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Improvement of cognition across a decade after stroke correlates with the integrity of functional brain networks

Johan Eriksson [a], Lars Nyberg [a,b], Eva Elgh [c], Xiaolei Hu [d,*]

[a] Umeå center for Functional Brain Imaging (UFBI) and Department of Integrative Medical Biology, Umeå University, 901 87 Umeå, Sweden
[b] Department of Radiation Sciences, Umeå University, 901 87 Umeå, Sweden
[c] Department of Psychology, Umeå University, 901 87 Umeå, Sweden
[d] Department of Community Medicine and Rehabilitation, Umeå University, 901 87 Umeå, Sweden

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ABSTRACT

Background and objective: We recently reported improvements of working memory across 10 years post stroke among middle-aged individuals. However, the mechanisms underlying working-memory recovery are largely unknown. This study investigated the associations between long-term improvement of working memory and resting-state functional connectivity in two frontoparietal networks: the frontoparietal network and the dorsal attention network.

Methods: Working memory was repeatedly assessed by the Digit Span Backwards task in 21 persons, within 1 year after stroke onset and again 10 years post stroke onset. Brain functional connectivity was examined by resting state functional magnetic resonance imaging at the 10-year follow-up.

Results: A significant improvement of working memory was found among 21 persons after stroke (median age = 64) at the 10-year follow-up compared to the within-one-year assessment. The magnitude of performance improvement on the Digit Span Backwards task was significantly positively correlated with stronger brain connectivity in the frontoparietal network ($r = 0.51$, $p = 0.018$) measured at the 10-year follow-up only. A similar association was observed in the dorsal attention network ($r = 0.43$, $p = 0.052$) but not in a visual network ($r = -0.17$, $p = 0.46$) that served as a control network. The association between functional connectivity within the above-mentioned networks and Digit Span Backwards scores at 10-year after stroke was in the same direction but did not reach significance.

Conclusions: The present work relate stronger long-term performance improvement on the Digit Span Backwards task with higher integrity of frontoparietal network connectivity.

1. Introduction

Working memory is a multicomponent system that plays a significant role in goal-directed behavior in daily living (Eriksson et al., 2015). Impairment of working memory affects other executive functions and also episodic memory formation and retrieval (Bergmann et al., 2013). Post-stroke working-memory dysfunction is substantially affected in the acute phase after stroke and remains prominent also in the chronic stage of stroke (Elgh and Hu, 2019; Lugtmeijer et al., 2021). Working-memory difficulties predicts increased disability, dependency, institutionalization and mortality (Lugtmeijer et al., 2021; Synhaeve et al., 2015) as well as episodic-memory impairment and increased risk for post-stroke dementia (Leys et al., 2005). Despite its importance for everyday functioning, the impairment of working memory often remains overlooked in stroke follow-up.

We have previously reported improvements in the Digit Span Backwards (DSB) task across 10 years post stroke among middle-aged individuals (average age 64 at 10-year follow-up) (Elgh and Hu, 2019). The DSB task requires participants to repeat digits in the reverse order of that presented by the examiner. The task therefore taxes attention and working-memory processes to a greater extent than short-term memory-maintenance tasks such as Digit Span Forward. However, the mechanisms underlying recovery of working memory remain largely unknown.

Neuroimaging studies indicate that the human brain is organized in

Abbreviations: DSB, Digit Span Backwards task; rfMRI, resting state functional magnetic resonance imaging; FPN, frontoparietal network; DAN, dorsal attention network.

* Corresponding author.
E-mail address: xiaolei.hu@umu.se (X. Hu).

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large-scale resting state networks (RSNs), defined by inter-regional functional connectivity from resting state functional magnetic resonance imaging (rfMRI). Previous studies have demonstrated altered patterns of functional connectivity both at acute and chronic phases after stroke (Baldassarre et al., 2016; Carrera and Tononi, 2014; Tao and Rapp, 2020). A limited number of studies have found that normalization of functional connectivity is accompanied by behavioral recovery in neglect and language after stroke (Ramsey et al., 2016; Sebastian et al., 2016). However, these prior studies had relative short follow-up time (in months) and did not examine recovery of executive functions.

