at 12 months follow-up. In a cross-sectional study by Sanders et al.[19] among 124 community-dwelling older adults without cognitive impairment, only 14% walked with errors during the FMT. Besides making more errors in the FMT, it should also be noted that our participants (with a mean age of 55 years) were a lot younger than the participants in Sanders' study (mean age of 78 years). For younger persons with stroke, impairments in spatial navigation at younger age potentially can lead to an even increasing problem with time due to age-related decline in navigational abilities.[39]

Furthermore, 23% of our participants reported problems with navigation at 12 months. This is a slightly lower proportion than was found in the study by van der Ham et al.,[23] where 29% reported navigational problems in the chronic phase after stroke. The population in van der Ham's study had similar age as our participants and included patients with mild stroke. Since these patients were included in a chronic stage (mean time after stroke was 40 months), they had not provided an NIHSS score, which makes it hard to compare the stroke severity between the two studies. Furthermore, the difference in results between the two studies can be due the use of different questionnaires. The Dutch study used the Wayfinding Questionnaire, which is a far more comprehensive questionnaire with several subscales covering different aspects of wayfinding, such as navigation, mental transformation, distance estimation, and sense of direction.[23]

The contributions from other cognitive domains are reflected in the two timed sections of the FMT (time spent planning how to walk the maze, and the time spent walking through the maze). The participants dedicated more time to route planning compared to IMT at all three test points. This is in line with the study of Sanders et al. (2008), where the study sample of community-dwelling participants also devoted more time to route planning.[19] This may indicate that most patients were able to remember and carry out the plan they had decided on during PT. Furthermore, in the logistic regression analyses with FMT-errors at 12 months as the dependent variable, TMT-B was the only variable significantly associated with this outcome. Previous studies, both in patients attending a memory clinic[38] and in community-

dwelling older adults,[19] have found that executive function, measured with the TMT-B, was associated with FMT. In the memory clinic study, although TMT-B was significantly associated with the FMT, the relatively low explained variance still indicates that the TMT-B does not adequately capture impairments in spatial navigation.[38]

The finding that women are more likely to report navigational impairments than men is in line with findings from other studies. Burke et al. (2012) showed that there were no gender differences in performance-based tests (real-world setting), but when answering self-report questionnaires, men were more confident compared to women about their wayfinding skills.[40] Others have also found that self-reported impairments in navigation ability are associated with being female, being older, and having more cognitive, anxiety or depressive complaints.[41,42] Neither age nor education was associated with impairments in spatial navigation. Our patients were quite young and well educated, which might explain why these well-known variables were not statistically significant in our study. In contrast to a previous study[27], but in line with another,[28] lesion side was not associated with spatial navigation. Taken together, it seems that lateralization of spatial navigation is complex, and when screening for navigational impairments after stroke, information about lesion side does not provide sufficient information to detect navigational impairments.

Research on navigational impairments in people after stroke has often focused on brain topography using case studies.[43] These studies are important for knowledge about brain structure and function but give little information in a clinical setting with a focus on patients' participation in an everyday life function. Navigational tests can be carried out in real-world situations, with a virtual reality equipment, or with questionnaires.[44] Self-report tools can give important information about a person's perception of navigation ability but are not necessarily associated with performance-based navigation in real-life situations.[44] After a stroke, assessments of cognitive function are routinely carried out, and guidelines emphasize visual neglect as an important cognitive function to assess.[45] Other aspects of spatial cognition, such as navigational abilities, have rarely been addressed, neither in the acute or subacute phase nor in the outpatient clinic.[16] Potentially, this could lead to underdiagnosing navigation ability impairments, which in turn might hinder persons with even mild stroke from participating in everyday activities.[46]

The major limitation of this study is the lack of pre-stroke information about spatial navigation ability, both performance-based and self-reported. There is a common acceptance that individual differences in sense of direction exist, and we cannot conclude that the observed impairments in spatial navigation at 12 months were caused by the stroke.[47] Furthermore, we do not have information about rehabilitation interventions after stroke, and could thus not adjust for this in the regression analyses. Several physical therapists were involved in the assessments, which may affect the inter-rater reliability. Here, we think the pre-study training of the assessment procedures might have limited this bias. Another limitation is the larger proportion of men included. More men than women experience a stroke at a younger age;[48] however, the presence of 80% men in this sample exceeded the anticipated gender bias, limiting the generalizability of our findings for female stroke patients. A major strength of the study is the large sample size with very few drop-outs, the longitudinal design and the use of performance-based as well as self-reported outcomes for spatial navigation.

