

Glioma of The Temporal Lobe That Impair Working Memory

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Abstract

Background: Working memory refers to the temporary storage and manipulation of information. Although working memory is generally considered to rely primarily on a fronto-parietal network, there is recent evidence that the temporal lobe has an important role in specific aspects of working memory.

Methods: In this study, we assessed 30 patients with temporal tumor and 30 healthy controls using a method that combined memory tests with working memory tasks (Digital span task, Spatial capacity N-back task and Emotional N-back task).

Results: The results revealed that there are no significant difference between the groups with regard to the neuropsychological functionings. For working memory tasks, statistically significant differences were not found on the 1-back tasks and forward versions of simple span tasks between the temporal patients group (TP) and the healthy controls group (HC). Analysis of correct responses of the experimental tasks suggested that the TP group was significantly different from the HC group in the 2-back tasks and backward versions of simple span tasks. For reaction times, spatial capacity 2-back task and emotional 2-back task showed the TP group were significantly different from the HC group.

Conclusion: These findings revealed that working memory capacity was impaired in patients with a temporal tumour and that the temporal lobe may be a certain neuroanatomical structure in the working memory network.

Introduction

Working memory (WM) is a capacity-limited short-term memory system that is engaged in the processing of currently active information [1]. The key role of WM in goal directed behavior makes it a significant predictor of a number of skills and abilities ranging from fluid intelligence to language learning, mathematical skills, and academic achievement [2, 3]. Due to the critical role that WM plays in human behavior, considerable research effort has focused on describing its structure, that is, its cognitive building blocks and their interrelationships, in more detail.

Neurobiological and neuroimaging findings over the last decades have conveyed the idea that WM might depend on specific anatomical structures. Neuroimaging studies to date have largely focused on the dorsolateral prefrontal cortex (dlPFC) and parietal cortex, key regions involved in WM processing [4, 5]. Though a larger network of WM-related dysfunction including the anterior cingulate cortex (ACC) and left frontal pole has also been proposed [6–8]. Evidence for local generators of WM theta oscillations in humans has been found in the occipital/parietal and temporal cortices and hippocampus using intracranial EEG (iEEG) [9]. A growing body of research indicates that the medial temporal lobe (MTL) is essential not only for long-term episodic memory but also for visual working memory (VWM) [10–12]. Additional analyses suggested that the medial temporal lobe per se was critical for accurate conjunction working memory. They proposed that the medial temporal lobe was critically involved in memory for conjunctions at both short and long delays [13].

However, the structure of WM is yet to be determined. Our present study primarily investigates the influence of WM in a group of homogenous patients with a glioma relatively limited to the temporal cortex. In our study, we enrolled insular patients for evaluation within one week after seizure symptom onset because there is evidence that long-term epilepsy impaired recognition is a component of the neuropsychological profile that is associated with epilepsy [14, 15].

In the present study, we simultaneously assessed WM in temporal patients through WM paradigms. Based on previous behavioral, functional and anatomical data, we hypothesized that (1) the temporal patient group would show deficits in WM (2) and that the temporal cortex may be a neuroanatomic structure in WM.

Materials And Methods

Participants

Thirty patients with a localized lesion that was limited to the temporal lobe (TP, N = 30) that were evaluated in the Department of Neurosurgery, the First Affiliated Hospital of USTC from September 2018 to March 2020 were considered for participation in the present study. Additionally, 30 right-handed healthy controls (HC, N = 30) were matched with the patients for age, gender, education and ethnicity. All participants had normal color vision and no previous or current neurological or psychiatric diseases. Patients were excluded if they failed to recognize frank hemiplegia and suffered from language deficits, anosognosia or motor limitations that could have affected their performance in the neuropsychological tasks in the present experiment. Tasks (Digital span task, Spatial capacity N-back task, Emotional N-back task and neuropsychological assessment) were performed in a random order. Picture stimulus, questions, and instructions were programmed into E-Prime (version 2.0), which was presented on a regular PC or notebook. Every participant was instructed to perform several exercises before the tasks. Each participant was given 300 Chinese yuan (about \$50) at the end of the experiment as financial compensation. All patients were examined using MRI scans before the experiment. They were identified and contacted based on this imaging data.

A professional neurosurgeon who was blinded to the study's hypotheses and the neuropsychological data performed the anatomical classification based on acute or recent MRIs. This study was approved by the hospital's ethics committee.

Experimental measures

Neuropsychological examinations

All participants completed the Beijing version of the Montreal Cognitive Assessment (MoCA). The NEO-Five-Factor Inventory was used to assess general personality traits and Raven's Progressive Matrices was applied to estimate basic intelligence. The Self-Rating Depression Scale (translated into Chinese) was administered to obtain a measure of depressive symptoms for the participants.