Anatomically, attention and working-memory processes depend on the integrity of frontoparietal brain circuits (Eriksson et al., 2015). Degree of frontoparietal functional connectivity is linked to working-memory performance, including connectivity in the frontoparietal system (Murphy et al., 2020). Frontoparietal lesions after stroke play a key role in working-memory deficits (Kornfeld et al., 2018; Lugtmeijer et al., 2021), suggesting that individual differences in resting-state functional connectivity in networks with marked frontoparietal involvement, such as the frontoparietal network (FPN) and the dorsal attention network (DAN) (Majerus et al., 2018) (Fig. 1), may relate to the degree of recovery of working memory post stroke. However, the association between working memory and connectivity of frontoparietal networks after stroke remains elusive. The rationale of the current study is that the changes in working memory might be associated with the status of functional connectivity of FPN and DAN among these persons more than a decade after stroke. Although longitudinal measures of both cognition and connectivity would have been ideal, we are here limited to the association between longitudinal cognitive changes and connectivity only at the 10-year follow-up.

This study aimed at investigating the associations between functional connectivity in FPN and DAN with long-term improvement on the DSB task ten years after stroke onset (Elgh and Hu, 2019). We hypothesized that improvement of working memory is related to stronger FPN and DAN connectivity. In the absence of connectivity data from the time near stroke onset, we could compute a change in DSB performance but not in degree of connectivity. In a control analysis, DSB performance was related to connectivity in a visual network, for which no DSB-connectivity association was expected. To the best of our knowledge, no prior study has related behavioral improvement over a decade to the integrity of network connectivity.

2. Materials and methods

2.1. Study design

This is a single-center prospective cohort study of stroke survivors. Ethical approval for the cognitive assessment was obtained from the regional Ethical Review Board in Umeå, Sweden, Dnr 2015/144–31. An ethical approval for the rfMRI examination study was approved by the Swedish Ethical Review Authority with Dnr 2019–02830.

2.2. Participants

The study was conducted at the Department of Neurorehabilitation, University Hospital of Umeå, and Umeå center for Functional Brain Imaging (UFBI), Umeå University. A total of 38 stroke survivors with previous neuropsychological assessments who participated in a 10-year follow-up cognitive study (Elgh and Hu, 2019, 2020) were informed about the current rfMRI study and were provided with written consent forms via letters. A research staff made contact via telephone with all eligible patients to improve the recruitment rate. Twenty-four participants provided their written informed consent to participate, while 13 declined and one had deceased (Fig. 2). Behavioral data for the DSB task at the early timepoints were missing for two participants, and one participant was excluded due to excessive head movements during scanning (mean frame-wise displacement more than three standard deviations from the group mean). Thus, 21 patients were included in the present analyses.

2.3. Basic demographic and clinical characteristics

Baseline data were collected from the *Riksstroke* registry (Register, 1994) and from patients' medical records. The clinical data were collected by various questionnaires one month prior to the scheduled

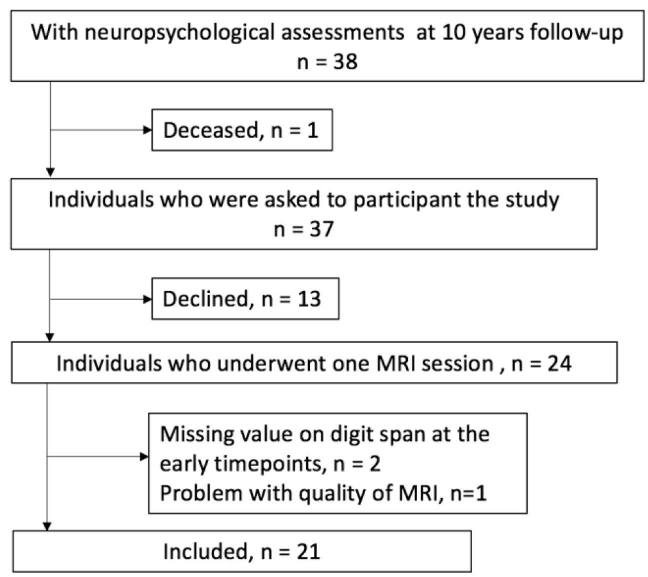

Fig. 2. Flow diagram of inclusion process.