In conclusion, the results indicate that approximately one in four patients with mild stroke experienced spatial navigation problems by performing errors while walking or by reporting navigational problems. We believe that these impairments may go undetected in the usual clinical follow-up. Future studies should focus on the impact of impairments in spatial navigation on participation in society and leisure.

Acknowledgments

We thank all the participants for taking part in this study. We also thank our colleagues at the two stroke units – especially Kristina Flornes Aalo, Berit Tronsmo, and Kathrine Karlsen – for their support and assistance in the data collection.

Funding

The study was funded by the Norwegian Fund for Postgraduate Training in Physiotherapy under Grant ID 76340.

Disclosure of interest

The authors report no conflict of interest

References

1. Lees KR, Emberson J, Blackwell L, et al. Effects of Alteplase for Acute Stroke on the Distribution of Functional Outcomes: A Pooled Analysis of 9 Trials. *Stroke.* 2016;47(9):2373-2379.
2. Collaboration SUT. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev.* 2013(9):CD000197.
3. Reeves M, Khoury J, Alwell K, et al. Distribution of National Institutes of Health stroke scale in the Cincinnati/Northern Kentucky Stroke Study. *Stroke.* 2013;44(11):3211-3213.
4. Moran GM, Fletcher B, Feltham MG, Calvert M, Sackley C, Marshall T. Fatigue, psychological and cognitive impairment following transient ischaemic attack and minor stroke: a systematic review. *Eur J Neurol.* 2014;21(10):1258-1267.
5. Stewart JC, Cramer SC. Patient-reported measures provide unique insights into motor function after stroke. *Stroke.* 2013;44(4):1111-1116.
6. Bejot Y, Bailly H, Durier J, Giroud M. Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med.* 2016;45(12 Pt 2):e391-e398.
7. Ramirez L, Kim-Tenser MA, Sanossian N, et al. Trends in Acute Ischemic Stroke Hospitalizations in the United States. *Journal of the American Heart Association.* 2016;5(5).
8. Bejot Y, Delpont B, Giroud M. Rising Stroke Incidence in Young Adults: More Epidemiological Evidence, More Questions to Be Answered. *Journal of the American Heart Association.* 2016;5(5).
9. Wolfenden B, Grace M. Returning to work after stroke: a review. *Int J Rehabil Res.* 2009;32(2):93-97.
10. Morris R. The psychology of stroke in young adults: the roles of service provision and return to work. *Stroke Res Treat.* 2011;2011:534812.
11. Nys GM, van Zandvoort MJ, de Kort PL, et al. The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology.* 2005;64(5):821-827.
12. Staub F, Bogousslavsky J. Fatigue after stroke: a major but neglected issue. *Cerebrovasc Dis.* 2001;12(2):75-81.
13. Edwards DF, Hahn M, Baum C, Dromerick AW. The impact of mild stroke on meaningful activity and life satisfaction. *J Stroke Cerebrovasc Dis.* 2006;15(4):151-157.
14. Goldstein LB, Bertels C, Davis JN. Interrater reliability of the NIH stroke scale. *Arch Neurol.* 1989;46(6):660-662.
15. Fischer U, Baumgartner A, Arnold M, et al. What is a minor stroke? *Stroke.* 2010;41(4):661-666.
16. van den Berg E, Ruis C. Space in neuropsychological assessment. In: Postma A, van der Ham IJM, eds. *The neuropsychology of space.* Cambridge: Elsvier Academic Press; 2016:361-378.
17. Gallistel CR. *The organization of learning* Camebridge: Bradfords Books/MIT Press; 1990.
18. van Asselen M, Kessels RP, Kappelle LJ, Neggers SF, Frijns CJ, Postma A. Neural correlates of human wayfinding in stroke patients. *Brain Res.* 2006;1067(1):229-238.
19. Sanders AE, Holtzer R, Lipton RB, Hall C, Verghese J. Egocentric and exocentric navigation skills in older adults. *J Gerontol A Biol Sci Med Sci.* 2008;63(12):1356-1363.
20. World Health Organization. International Classification of Functioning, Disability and Health. https://www.who.int/classifications/icf/en/. Published 2001. Accessed.
21. Wolbers T, Hegarty M. What determines our navigational abilities? *Trends Cogn Sci.* 2010;14(3):138-146.

