Verbal working memory: magnetic resonance morphometric analysis and a psychophysiological model

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Neuropsychological characteristics of verbal working memory (memory capacity, permanency, and different types of memory errors) of 43 healthy subjects of older age were compared with the anatomical characteristics of their brain structures (volume of the hippocampi and the caudate nuclei, size of the cingulate-cortex regions of both hemispheres). The obtained data demonstrate a correlation between the permanency of verbal-information maintenance and left caudate-nucleus volume and a positive correlation between associative-memory capacity and left hippocampus volume. A decline in the number of verbal-memory errors (confabulations) is related to the increased size of the left anterior cingulate cortex. Furthermore, verbal working-memory capacity and permanency correlate negatively with the size of the left posterior dorsal cingulate cortex, whereas the number of fluctuations and word replacements correlate positively with the increased size of this brain region. We suggest a psychophysiological model of verbal-stimulus maintenance in working memory based on the results of our study and published research data.

Keywords: magnetic resonance morphometric analysis, working memory, verbal memory, caudate nucleus, cingulate cortex, hippocampus, working-memory model

Neurophysiological mechanisms of verbal information processing are traditionally related to the functioning of the temporal cortex of the left hemisphere of the brain. This hypothesis is supported by the fact that a lesion in this brain region usually causes trouble in speech perception, as well as other problems with audio-verbal information processing, including severe verbal-memory impairment. However, the temporal cortex is not the only brain structure that takes part in this cognitive process; moreover, from all appearances, verbal memory is related to the combined functioning of several brain regions.

It has been revealed that verbal memory is related to the hippocampus, which is a part of the limbic system of the brain. According to the results of fMRI studies, the hippocampus is activated during the performance of verbal-memory tasks. Furthermore, it is activated more frequently in the stage of information retrieval than in the stage of its consolidation (Karlgodt, Shirinyan, van Erp, Cohen, & Can-
Abnormal activation of this brain structure is seen in patients with multiple sclerosis (Sweet, Rao, Primeau, Durgerian, & Cohen, 2006) and epilepsy (Campo et al., 2009). Also, hippocampus size is related to verbal-memory capacity in patients with epilepsy (Kalviainen et al., 1997) and Alzheimer’s disease (de Toledo-Morrell et al., 2000).

Furthermore, an important role in verbal-memory functioning belongs to the cingulate cortex, which is also a part of the limbic system along with the hippocampus. For example, some studies show that the anterior cingulate cortex is involved in the process of semantic coding in verbal working memory (Kaneda & Osaka, 2008). Also, the posterior cingulate cortex activates recognition of familiar words, objects, and places (Sugiura, Shah, Zilles, & Fink, 2005; Heun et al., 2006).

Some studies also show that the caudate nuclei activate during the functioning of working memory (Hart et al., 2013; Moore, Li, Tyner, Hu, & Crosson, 2013). Lesions in this structure in humans result in working-memory impairment (Partiot et al., 1996).

Recent studies of different brain regions involvement in cognitive processes use magnetic resonance morphometric analysis. For example, some studies show that the size of the hippocampus and its subdivisions correlates with memory processes (Kozlovskiy, Sozinova, Skvortsova, & Vartanov, 2009; Maguire, Woollett, & Spiers, 2006; Vartanov, Kozlovskiy, Skvortsova, & Sozinova, 2009). It has also been demonstrated that reduced hippocampus size in elderly people is accompanied by verbal-memory decline (Hackert et al., 2002). Moreover, anterior hippocampus volume is related to delayed verbal memory, whereas posterior hippocampus volume is associated with spatial memory (Chen, Chuah, Sim, & Chee, 2010). Decreased size of the hippocampus and the amygdala is found in close relatives of schizophrenia patients, who also tend to have trouble with delayed verbal memory while immediate verbal memory remains intact (O’Driscoll et al., 2001).

Far less is known about the correlation between the size of different cingulate-cortex regions and verbal-memory processes. Some studies show that anterior cingulate-cortex atrophy, such as in Alzheimer’s disease, can cause severe confabulations (Lee et al., 2009); anterior cingulate-cortex atrophy is also seen in schizophrenics, who suffer from memory errors, such as confabulations (Choi et al., 2005; Koo et al., 2008; Mitelman, Shihabuddin, Brickman, Hazlett, & Buchsbaum, 2005). According to some studies, an increase in several areas of the cingulate cortex correlates with a decrease in the number of errors in memory tests. However, a decrease in the number of errors not only does not improve overall memory performance but actually tends to deteriorate total recall (Kozlovskiy, Vartanov, et al., 2012; Kozlovskiy, Velichkovsky, et al., 2012).