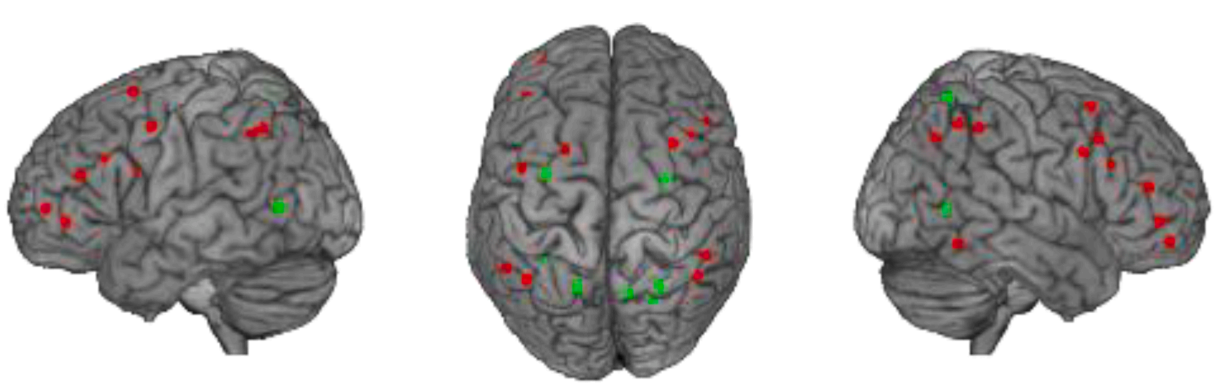

Fig. 1. Nodes of the "frontoparietal" (red) and "dorsal attention" (green) resting-state networks, as defined in the parcellation by Powers and colleagues (Power et al., 2011). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

appointment for neuropsychological assessments and are described in more detail below and in the previous study (Elgh and Hu, 2019).

2.4. Functional status assessment

Functional status assessment examined patients' independency in their daily activity. The simplified modified Rankin Scale questionnaire (smRSq) is a standardized, practical, and validated questionnaire for the reliable assessment of a person's functional and disability status (Bruno et al., 2010). The assessed patients' answers five questions with either 'yes' or 'no', and a value on a scale from 0 (no symptoms) to 5 (total physical dependence) is obtained. Scores of 2 or less are considered to represent total independence (Bruno et al., 2010).

2.5. Depression and anxiety assessments

Depression and anxiety have negative impact in stroke recovery. Depression was assessed using the Beck Depression Inventory-II (BDI-II) (Kapci et al., 2008); a self-rating scale that measures depression in adults and adolescents. The test contains 21 questions, each being answered by a single score on a 0–3 point scale. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs of the BDI-II are $\leq$ 13 for minimal depression, 14–19 for mild depression, 20–28 for moderate depression, and 29–63 for severe depression.

Anxiety was assessed using the Beck Anxiety Inventory (BAI) (Carney et al., 2011); a 21-item multiple-choice self-report inventory. Each answer was given as a score describing how much the patient has suffered from a particular symptom, with the scale ranging from 0 (not at all) to 3 (severely). Higher total scores indicate more severe anxiety symptoms. The standardized cutoffs are $\leq$ 7 for minimal anxiety, 8–15 for mild anxiety, 16–25 for moderate anxiety, and 26–63 for severe anxiety.