Working Memory Tests

The WM test battery included ten WM tests that encompassed four different task paradigms: Simple digital span task, Spatial capacity N-back task, Emotional N-back task.

Simple digital span task

Simple span tasks are assumed to predominantly tap WM storage (Fig 1). In simple span tasks, lists of stimulus items with varying length are to be reproduced while maintaining the order of presentation. Both forward versions (repeating the list in the same order) and backward versions (repeating the list in the reverse order) have been used extensively in the literature, and they are part of common standardized neuropsychological and IQ tests. Within the verbal domain, the backward version is generally more difficult than its forward counterpart, while the pattern is somewhat less clear when it comes to visuospatial material.

For the simple span tasks used here, stimulus lists (digits) of unpredictable length were presented. At the end of each list, participants were required to report the items in the exact order in which they had been presented in the forward version of the task, while the items were to be reported in the reverse order in the backward version of the task. Each test included two initial practice trials that consisted of one three-item list and one four-item list. In case of error, the practice trials were repeated until the participant answered correctly or until the practice was presented three times. This practice was followed by an additional practice trial consisting of a list with nine items (longest list length) to demonstrate the range. None of the practice trials were included in the dependent measures. The actual tests included seven trials involving list lengths ranging from three to nine.

Spatial capacity and Emotional N-back task

The n-back tests used here consisted of a 1- and 2-back task. In the 1-back task, the participant was to respond whether the currently visible item was the same (target), or not (no-target), as the previous item by pressing the N (target) and M (no-target) keys on the computer keyboard. In the 2-back task, the participant was required to indicate whether the currently presented item was the same as the item that was presented two steps back.

Spatial squares were used as the major stimuli in spatial WM (Fig 2). There were two blocks, and each block was composed of 40 trials. Each trial sequence began with the presentation of a memory item for 1500 ms. Then, a memory item was presented for 6000 ms. Next, a test item was presented for 6000ms. If the spatial test stimulus was the "same" as the memory array stimuli, subjects were instructed to press "N" otherwise, press "M".

Emotional pictures were used as the major stimuli in object WM (Fig 3). Eight blocks were included, and each block comprised 40 trials. Each trial sequence began with the presentation of a fixation for 1500 ms. Then, a memory item was presented for 6000 ms. Next, a test item was presented for 6000ms.

Subsequently, participants were instructed to press a button. If the test stimulus was the “same” as the memory array stimuli, subjects were instructed to press “N” otherwise, press “M”.

Statistical methods

All statistical analyses were performed using SPSS 23.0, and the level of significance was set at $p=0.05$ after correction. We utilized the mean values (the standard deviations) that denoted the results that were normally distributed and used medians (P75–P25) to express the results that were not normally distributed. We compared demographic characteristics between groups using independent samples t-tests for continuous variables and chi-square tests for categorical variables.

Results

Neuropsychological functioning

The independent samples t-tests revealed no significant difference between the groups with regard to MoCA scores, age, education, NEO-Five-Factor Inventory, Raven’s Progressive Matrices, and Self-Rating Depression Scale. See Table 1.

Table 1. Clinical and demographic characteristics of the study groups

Variable	Groups, Mean (SD)/ Median(P75-P25)		
	TP (N = 30)	HC (N = 30)	<i>p</i> -Value
Sex (%men)	50.00	43.33	0.79
Age, mean (SD)	42.27.06 (6.31)	41.57(6.41)	0.85
Years of education, mean (SD)	9.10 (2.09)	8.83(2.01)	0.72
Laterality	Right = 17 Left = 13		
Tumor volume (cm ³)	31.91 (9.87)		
Raven, mean (SD)	44.43(3.17)	45.37(3.09)	0.84
MoCA, Median(P75-P25)	26.00(26.00-25.00)	26.00(26.00-26.00)	0.18
NEO-FFI-60, mean (SD)	120.03(9.46)	118.27(10.40)	0.57
SDS, mean (SD)	38.16(5.86)	39.40(6.84)	0.43

Abbreviations: HC, healthy controls; TP, temporal patients.

Working Memory Tests

Simple digital span task, Spatial capacity N-back task, Emotional N-back task.

The means, standard deviations, independent samples t-tests analysis of group differences in these tasks are reported in Table 2. Statistically significant differences were not found on the 1-back tasks and forward versions of simple span tasks. Analysis of correct responses of the experimental tasks demonstrated that temporal patients group was significantly different from the HC group in the 2-back tasks and backward versions of simple span tasks. For reaction times, spatial capacity 2-back task and emotional 2-back task showed the TP group were significantly different from the HC group. See details in the Table 2.

