



Short communication

Long-term consequences of subarachnoid hemorrhage: Examining working memory



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ABSTRACT

Working memory impairments are prevalent among survivors of aneurysmal subarachnoid hemorrhage (SAH), but few studies have examined specifically these impairments. Such an examination is important because working memory processes are vital for daily cognitive functioning. In the current study, patients with SAH and healthy control participants were administered the word-span and alpha-span test – experimental tests of working memory. In the word-span test, participants recalled increasingly longer word-lists, requiring the maintenance of information in mind. In the alpha-span test, participants recalled the word-lists in alphabetical order, requiring both the maintenance and manipulation of information. Patients with SAH were no different from healthy controls on a battery of standard neuropsychological measures or on the word-span test. They were, however, significantly impaired on the alpha-span test, suggesting a deficit in the manipulation components of working memory. That is, impairment resulting from SAH is present when a working memory task requires additional executive processing demands. This deficit in patients with SAH does not appear to be influenced by aneurysm location, suggesting that some of the effects of SAH on cognition are from diffuse rather than focal pathology; however, a larger sample size is needed to reinforce this claim.

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1. Introduction

There is a high prevalence of cognitive deficits after aneurysmal subarachnoid hemorrhage (SAH). These cognitive impairments, much like those that result from other diffuse injury, cut across multiple domains including memory and executive function [1]. As such, patients recovering from SAH often experience deficits in a broad range of tasks, true even for those who are functionally independent and classified as having made a good clinical recovery [2–4]. To date, we have a limited understanding of the broad characteristics of these impairments, yet such understanding is critical given that they lead to a consequential decrease in quality of life for patients after SAH [5,6]. In this report, we focused on understanding deficits in working memory, the short term, temporary storage and manipulation of information in consciousness [7], following SAH because it is a critical process for many activities in

daily life. Specifically, we sought to determine if SAH impairs working memory broadly or only when there are additional demands on executive function.

Working memory tasks require simple storage of information and in more complex tasks, the stored information needs to be manipulated online, requiring additional executive resources such as attention allocation [8]. Studies that have examined how SAH affects working memory have used tasks that require only the storage of information online, with variable results [9,10]. To our knowledge, no study has specifically examined the different components of working memory (storage and manipulation).

Given that standard neuropsychological measures used to assess cognitive function include multiple processes and may not pick up upon the specificity of such impairment following SAH [11], we chose to use an experimental measure of working memory with and without additional executive processing demands, the word- and alpha-span test [12]. If impairments in working memory following SAH are specific to when additional processing are required, then patients recovering from SAH should perform normally on the test that requires the serial recall or temporary storage of information (word-span test), but impaired on a test that requires the ability to manipulate the stored information (alpha-span test).

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2. Methods

2.1. Participants

Twenty-one patients with surgically treated SAH (seven treated with neurosurgical clipping and fourteen with endovascular coiling) were recruited from the neurovascular clinic at St. Michael's Hospital. The mean age of the patients was 56.4 years (SD = 7.8). Thirteen of the patients were female. All patients had at least ten years of education. The ruptured aneurysms were in the anterior communicating artery [10], middle cerebral artery [7] and posterior communicating artery [2] or in the posterior circulation system (basilar tip; 2). The mean time from SAH to testing was 59 months (SD = 96.8). No patient was clinically amnesic as determined by clinical interview. The neuropsychological battery collected for research purposes confirms this as only one participant was greater than two standard deviations below the normative score of the California Verbal Learning Test (CVLT) long delay score.

The initial appearance of the hemorrhages was classified according to Fisher Grade [13] based on their computed tomography (CT) at admission (range = 1 to 4; median = 3). The severity of the subarachnoid hemorrhage was graded according to the World Federation of Neurosurgical Societies Grade (WFNS) classification (range = 1 to 4; median = 2.5). Global impairment disability status of the patient was noted via clinical interview with the range of deficits from non neurological deficits [15] to no functional limitation (1), issues with anxiety (1) to some short-term memory issues (4).