2.6. Cognitive assessment with Digit Span

Data in this study were collected in a single-centre prospective, longitudinal cohort study of stroke survivors with three consecutive follow-ups over a 10-year period after a first-ever stroke (Elgh and Hu, 2019). Digit Span from Wechsler Adult Intelligence Scale (WAIS)-IV was used to assess working memory. Notably, WAIS-R and WAIS-III used at one week and 7-month follow-ups was replaced by WAIS-IV at the 10-year follow-up due to practical reasons. Previous validation studies have shown that WAIS-IV has the same construction as WAIS-III/R (Tulsky et al., 1997) with very high correlation between subscales ($r = 0.82$–94) (Weschler, 2010).

The cognitive functions of stroke survivors were assessed prospectively at the 10-year follow-up, then compared retrospectively with data collected 1 week- and 7 months after stroke in the medical records before the study was planned. By following the same assessment protocol, the assessments were performed by the different test administrators at the different time points. For this reason, there were some missing values at the early timepoints. Among 21 participants at the 10-year follow-up, only 17 participants had Digit Span data from the one-week, and 12 participants had Digit Span data at seven-months after stroke onset. Furthermore, no significant difference ($p = 0.72$) on the means (SD) of Digit Span data was observed between one-week (5.5 (1.8)) and 7-month (6.0 (2.6)) follow-ups in the present cohort. The change in performance was therefore calculated as performance at 10 years minus the average performance across one week and seven months when available ($n = 8$), and otherwise relative to performance at the initial test phase when data was available (one week: $n = 9$; seven months: $n = 4$).

2.7. Scanning procedure

The MRI data were collected with a GE 3 Tesla Discovery MR750 scanner (32-channel receive-only head coil). Each participant underwent one MRI session which included a resting-state fMRI examination, a high-resolution structural imaging protocol (T1), two T2 sequences (FLAIR and PROPELLER) to support neuroradiological examination, and a B0 sequence to correct for field inhomogeneities during preprocessing of the fMRI data.

For resting-state fMRI, a T2*-weighted gradient echo pulse sequence (echo planar imaging) was used, field of view = 25 cm, matrix size = 96 × 96, slice thickness = 3.4 mm, 37 slices with no interslice skip and an ASSET acceleration factor of 2. The volumes covered the whole cerebrum and most of the cerebellum. The acquisition orientation was oblique axial and aligned with the anterior and posterior commissures, and the slices were acquired in interleaved order with TE = 30 ms, TR = 2 s, flip angle = 80°. A high-resolution T1-weighted structural image was collected using fast spoiled gradient echo with TE = 3.2 ms, TR = 8.2 ms, TI = 450 ms, and flip angle = 12°. Pulse and respiration data was collected during fMRI using a photoplethysmograph and a breathing belt, respectively. Before image acquisition, 10 dummy scans were collected and discarded. The participants were instructed to fixate on a crosshair centered on a display throughout the sequence.

2.8. Preprocessing of fMRI data

Image pre-processing was conducted with SPM12 (Wellcome Department of Imaging Neuroscience, London, UK) running in Matlab 8.4 (Mathworks, Inc., Sherbon, MA, USA) using custom-made Matlab scripts. Functional images were corrected for slice-time differences, realigned to the first image of the time series to correct for head movement and unwarped to remove residual movement-related variance, including adjustment for B0 field inhomogeneities, and co-registered to high-resolution structural data. Structural images were normalized to the MNI (Montreal Neurological Institute) template using DARTEL (Ashburner, 2007) and the resulting parameters were used for functional image normalization, which were resampled to 2 mm isotropic voxel size. Finally, functional images were smoothed with an 8 mm FWHM Gaussian kernel.

2.9. Overlap between stroke lesions and network nodes

To investigate a possible relation between network connectivity and node-lesion overlap, we identified stroke lesions in T1 and FLAIR images, as apparent at the time of resting-state data collection. Possible overlap with network nodes was identified visually by a clinician, by projecting the nodes on the normalized structural images using the MRICroN software (Rorden et al., 2007). The number of partial or complete lesion-node overlap was counted for each participant and network separately. The unit of analysis with regard to lesion overlap was nodes rather than voxels, such that partial or complete overlap would both count as 1 unit of overlap.