According to some studies, a decrease in caudate-nuclei volume leads to a decline in performance on most verbal and visual memory tests, mostly because of a decline in cognitive control (Bartrés-Faz et al., 2002; Kozlovskiy, Skvortsova, Sozinova, Vartanov, & Nikonova, 2010).

However, such morphometric studies usually compare working-memory processes with a single brain structure, whereas, as demonstrated above, verbal-memory functioning is defined by simultaneous activation of several brain structures. In the present study we explored the relationship between the sizes of a range of brain structures (the hippocampus, the caudate nuclei, and the cingulate cortex).
and different aspects of the verbal-memory process. We used neuropsychological memory tests to assess a variety of verbal-memory properties, such as verbal-memory capacity and permanency and different types of verbal-memory errors. Neuropsychological methods also allow comparison of the received data with the results of other studies. The present study included healthy elderly subjects, which provides valuable information, due to the fact that the individual anatomical and psychological differences become even more expressed in older age.

**Method**

**Participants**

Participants in the study were 43 right-handed women (the mean age was 60.4 +/- 16.6 years) with no previous brain trauma, strokes, psychological or neurological diseases.

**Procedure**

The study consisted of two parts, an MRI study and a neuropsychological assessment.

During the MRI study all participants were scanned on a 3.0 MRI scanner; T1 three-dimensional images of the brain were obtained. On standardized sagittal slices of the images in each direction we highlighted the relevant areas, which included the left and right hippocampus, and measured their volumes (in mm³). We also calculated the volume of the left and right caudate nucleus. Furthermore, we highlighted relevant areas, including the cingulate cortex of both hemispheres. In each hemisphere we divided the cingulate cortex into three regions—anterior (Brodmann areas 24, 33), posterior ventral (Brodmann area 23), and posterior dorsal (Brodmann area 31). Then we calculated absolute squares of the surfaces of all highlighted cingulate-cortex regions (in mm²).

The neuropsychological part of the study included Luria’s neuropsychological assessment of cognitive processes as modified by Glozman (1999) to allow quantitative analysis of memory processes. The following tests were used to assess the verbal working-memory process: immediate and delayed recall of 10 words, two groups of words and sentences, semantic coding (memorizing 12 words by including them in random sentences and recalling them in 10 minutes of heterogenic interference), associative memory tests (memorizing pairs of words, recall of the second word after hearing the first one). For each memory type we defined memory capacity (total of recalled elements), permanency (total of delayed recall), and the number of memory errors. We separated several kinds of errors, such as replacement of one element with another one, confabulations (including new elements), contaminations (mixing several elements), perseverations (recalling a single element more than once), and sequence errors.

Obtained data were statistically analyzed by calculating nonparametric correlations (Spearman correlation coefficient) between individual behavioral and anatomical measurements. Further analysis included only statistically significant correlations ($p < 0.05$).
Results

The obtained data revealed significant correlations between various neuropsychological aspects of verbal working memory and the anatomical characteristics of several brain structures.

Table 1 shows significant correlations between the size of different brain structures and the capacity and permanency of verbal working memory.

Table 1. Significant correlations between the size of brain structures and the capacity and permanency of verbal working memory

<table>
<thead>
<tr>
<th>Brain structures</th>
<th>Recall of 10 words</th>
<th>Recall of 2-word or 2-sentence groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Memory capacity</td>
<td>Memory permanency</td>
</tr>
<tr>
<td>Left caudate nucleus</td>
<td>—</td>
<td>0.39</td>
</tr>
<tr>
<td>Left posterior dorsal cingulate cortex</td>
<td>—0.35</td>
<td>—0.33</td>
</tr>
</tbody>
</table>

According to Table 1, verbal-memory capacity correlates negatively with the size of the left posterior dorsal cingulate cortex. Thus, an increase in the size of this brain region leads to a decline of verbal-memory capacity. Verbal-memory permanency correlates positively with the volume of the left caudate nucleus, whereas its correlation with the left posterior dorsal cingulate cortex is negative both for the recall of 10 words and for the recall of two groups of verbal stimuli.

Table 2 indicates significant correlations between the size of several brain structures and the number of different types of verbal-memory errors in the neuropsychological tests.