Twenty-one matched healthy control participants, free from neurological or psychiatric illness were recruited from the community via online advertisements. Table 1 shows the demographics and performance of the two groups on standardized neuropsychological tests. The Hospital Research Ethics Board approved the study and all participants gave informed consent.

3. Materials

The word-span and alpha-span tests were administered alongside a set of standardized tests (Table 1). These are commonly used experimental tasks to assess working memory [14]. Each list contained common one-syllable words (e.g., edge; bag) that were matched for concreteness and frequency. For both tasks, participants were read aloud the lists of random words at the rate of approximately one word per second. A list length of two (words) is first used. After completion of a pair at the given list length, the length is increased by one and another pair is given. This continues to a maximum list length of

eight or until the participant fails at both list-pairs of a particular length. The participants were unaware of this stopping rule. In the word-span test, participants are asked to repeat back the words in the same order in which they heard the words. In the alpha-span test, participants are asked to repeat the words back in alphabetical order.

In both conditions, the span score (total score) corresponded to the length of the list for which at least one of the pairs was recalled correctly. A partial score was calculated by awarding one point to each member of a correctly recalled adjacent pair for each list in both conditions. An individual score $([(\text{score in word-span} - \text{score in alpha-span}) / \text{word-span}] \times 100)$ was calculated to assess performance impairment in the alpha-span relative to the word-span test.

4. Results

4.1. Total scores

To examine the effect of both group (SAH versus control) and span type (word versus alpha) on the total scores, a repeated-measures analysis of variance (ANOVA) was run. There was a main effect of span type on the total score ($F(1,38) = 19.063, p < 0.001$), but there was no effect of group ($F(1,38) = 0.889, p = 0.352$) nor an interaction between group and span task type on the total scores ($F(1,38) = 1.238, p = 0.273$; Fig. 1: left).

4.2. Partial scores

A repeated-measures analysis of variance (ANOVA) with span type as a within-subjects variable and group as a between-subjects variable revealed a significant interaction between span type and group ($F(1,38) = 4.109, p = 0.050$) as well as a main effect of span type ($F(1,38) = 7.208, p = 0.011$) when examining partial scores. Exploring this interaction effect more closely, planned comparisons revealed no significant difference in the word-span condition ($F(1,39) = 0.699, p = 0.409$), but a significant difference between patients with SAH and controls for the alpha-span ($F(1,39) = 4.916, p = 0.03$; Fig. 1: right).

To remove biases within individual output, we also examined score differences $([(\text{word-span score} - \text{alpha-span score}) / \text{word-span score}] \times 100)$. An ANOVA determined a significant difference between patients with SAH and controls in terms of score differences ($F(1,39) = 7.262, p = 0.01$). Patients with SAH were more impaired in the alpha-span condition compared to control participants when we controlled for word-span scores (Fig. 2).

For all analyses, neither the aneurysm location, type of surgical intervention, Fisher grade nor Hunt and Hess scores related to span scores, as assessed with univariate analyses, although our small sample size likely does not give us power to detect any potential differences.

5. Discussion

This study reports that working memory impairment after SAH is present not on a global level but rather only when a working memory task requires additional executive processes to manipulate information held online. Compared to healthy control participants, patients with SAH were impaired on a working memory test that required the maintenance and manipulation of information (alpha-span) but not on a task that required simply storing information in consciousness (word-span). We speculate that this is evidence that impairments after SAH is due to a disconnection of cognitive processes that are needed to work in concert for demanding tasks, and not necessarily impairment in independent cognitive processes, as suggested by the intact neuropsychological profile of the patients with SAH. There was no effect of aneurysm variables (location or surgical

Table 1

Demographic characteristics and average scores (standard deviations shown in the parentheses) for the patients with SAH and the control participants for neuropsychological tests (p-values resulting from independent sample t-tests between the groups).