22. Rochette A, Desrosiers J, Bravo G, St-Cyr-Tribble D, Bourget A. Changes in participation after a mild stroke: quantitative and qualitative perspectives. *Top Stroke Rehabil.* 2007;14(3):59-68.
23. van der Ham IJ, Kant N, Postma A, Visser-Meily JM. Is navigation ability a problem in mild stroke patients? Insights from self-reported navigation measures. *J Rehabil Med.* 2013;45(5):429-433.
24. Barrash J, Damasio H, Adolphs R, Tranel D. The neuroanatomical correlates of route learning impairment. *Neuropsychologia.* 2000;38(6):820-836.
25. Busigny T, Pages B, Barbeau EJ, et al. A systematic study of topographical memory and posterior cerebral artery infarctions. *Neurology.* 2014;83(11):996-1003.
26. Kessels RP, de Haan EH, Kappelle LJ, Postma A. Varieties of human spatial memory: a meta-analysis on the effects of hippocampal lesions. *Brain Res Brain Res Rev.* 2001;35(3):295-303.
27. Jacobs J, Korolev IO, Caplan JB, et al. Right-lateralized brain oscillations in human spatial navigation. *J Cogn Neurosci.* 2010;22(5):824-836.
28. Ruggiero G, Frassinetti F, Iavarone A, Iachini T. The lost ability to find the way: topographical disorientation after a left brain lesion. *Neuropsychology.* 2014;28(1):147-160.
29. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2013;44(7):2064-2089.
30. Jorm AF. The Informant Questionnaire on cognitive decline in the elderly (IQCODE): a review. *Int Psychogeriatr.* 2004;16(3):275-293.
31. Harrison JK, Fearon P, Noel-Storr AH, McShane R, Stott DJ, Quinn TJ. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a general practice (primary care) setting. *Cochrane Database Syst Rev.* 2014(7):CD010771.
32. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg.* 2014;12(12):1495-1499.
33. Burton L, Tyson SF. Screening for cognitive impairment after stroke: A systematic review of psychometric properties and clinical utility. *J Rehabil Med.* 2015;47(3):193-203.
34. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975;12(3):189-198.
35. Cumming TB, Churilov L, Linden T, Bernhardt J. Montreal Cognitive Assessment and Mini-Mental State Examination are both valid cognitive tools in stroke. *Acta Neurol Scand.* 2013;128(2):122-129.
36. Reitan RM. The relation of the trail making test to organic brain damage. *J Consult Psychol.* 1955;19(5):393-394.
37. Saa JP, Tse T, Baum C, et al. Longitudinal evaluation of cognition after stroke - A systematic scoping review. *PLoS One.* 2019;14(8):e0221735.
38. Tangen GG, Engedal K, Bergland A, Moger TA, Hansson O, Mengshoel AM. Spatial navigation measured by the Floor Maze Test in patients with subjective cognitive impairment, mild cognitive impairment, and mild Alzheimer's disease. *Int Psychogeriatr.* 2015:1-9.
39. Head D, Isom M. Age effects on wayfinding and route learning skills. *Behav Brain Res.* 2010;209(1):49-58.
40. Burke A, Kandler A, Good D. Women who know their place : sex-based differences in spatial abilities and their evolutionary significance. *Human nature (Hawthorne, NY).* 2012;23(2):133-148.
41. Coluccia E, Louse G. Gender differences in spatial orientation: A review. *J Environ Psychol.* 2004;24:329-340.
42. Moffat SD. Aging and spatial navigation: what do we know and where do we go? *Neuropsychol Rev.* 2009;19(4):478-489.