Lesion information was not used to constrain the connectivity estimation. That is, all voxels and nodes were included in the connectivity calculations regardless of possible lesion-node overlap, thus allowing for the evaluation of a possible effect from lesion-node overlap across participants.

2.10. Data analyses and data presentations

2.10.1. Resting-state connectivity

Resting-state connectivity was calculated as the mean Pearson correlation between nodes within a given network, where each network was defined according to the Power parcellation of 264 nodes (Power et al., 2011) (labeling of network nodes from the original publication is available at https://www.jonathanpower.net/2011-neuron-bigbrain.html). The relevant signal change was calculated as the average signal across the included voxels for each node. Mean network correlations were calculated for the frontoparietal and the dorsal attention networks to test the hypothesis of recovery-network-integrity associations, and in the visual network as a control condition. Head movement was included as nuisance regressors using the Friston 24 expansion of the realignment parameters. Mean signal in cerebrospinal fluid (CSF) and white matter were also included as nuisance regressors, together with regressors generated using RETROICOR (Glover et al., 2000) based on pulse and respiration data, implemented in the physIO toolbox (Kasper et al., 2017). Additional nuisance regressors for each time point where frame-wise displacement was larger than 0.2 were also included. Given the inclusion of signal change related to pulse and respiration, as well as CSF and white matter, it was not deemed relevant to include global signal change as an additional nuisance regressor (Ciric et al., 2017; Power et al., 2017).

In group-level analyses the change in behavioral performance on the digit-span backwards task across ten years (see above) were correlated with mean connectivity within networks, while controlling for mean-centered frame-wise displacement (FD) and squared mean FD (Power et al., 2015; Satterthwaite et al., 2012). That is, the residuals after regressing mean-centered FD and FD squared on mean connectivity were added to the constant term in the same regression (i.e., the average correlation in the group), resulting in connectivity values adjusted for FD and FD squared. The adjusted values were then correlated with cognition.

2.10.2. Demographic and behavioral data

Demographic characteristics are presented as Mean ± SD, number with/without number of cases (%). Statistical analyses for alterations of DSB over time (paired *t*-test) were performed using SPSS software version 27, with a p value < 0.05 being considered significant.

3. Results

3.1. Demographic and medical characteristics

Demographic and medical characteristics of the participants at the 10-year follow-up session after stroke onset are presented in Table 1. The median age of participants was 64 with mostly female participants (57 %). Most of the participants (n = 18, 86 %) had no or only slight disability (mRS = 0–2). Most of the participants were slightly overweight without suffering either depression or anxiety. Ischemia was the dominate stroke sub-type (67 %). More than half of the participants (62 %) had more than 12 years education. At the time of neuropsychological assessments at 10-year follow-up, 38 % participants were still working.

Table 1
Demographic and clinical characteristics of 21 participants at 10-years follow-up after stroke onset.

Mean of Age at 10-year follow-up (SD)	62.3 (8.8)
Age at stroke onset (mean (SD))	52.7 (8.3)
Men/Women	9/12
Residential status (Live alone/live with somebody/unknown)	5/15/1
Stroke subtype	
Ischemia (%)	14 (67%)
Hemorrhage (%)	6 (29%)
Unknown (%)	1 (5%)
Mean of mRS (SD)	1 (1)
Mean of BMI (SD)	27.5 (4.0)
Mean of BAI (SD)	8.0 (7.9)
Mean of BDI-II (SD)	11.8 (8.7)
Level of education (years)	
9	2 (10%)
12	6 (29%)
greater than12	13 (62%)
Employment (number of case (%))	
Full-time job	3 (14%)
Part-time job	5 (24%)
Retired/Unemployed	12 (57%)

3.2. Improvement of working memory

We verified that the previously reported improvement in DSB across 10 years post stroke (Elgh and Hu, 2019) also applied to the current sub-sample. Indeed, the change (M = 2.29, 95 % CI = 1.29–3.28; Fig. 3A) in DSB scores was significant ($t_{20} = 4.80$, $p = 0.00011$).