	SAH patients	Healthy controls	p Value
<i>Demographic</i>			
Age	56.4 (7.8)	60.3 (10.4)	0.21
Education	14.6 (2.6)	14.9 (2.3)	0.81
Number of females	13	11	
<i>Neuropsychological tests</i>			
NART [Ⓢ] est. IQ	106 (9.8)	112 (6.5)	>.05
CVLT [Ⓢ] learning (trial 1 to 5)	47.9 (8.5)	51.5 (14.6)	0.53
CVLT delay	10.6 (2.8)	10.6 (4.2)	0.91
Digit span forward	8.9 (2.1)	10.0 (2.0)	0.17
Digit span backward	6.3 (1.8)	7.1 (2.5)	0.62
DSST [Ⓢ] (120 seconds)	59.9 (14.9)	67.1 (19.2)	0.23
Trails A (seconds)	28.2 (11.1)	31.9 (12.1)	0.69
Trails B (seconds)	70.6 (29.3)	65.2 (24.3)	0.90

[Ⓢ] National Adult Reading Test; [Ⓢ] California Verbal Learning Test; [Ⓢ] Digit Symbol Substitution Test.

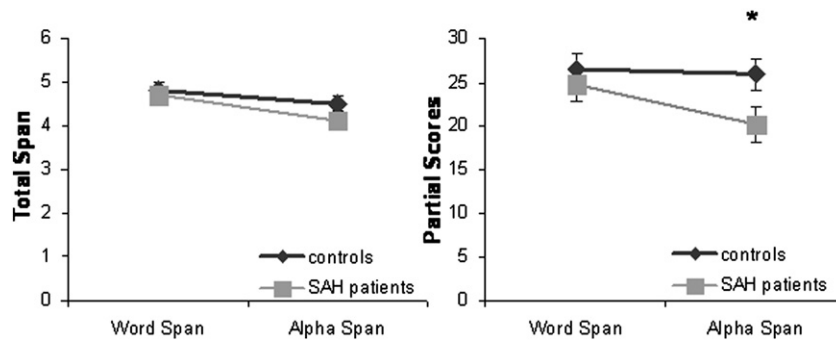


Fig. 1. Left: the average total scores (span length) for SAH patient and control participants. Right: The average partial scores for SAH patient and control participants for the word-span and alpha-span conditions. Standard error bars are shown.

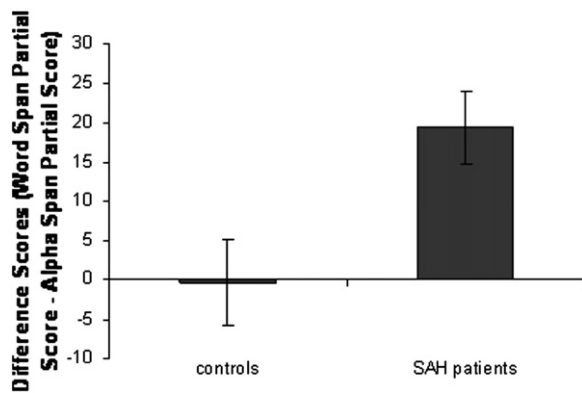


Fig. 2. Average individual difference scores $([(\text{score in word-span} - \text{score in alpha-span}) / \text{score in word-span}] \times 100)$ indicating alpha-span impairment relative to word-span performance. Standard error bars are shown.

intervention), which is consistent with findings that some cognitive impairment after SAH are the result of diffuse damage rather than focal effects [15]. However, this current report includes a very limited number of participants. A future investigation with a larger sample size is needed to better address the finding of a null effect of aneurysm location.

In relation to real-world functioning, tasks such as various household chores, shopping for recipe items and conversational ability all require memory and executive processes to work in concert. Deficits in these and other functions may reflect deficits in daily living, which has been the case for other clinical populations [16].

Working memory functioning has not been the focus of many prognostic or rehabilitation tools offered to recovering patients with SAH. Based on findings of successful working memory interventions with other clinical populations [17,18], future rehabilitative techniques should apply similar techniques to those recovering from SAH.

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Conflict of interest statement

None of the authors have any conflicts of interest to state.