Table 2. Behavioral data of span tasks, 1-back and 2-back conditions

Outcome	Groups, Mean (SD) / Median(P75-P25)		
	TP (N = 30)	HC (N = 30)	<i>p</i> - Value
Simple span tasks			
<i>Forward versions</i>	4.00 (5.00-3.00)	4.00(5.00-3.00)	0.82
<i>Backward versions</i>	2.00 (3.00-2.00)	5.00 (5.00-4.00)	<0.01
Spatial capacity 1-back task			
<i>Percent correct (%)</i>	0.79 (0.10)	0.80 (0.09)	0.19
<i>Mean RT(ms)</i>	2632.81 (443.29)	2447.12 (440.44)	0.81
Spatial capacity 2-back task			
<i>Percent correct (%)</i>	0.61 (0.05)	0.86(0.06)	0.04
<i>Mean RT(ms)</i>	3388.20 (680.23)	2351.35 (770.85)	<0.01
Emotional 1-back task			
<i>Percent correct (%)</i>	0.83(0.08)	0.90(0.06)	0.19
<i>Mean RT(ms)</i>	2993.27 (359.19)	2759.61 (339.04)	0.79
Emotional 2-back task			
<i>Percent correct (%)</i>	0.62 (0.06)	0.75 (0.08)	0.03
<i>Mean RT(ms)</i>	4093.27 (772.22)	2992.95 (461.09)	<0.01

Abbreviations: HC, healthy controls; TP, temporal patients.

Discussion

In this case-control study we investigated the central neuroanatomic structure underlying WM in temporal patients, and healthy participants. We assessed WM abilities with paradigms (simple digital span task, spatial capacity N-back task, emotional N-back task) . The present study provides neuropsychological evidence of (a) WM being impaired in patients with an insular glioma when compared to a healthy group matched on sex, age, education and ethnicity and (b) the temporal cortex may be a neuroanatomic structure in WM.

Working memory (WM) is an important cognitive function that is frequently used in everyday life. It requires a complex interaction between different cognitive functions such as stimulus encoding, storage, retrieval, replacement, and manipulation [16]. In broad terms, models of WM can be differentiated by their emphasis on content material (e.g., verbal and visuospatial) vs. constituent processes (e.g., updating and maintenance). With respect to content, previous behavioral, neuropsychological and neuroimaging research has consistently indicated that WM can be separated into verbal and visuospatial stores which mainly subserve maintenance functions [17,18]. Many of the studies listed above have employed factor analysis to investigate the functional structure of WM. In contrast to some earlier studies, we included an extensive WM test battery and a large and diverse adult sample. The present tasks represented typical hypothetical WM processes: simple span tasks have been argued to primarily tap WM maintenance, complex span tasks have been considered to reflect both maintenance and manipulation [19], and running memory tasks as well as n-back tasks are thought to measure higher-order WM processes, including updating and attention control [20]. In our study, temporal patients had significantly lower scores in the backward version of span tasks and 2-back tasks.

In accord with the presumed role of the temporal in subjective WM and previous neuroimaging studies that reported temporal activation during the observation and experience of working memory tests, the temporal is typically related to WM. However, some studies have reported that the temporal may also be involved in processes of WM [21-23]. To date, these results do not yet provide causal evidence for the role of the temporal in WM. We are the first to evaluate WM in a comprehensive manner, wherein we observe lower scores in backward version of span task and significantly poorer performance on the 2-back tasks in those temporal patients. Thus, our results suggested that the damaged temporal impaired the WM based on the simple digital span task and WM paradigms.

Limitation

One limitation of our study is the fact that some gliomas infiltrated the operculo-insula rather than purely the temporal cortex. Prominent subcortical fiber bundles, including the uncinate and the arcuate fascicle, connect to the frontoorbital regions. Damage to the frontoorbital regions or fiber might have impacted the performance on WM in some patients [24]. Furthermore, a larger sample size would have allowed for comparisons according to the particular location of the temporal cortex lesions (lateral anterior, lateral posterior versus medial), which could be of special interest given the functional segregation within the temporal cortex revealed by functional imaging and intracerebral electrical stimulation studies [25,26]. Finally, we did not explore the difference between WM in left temporal versus right temporal lesions, although a recent study suggest that patients with LTL glioma exhibited more memory impairments than RTL patients [27,28].