3.3. Positive associations between FPN, DAN and improvement of working memory

The change in performance on DSB across 10 years correlated positively with mean connectivity within the frontoparietal network ($r_{19} = 0.51$, $p = 0.018$), and at trend level with connectivity within the dorsal attention network ($r_{19} = 0.43$, $p = 0.052$; Fig. 3B-C). We also correlated the change in performance with connectivity in the visual 'control' network, where we had no a priori reason to expect a significant correlation. The change did not correlate with mean connectivity within the visual network ($r_{19} = -0.17$, $p = 0.46$; Fig. 3D).

The relation of DSB performance at the 10-year follow-up with connectivity in the FPN and DAN networks was in the same direction as for the DSB change score but did not reach significance (FPN: $r_{19} = 0.25$, $p = 0.27$; DAN: $r_{19} = 0.27$, $p = 0.42$; Fig. 3E, F).

3.4. No association between network connectivity and node-lesion overlap

There was an overlap between network nodes and stroke lesions in five out of the 21 participants for the frontoparietal network (range: 2–7 out of 25 nodes), and in two participants for the dorsal attention network (1 and 3 out of 11 nodes). With so few individuals with any overlap, estimations of possible correlations between connectivity and lesion overlap would be underpowered. Qualitatively, we note that four out of five individuals with a lesion-node overlap had a frontoparietal network connectivity value within 1.5 SD of the group mean and that two out of the five was above the mean. For the dorsal attention network, one of the individuals with lesion-node overlap had a connectivity value above, and one below, the group mean. The correlation between DSB change and connectivity increased for the FPN when excluding participants with a node-lesion overlap ($r_{14} = 0.56$, $p = 0.024$) and decreased slightly for the DAN ($r_{17} = 0.40$, $p = 0.094$). Taken together, we found no evidence for a relation between degree of network connectivity and node-lesion overlap.

4. Discussion

The current study investigated whether individual differences in degree of long-term improvement of working memory assessed by the DSB task relate to resting-state functional connectivity in two fronto-parietal networks (FPN and DAN). We found a significant improvement of working memory at 10-year follow-up compared to that within one year after stroke onset. Notably, we demonstrated that a larger performance improvement on the DSB task was significantly and positively correlated to stronger FPN connectivity measured only at 10 years after stroke onset, with a corresponding trend for the DAN.

4.1. Recovery of working memory across a decade

Consistent with our previous findings (Elgh and Hu, 2019, 2020), the amelioration of working memory capacity was demonstrated in the cohort of 21 participants examined by rfMRI in the current study. Since DSB among the healthy population is commonly reported constant during middle adulthood (GrÉGoire and Van Der Linden, 1997) and declining in late adulthood (Hester et al., 2004; Karakas et al., 2002), we assumed that increased DSB at 10-year follow-up in the sample reflected recovery of working memory. Similar to our previous studies (Elgh and Hu, 2019, 2020), the significant recovery of working memory as assessed by the DSB task was demonstrated only at 10 years, although