Table 2. Significant correlations between the size of brain structures and the number of verbal-memory errors

<table>
<thead>
<tr>
<th>Brain structures</th>
<th>Recall of 10 words</th>
<th>Recall of 2-word or 2-sentence groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fluctuations</td>
<td>Replacement of words</td>
</tr>
<tr>
<td>Left caudate nucleus</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Left posterior dorsal cingulate cortex</td>
<td>0.46</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 2 shows that the size of the left posterior dorsal cingulate cortex correlates positively with the number of fluctuations during the 10-word recall and with the number of word replacements during the recall of the two stimuli groups. Thus, an increase in the size of this cingulate-cortex region is related to an increase in the number of these verbal-memory errors. Fewer contaminations of stimuli groups are related to an increase in the size of the left caudate nucleus.

Table 3 shows the significant correlations between the sizes of several brain structures and different characteristics of associative memory.
Table 3. Significant correlations between the size of brain structures and the characteristics of associative memory

<table>
<thead>
<tr>
<th>Brain structures</th>
<th>Associative-memory test</th>
<th>Semantic-coding test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Memory capacity</td>
<td>Memory capacity</td>
</tr>
<tr>
<td>Left hippocampus</td>
<td>0.31</td>
<td>—</td>
</tr>
<tr>
<td>Left anterior cingulate cortex</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Left caudate nucleus</td>
<td>—</td>
<td>0.31</td>
</tr>
</tbody>
</table>

According to Table 3, the size of the left hippocampus correlates positively with associative-memory capacity. Moreover, an increase in the size of the left caudate nucleus is related to increased memory capacity on the semantic-coding test, whereas an increase in the size of the left anterior cingulate cortex leads to a decrease in the number of confabulations on the same test.

Discussion and Conclusions

The results of the present study demonstrate significant correlations between the anatomical characteristics of different brain structures and the ability to maintain a trace in verbal working memory. However, these correlations vary for different memory characteristics and brain structures.

According to our data, the volume of the caudate nucleus in the left hemisphere correlates with the permanency of maintaining verbal information after the introduction of interfering stimuli in different memory tests, but it does not correlate with verbal-memory capacity. Thus, we can suggest that the role of this brain structure in verbal memory is to resist external interference. In order to permanently maintain a trace in verbal memory, the influence of external sensory interference should be decreased. Furthermore, other studies show that lesions or malfunctioning of the caudate nuclei in rats (Döbrössy, Svendsen, & Dunnett, 1995) and humans (Partiot et al., 1996) leads to trouble in delayed-reaction tests, which require the functioning of working memory. Moreover, working-memory dysfunctions related to trouble in the selection of relevant information and the suppression of irrelevant information are registered in various diseases, which lead to caudate-nuclei lesions. For example, working-memory dysfunctions are noted in patients with Parkinson’s disease (Lewis, Slabosz, Robbins, Barker, & Owen, 2005) and Huntington’s disease (Lawrence, Watkins, Sahakian, Hodges, & Robbins, 2000), as well as in patients with Tourette’s, ADHD, and schizophrenia (Keri, 2008; Ross, Harris, Olincy, & Radant, 2000). Our data correspond well with the model of information maintenance in the working memory created by Ashby, Ell, Valentin, and Casale (2005). According to this model, which is called FROST, there is an activation loop between the prefrontal cortex, the caudate nuclei, the globus pallidus, and the thalamus (FROST is an abbreviation for FROntal–Striatal–Thalamic). The authors of the model suggest that this loop is responsible for trace maintenance in working memory. However, this model does not account for differences in the functions of
the prefrontal cortex and the basal ganglia in the working-memory process. According to some studies (Awh & Vogel, 2008; Koziol & Budding, 2009), during the working-memory process the prefrontal cortex supports the activation level and the attention focus on the relevant information, while the basal ganglia—for example, the caudate nuclei—provide information filtration, selection of relevant stimuli, and suppression of irrelevant ones. This filtration is possible because the caudate nuclei suppress the thalamic nuclei through the globus pallidus, while the thalamic nuclei allow the entrance of sensory information into the brain. It is known from the literature that the left and right caudate nuclei have slightly different functions. For example, a lesion in the left caudate-nucleus head leads to impairment of verbal working memory, whereas a lesion in the right caudate nucleus results in visual-memory decline (Buklina, 1999; Kumral, Evyapan, & Balkir, 1999). Our data also support inter-hemispheric asymmetry in caudate-nuclei functioning. We suggest that a better-developed left caudate nucleus, which receives a signal from the prefrontal cortex, more effectively suppresses the left thalamus, which allows the entrance of verbal information into the left hemisphere. As a result, the impact of external sensory interference is slightly less, and, in turn, the permanence of verbal-information maintenance is increased.