Conclusion

In summary, by simultaneously measuring WM paradigms in the homogenous, well-matched cohort of temporal glioma patients and demographically matched healthy volunteers, we confirmed previous

results associating wm impairment with exposure to temporal damage. Finally, we could not identify obvious laterality effects on WM and deficits in intelligence and personality in temporal lesions. Although not providing mechanistic evidence and the study's limitations, these results are consistent with 1) temporal glioma patients having impaired WM; and 2) temporal contributing to WM processing. In the past few years, we have been attempting to better understand the neural basis of WM. Identifying critical subcomponents and brain network interactions that are involved in WM contributes to understanding of the generation of this multifaceted experience at the crucial intersection of human emotional and social behavior. Therefore, such studies may also guide the development of clinical and subclinical groups that are associated with deficient WM ability, such as individuals with conduct disorder, autism spectrum disorder (ASD) [29], and alexithymia [30]. Clinicians should recognize this important social disability and appropriate counseling should be provided to guardians.

Declarations

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Authors' contributions

Shengyuan Ni, Peng Chen, Yang Yang and Dejun Bao contributed to the manuscript's conception, design, preparation, conducting experiments, acquisition, analysis, and interpretation. Rui Zhang and Pang Qi made substantial contributions in drafting the manuscript and revising it critically for important intellectual content. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets are available from the corresponding author on formal and logical request.

Ethics approval and consent to participate

The study protocol was also confirmed by the ethics committee of University of Science and Technology of China.

Consent for publication

Not applicable.

Competing interests

The authors take full responsibility for the writing and content of this article and confirm that there are no conflicts of interests associated with this academic publication.

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Figures

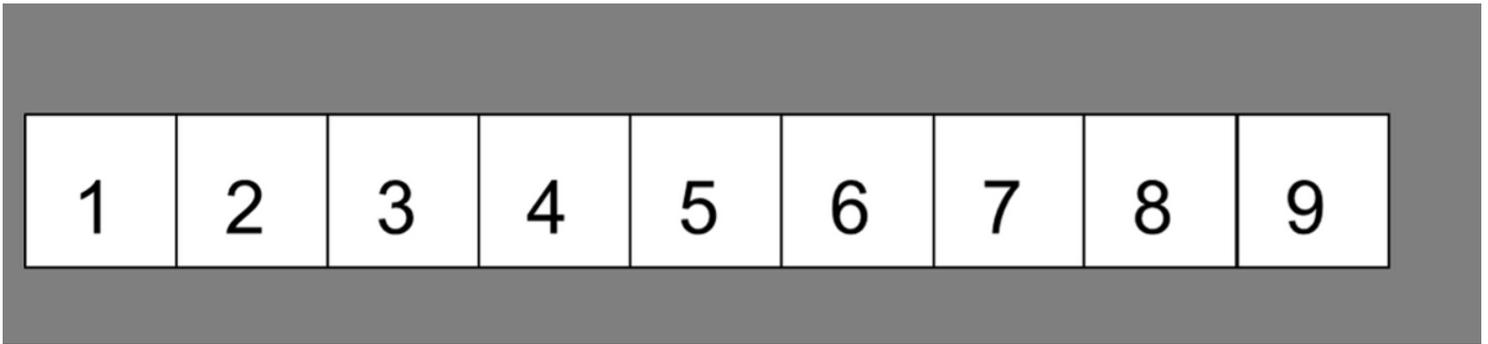


Figure 1

Simple digital span task. Response screens in the simple span tasks.

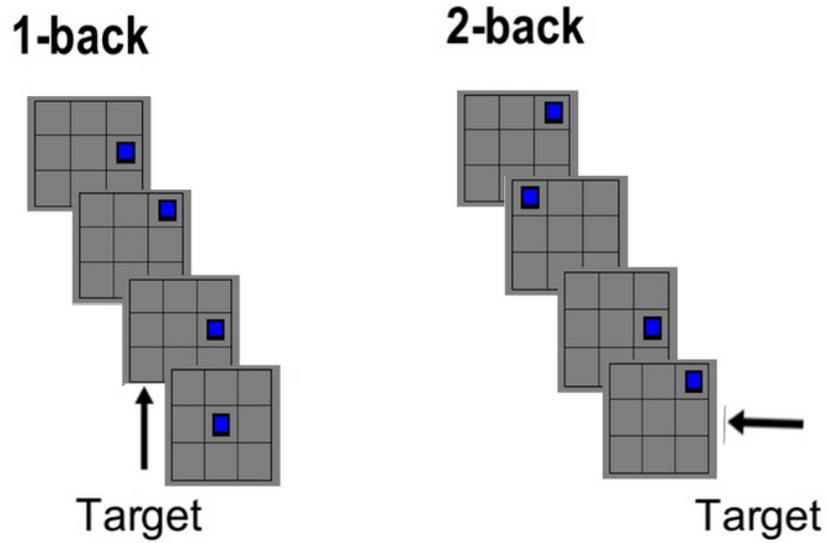


Figure 2

Spatial capacity N-back task. Schematic representation of the 1-back and 2-back condition.

1-back



2-back



Figure 3

Emotional N-back task. Schematic representation of the 1-back and 2-back condition.