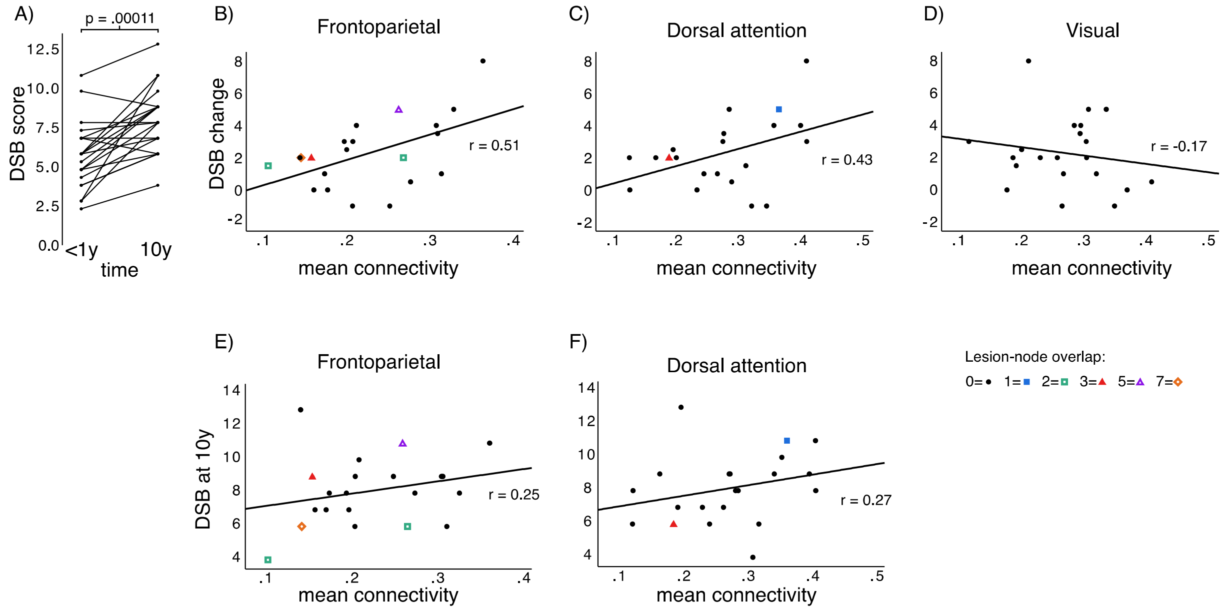

Fig. 3. A) The change in performance on the digit span backwards test is shown as lines from timepoint 1 (<1 year after stroke) to timepoint 2 (10 years after stroke). Each line represents one individual. B-D) Scatter plots and regression line for change in performance over a decade after stroke (y axes) as a function of mean connectivity (x axes) within resting-state networks. E-F) Scatter plots and regression line for the relation between DSB performance at 10-year follow-up and mean connectivity. Colored dots indicate individuals with an overlap between network nodes and lesions; colors represent number of nodes that overlap with lesions (see bottom right of figure for key). The connectivity values are mean correlations adjusted for framewise displacement (FD) and FD squared (see methods).

there was a non-significant tendency of the DSB improvement at 7 months when comparing to that at one week after stroke. This is consistent with the recent findings in *meta*-analysis studies that have demonstrated stable impairment of working memory at chronic stage, i. e. at 3–36 month post-stroke (Lugtmeijer et al., 2021; Sachdev et al., 2009). Long-term cognitive declines have recently been demonstrated from one to three-year post-stroke (Lo et al., 2022). However, the time course of the recovery of working memory we found in this study is much longer than the common concept that most recovery occur within the first three months after stroke (Ramsey et al., 2017). The later recovery of working memory at 10-year follow-up could be explained by an appropriate activity training, such as activities in daily life, which may reopen the critical window of neuroplasticity (Laaksonen and Ward, 2022; Ward, 2017). Taken together, the current finding may suggest that more complicated functions, such as working memory, require longer time (more than a few years) to recover (Elgh and Hu, 2019, 2020).

To our knowledge, the participants received no specific cognitive rehabilitation treatment after stroke onset. The high education (62 % with university education) combined with being active in daily activities (median of mRS = 1) and occupations (38 % participants remained working part or full time) as well as a relative young age at stroke onset (median age of 54 years old) may be important contributors to the improvement of working memory in the present cohort (Lo et al., 2022; Shin et al., 2020). This is consistent with previous studies suggesting that activities or rehabilitation under a long time may induce improvement of working memory (Elgh and Hu, 2019; Kessels et al., 2017; Shin et al., 2020). In this selected study sample, the above-mentioned contributors may partially explain why the DSB data at 10-year follow-up are higher than published data in people with chronic stroke (Lugtmeijer et al., 2021). Consistent with our previous studies (Elgh and Hu, 2019, 2020), the current findings suggested that a prolonged recovery phase needs to be considered in clinical practice, especially for more complicated functions like working memory, in comparison to the common view of a recovery plateau reached after 6 months post stroke (Bernhardt et al., 2017). Thus, the current study establishes a hypothesis that the late recovery of working memory may occur several years after stroke. This need of course to be confirmed by larger longitudinal stroke datasets.