43. Claessen MHG, Visser-Meily JMA, Meilinger T, Postma A, de Rooij NK, van der Ham IJM. A systematic investigation of navigation impairment in chronic stroke patients: Evidence for three distinct types. *Neuropsychologia.* 2017;103:154-161.
44. Nadolne MJ, Stringer AY. Ecologic validity in neuropsychological assessment: prediction of wayfinding. *J Int Neuropsychol Soc.* 2001;7(6):675-682.
45. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* 2016;47(6):e98-e169.
46. de Rooij NK, Claessen MHG, van der Ham IJM, Post MWM, Visser-Meily JMA. The Wayfinding Questionnaire: A clinically useful self-report instrument to identify navigation complaints in stroke patients. *Neuropsychol Rehabil.* 2017:1-20.
47. Piccardi L, Risetti M, Nori R. Familiarity and environmental representations of a city: a self-report study. *Psychol Rep.* 2011;109(1):309-326.
48. Sealy-Jefferson S, Wing JJ, Sanchez BN, et al. Age- and ethnic-specific sex differences in stroke risk. *Gend Med.* 2012;9(2):121-128.

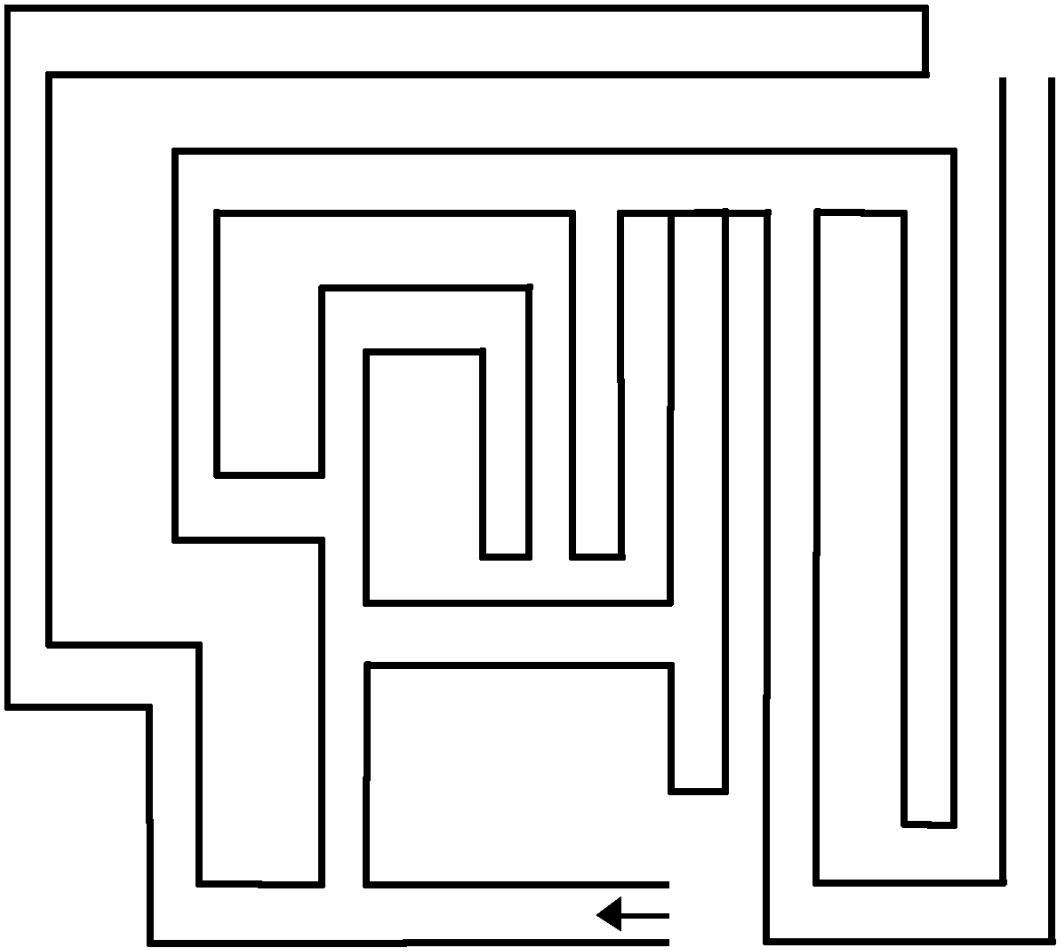

Figure 1. The Floor Maze Test.

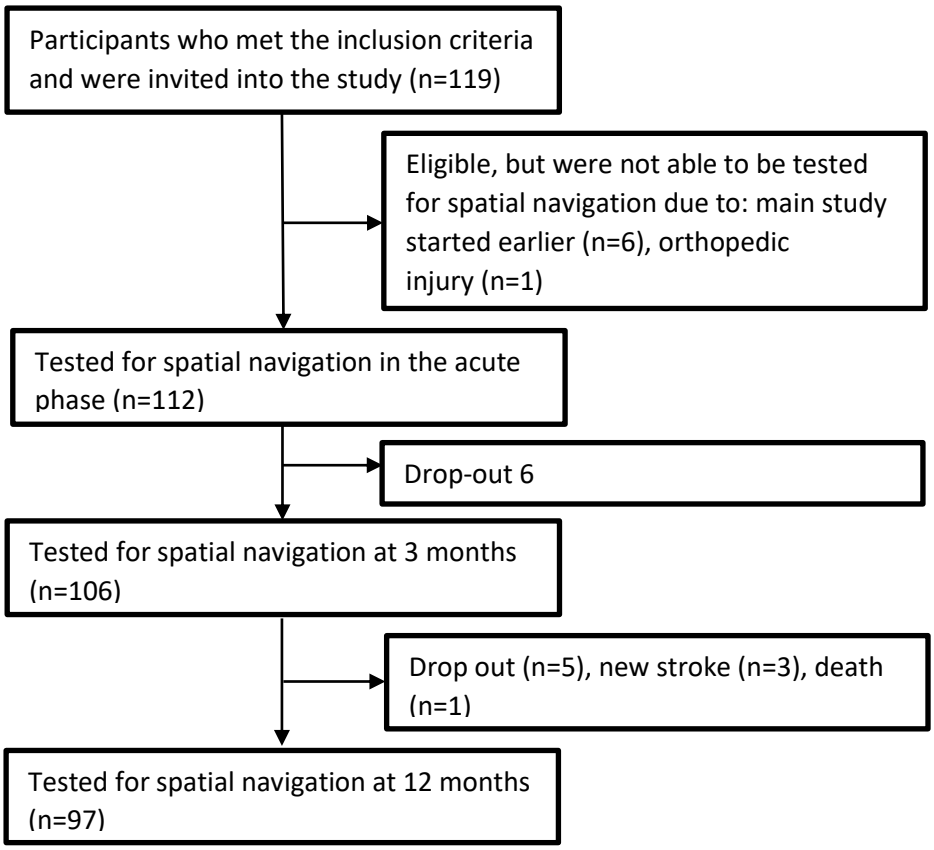

Figure 2. Flowchart for inclusion of the study participants.

Table 1. Baseline Sociodemographic and Clinical Characteristics of the Participants.