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References

- [1] Hutter BO, Kreitschmann-Andermahr I, Mayfrank L, Rohde V, Spetzger U, Gilsbach JM. Functional outcome after aneurysmal subarachnoid hemorrhage. *Acta Neurochir Suppl* 1999;72:157–74 [Comparative Study Review].
- [2] Schweizer TA, Al-Khindi T, Macdonald RL. Mini-Mental State Examination versus Montreal Cognitive Assessment: rapid assessment tools for cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *J Neurol Sci* 2012 May 15;316(1–2):137–40 [Comparative Study Research Support, Non-U.S. Gov't].
- [3] Al-Khindi T, Macdonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. *Stroke* 2010 Aug;41(8):e519–36 [Research Support, Non-U.S. Gov't Review].
- [4] Buchanan KM, Elias LJ, Goplen GB. Differing perspectives on outcome after subarachnoid hemorrhage: the patient, the relative, the neurosurgeon. *Neurosurgery* 2000 Apr;46(4):831–8 [Research Support, Non-U.S. Gov't, discussion 8–40].
- [5] Hop JW, Rinkel GJ, Algra A, van Gijn J. Quality of life in patients and partners after aneurysmal subarachnoid hemorrhage. *Stroke* 1998 Apr;29(4):798–804.
- [6] Mayer SA, Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, et al. Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. *Neurology* 2002 Dec 10;59(11):1750–8 [Clinical Trial Research Support, Non-U.S. Gov't].
- [7] Baddeley AD. Short-term and working memory. In: Tulving E, Craik FIM, editors. *The Oxford Handbook of Memory*. New York: Oxford University Press; 2000. p. 77–92.
- [8] Cowan N. Working Memory. In: Salkind NJ, editor. *Encyclopedia of Educational Psychology*. London: Sage Publications; 2008. p. 1015–6.
- [9] Hutter BO, Gilsbach JM. Which neuropsychological deficits are hidden behind a good outcome (Glasgow = 1) after aneurysmal subarachnoid hemorrhage? *Neurosurgery* 1993 Dec;33(6):999–1005 [discussion 6].
- [10] Larsson C, Forsell A, Ronnberg J, Lindberg M, Nilsson LG, Fodstad H. Subarachnoid blood on CT and memory dysfunctions in aneurysmal subarachnoid hemorrhage. *Acta Neurol Scand* 1994 Nov;90(5):331–6 [Research Support, Non-U.S. Gov't].
- [11] Sheldon S, Macdonald RL, Schweizer TA. Free recall memory performance after aneurysmal subarachnoid hemorrhage. *J Int Neuropsychol Soc* 2012 Mar;18(2):334–42 [Research Support, Non-U.S. Gov't].
- [12] Craik FIM. A functional account of age differences in memory. In: Klix F, Hagemendorf H, editors. *Human memory and cognitive capabilities*. Amsterdam: North-Holland; 1986. p. 409–22.
- [13] Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. *Neurosurgery* 1980 Jan;6(1):1–9 [Comparative Study Research Support, U.S. Gov't, P.H.S.].
- [14] Schmiedek F, Hildebrandt A, Lovden M, Lindenberger U, Wilhelm O. Complex span versus updating tasks of working memory: the gap is not that deep. *J Exp Psychol Learn Mem Cogn* 2009 Jul;35(4):1089–96 [Research Support, Non-U.S. Gov't].
- [15] Ogden JA, Mee EW, Henning M. A prospective study of impairment of cognition and memory and recovery after subarachnoid hemorrhage. *Neurosurgery* 1993 Oct;33(4):572–86 [Research Support, Non-U.S. Gov't, discussion 86–7].
- [16] Bottari C, Dassa C, Rainville C, Dutil E. The criterion-related validity of the IADL Profile with measures of executive functions, indices of trauma severity and sociodemographic characteristics. *Brain Inj* 2009 Apr;23(4):322–35 [Research Support, Non-U.S. Gov't].
- [17] Vallat C, Azouvi P, Hardisson H, Meffert R, Tessier C, Pradat-Diehl P. Rehabilitation of verbal working memory after left hemisphere stroke. *Brain Inj* 2005 Dec;19(13):1157–64 [Case Reports].
- [18] Vallat-Azouvi C, Pradat-Diehl P, Azouvi P. Rehabilitation of the central executive of working memory after severe traumatic brain injury: two single-case studies. *Brain Inj* 2009 Jun;23(6):585–94 [Case Reports].