4.2. Strength of functional connectivity is associated with working memory recovery

To the best of our knowledge, our results for the first time show that the improvement of working memory over a decade related positively to the integrity of network connectivity of FPN and DAN at the chronic phase after stroke. Our results are in line with the suggestion that frontoparietal lesions after stroke play a key role in working-memory deficits at the acute stage (Kornfeld et al., 2018; Lugtmeijer et al., 2021). It supports the view that the integrity and degree of frontoparietal functional connectivity is linked to working-memory performance (Eriksson et al., 2015; Murphy et al., 2020). Our results are encouraging because they provide unique evidence for higher integrity of frontoparietal functional connectivity concurrent with working-memory recovery among persons even a decade after stroke onset.

Even though one may expect the degree of connectivity to be related to the magnitude of the working memory score, the correlation between functional connectivity of FPN and DAN with DSB scores at 10-year follow-up was not significant despite of a similar trend. Instead, stronger connectivity of FPN was significantly correlated with improvement of DSB scores over a decade after stroke. The reason for this discrepancy remains unclear.

4.3. Limited overlap between lesions and network nodes

The limited overlap between lesions and networks may also be a relevant factor for enabling cognitive improvement since the lesions in frontoparietal networks are associated with working memory impairment (Lugtmeijer et al., 2021). However, it remains largely unknown how these diverse lesions affected the functional connectivities of FPN and DAN at the acute stage since rfMRI were performed only after 10 years in the study. Presumably, like in the visuospatial attention system (Carter et al., 2017; Siegel et al., 2016), the stroke lesions should negatively affect the integrity of functional connectivity in some ways since working memory showed significant impairments within the first year after stroke in this cohort (Elgh and Hu, 2019, 2020). However, the question remains why degree of recovery of working memory is not directly related to stroke lesions' localization, side and size. Possibly, unlike visual and motor impairment, working memory is better predicted by functional connectivity than lesion topography (Siegel et al., 2016).

4.4. Strengths and limitations

A strength of the current study was to be able to present both behavioral improvement over a decade and functional connectivity within this unique cohort. However, we could only measure brain connectivity at the end of this period, making the nature of a change-change association unclear in the absence of time-point 1 connectivity data. We are also aware of the issue of the small number of participants ($n < 25$) for the correlation analyses and the potential pitfalls of using a single measurement of working memory. Also, even though different test administrators were used at the different time points, the standard test protocol was followed to enhance interrater reliability and minimize the potential variability in the present study. Furthermore, no celling effect was observed in this cohort since there was a significant improvement across 10 years. Nevertheless, rather than generalizing the findings to the entire young stroke population, the current study suggests mainly that improvement of working memory correlates with functional connectivity of the FPN and DAN in the brain and does occur during the chronic phases after first-ever stroke, at least among some young stroke survivors who are actively living in the community. These findings require verification by a large-scale study.

In the current study, the visual network was used as a control condition because it is not directly related to working memory performance. However, as the visual network is also more circumscribed/localized compared to the FPN and DAN, it may in addition be less susceptible to stroke-related damage. Although we did not find support for a relation between lesion extent and the DSB-connectivity association, this limitation in the use of the visual network as a control may be noted.

5. Conclusion

The present work points to a stronger performance improvement on the DSB with higher integrity of frontoparietal network connectivity, over a decade after first-ever stroke onset among middle-aged individuals. The current study suggests that higher FPN functional connectivity may be an indicator of a greater recovery of working memory among persons with stroke. This hypothesis needs confirmation by larger longitudinal stroke datasets.

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CRediT authorship contribution statement

Johan Eriksson: Conceptualization, Visualization, Data curation, Writing – original draft, Writing – review & editing. **Lars Nyberg:** Conceptualization, Writing – review & editing. **Eva Elgh:** Conceptualization, Writing – review & editing. **Xiaolei Hu:** Conceptualization, Resources, Data curation, Visualization, Writing – original draft, Writing – review & editing, Funding acquisition, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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