Variable	Total (n=97)
Female, n (%)	20 (20.6)
Age (y), mean (SD)	55.4 (11.4)
Years of education, mean (SD)	15.3 (3.6)
Stroke characteristics	
NIHSS at inclusion, median (Q_1, Q_3)	0.0 (0, 0.9)
Topography, MRI-findings, n (%)	
Right hemisphere	35 (36.1)
Left hemisphere	28 (28.9)
Cerebellum	15 (15.5)
Multiple brain regions	14 (14.4)
No acute lesions on MRI	5 (5.2)
Mobility	
Gait speed (m/s), mean (SD)	1.03 (0.23)
Cognition	
MMSE (points), median (Q_1, Q_3)	29.0 (28.0, 30.0)
TMT-A (s), median (Q_1, Q_3)	35.5 (27.0, 46.8)
TMT-B (s), median (Q_1, Q_3)	84.5 (63.5, 123.8)

Y = year, SD = standard deviation, NIHSS = National Institute of Health Stroke Scale, Q = quartile, MRI = magnetic resonance imaging, MMSE = Mini-Mental State Examination, TMT-A = Trail Making Test-A, TMT-B = Trail Making Test-B. Data are reported as numbers (percentages) of participants unless otherwise indicated.

Table 2. The Floor Maze Test performance across the test points (acute phase, 3, and 12 months) with pairwise comparisons (n=97).

	Test times				Pairwise comparisons					
	Acute phase	3 months	12 months		Acute phase – 3 months		3– 12 months		Acute phase – 12 months	
	Median (Q1,Q3)	Median (Q1,Q3)	Median (Q1,Q3)	P[a]	Difference Mean (SD)	p[b]	Difference Mean (SD)	p[b]	Difference Mean (SD)	p[b]
PT (s)	21.2 (12.8, 41.5)	18.8 (11.6, 34.1)	16.1 (10.1, 30.8)	0.03	6.8 (37.7)	.08	4.6 (25.6)	.08	11.5 (38.0)	.004
IMT (s)	17.3 (13.4, 25.2)	15.1 (12.5, 20.2)	15.1 (12.2, 17.5)	<0.001	9.1 (51.8)	.09	5.6 (27.1)	.04	14.7 (46.5)	.006
Total-MT (s)	44.8 (31.4, 71.5)	38.0 (27.3, 56.6)	31.4 (25.2, 47.2)	<0.001	15.9 (72.6)	.03	10.3 (36.3)	.006	26.2 (62.6)	<.001

PT = Planning Time, IMT = Immediate Maze Time, Total-MT= Total Maze Time (PT + IMT), SD = Standard Deviation. [a]Friedman test,

[b]Wilcoxon Signed Pair Test. Bonferroni post hoc comparisons $p = .017$

Table 3. Multiple logistic regression analyses with the Floor Maze Test-errors (FMT-errors) at 12 months and self-reported spatial impairments at 12 months as dependent variables.

Variables, acute phase	FMT-errors				Self-reported spatial impairment			
n=92	Unadjusted model		Adjusted model		Unadjusted model		Adjusted model	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age (years)	.99 (.95-1.03)	.49	.97 (.93-1.02)	.27	1.00 (.96-1.05)	.83		
Sex (ref: female)	1.52 (.50-4.61)	.46	1. (.71-9.88)	.30	3.07 (1.04-9.04)	.04	3.68 (1.11-12.18)	.03
Education (years)	.98 (.85-1.12)	.73			0.91 (.79-1.05)	.20	0.95 (.82-1.10)	.51
NIHSS at inclusion (points)	1.62 (.99-2.66)	.06	1.32 (.75-2.32)	.34	1.14 (.68-1.91)	.62		
Topography (ref: right hemisphere)	1.13 (.43-2.93)	.81			1.59 (.61-4.18)	.34	1.87 (.65-5.37)	.25
MMSE (points)	.86 (.68-1.07)	.17	1.03 (.78-1.35)	.86	0.96 (.76-1.21)	.72		
TMT-B (s)	1.01 (1.00-1.02)	.01	1.00 (1.00-1.03)	.02	1.00 (.10-1.01)	.45	1.00 (1.00-1.01)	.30
Gait speed (m/s)	.68 (.09-5.04)	.71			0.63 (.08-4.67)	.63		

Ref = reference category, NIHSS = National Institute of Health Stroke Scale, MMSE = Mini-Mental State Examination, TMT-B = Trail Making Test – B.