The obtained data also demonstrate a relationship between the sizes of different cingulate-cortex regions and the characteristics of verbal working memory. Furthermore, different cingulate-cortex regions probably have different functions in this cognitive process. Thus, according to our data, the left anterior cingulate cortex is related to resistance to confabulations in the semantic-coding test. We suggest that the role of the left anterior cingulate cortex in verbal-memory functioning is to suppress irrelevant information and to resist internal semantic interference. This hypothesis is supported by the results of other studies. If the anterior cingulate cortex is seen as the “noise”-suppression system, it becomes clear why this structure is activated in most tasks that require the filtration of irrelevant information. This role of the anterior cingulate cortex also applies to information recall because this process includes filtering and denying false and uncertain memories, imagination, and so forth. Such filtering explains anterior cingulate-cortex activity in information recall from working memory (Schöning et al., 2009), verbal-declarative memory (Bremner, Vythilingam, Vermetten, Vaccarino, & Charney, 2004), spatial memory (Teixeira, Pomedli, Maei, Kee, & Frankland, 2006), episodic memory (Herrmann et al., 2001), and emotional memory (Tang et al., 2005). The role of information filtering and resistance to internal interfering stimuli is also highlighted in the inhibitory-control theory of Kane and Engle (2000). According to this theory, proactive interference has an influence on total working-memory capacity, while smaller capacity leads to the greater influence of interference on task results. Despite these facts, the ability to resist interference depends not only on memory but also on inhibition—that is, on the mechanism that suppresses irrelevant information (Conway, Cowan, & Bunting, 2001). However, the authors of the inhibitory-control theory did not account for the neurophysiological data and did not propose any hypothesis about the role of different brain structures in interference-resistance processes.

According to our data, the size of the left posterior dorsal cingulate cortex correlates negatively with verbal working-memory capacity and permanency. It also
correlates positively with the number of different memory errors. We suggest that the role of this brain region is to subtract relevant information and to receive a “signal” from the informational “noise.” This hypothesis explains some results of other studies, such as those regarding the activation of the posterior cingulate cortex during the recognition of familiar words, objects, or places (Heun et al., 2006; Sugiura et al., 2005).

The results of our study also revealed positive correlations between hippocampus volume and associative-memory capacity. However, these correlations are present only for the left hippocampus. This fact corresponds well with the results of other studies. For example, hippocampus lesions in rats lead to associative-memory impairment (Peinado-Manzano, 1994). A decline in associative-memory functioning is found in patients with Alzheimer’s disease, as well as in normal aging, which leads to a decrease in hippocampal volume (Atienza et al., 2011). Associative-memory decline in patients with mild cognitive impairment is related to atrophy of the left anterior hippocampus or to hypoactivation (Hanseeuw et al., 2011). Recent fMRI data show that different working-memory processes are provided by the functioning of several brain structures, but hippocampus activation is revealed particularly in associative-memory tasks (Hales & Brewer, 2010).

To summarize, information processing, classification, and cataloging are important parts of trace maintenance in verbal working memory. According to the obtained results, along with the data in the literature, this process is provided by such structures as the left posterior dorsal cingulate cortex and the left hippocampus. Our suggestion of the significance of information classification is partly in line with the SIMPLE memory model (Brown, Neath, & Chater, 2007; Hulme et al., 2006). According to this model, the speed of the retrieval of objects from memory depends on the amount of the specific qualities of that object. Thus, the more specific qualities the object has, the faster it is retrieved. However, this model explains only free retrieval, not sequence recall (Lewandowski, Brown, Wright, & Nimmo, 2006; Nimmo & Lewandowsky, 2005). Along with the inhibitory-control theory, the SIMPLE model was not connected to any neurophysiological data.

Therefore, according to the obtained results and the experimental data described in the literature, trace maintenance in working memory appears to be a more complex process than those described in existing working-memory models. The FROST model emphasizes the role of the fronto-striato-thalamic interaction in the signal-maintenance process in working memory (Ashby et al., 2005); the inhibitory-control theory (Kane & Engle, 2000) points out the significance of internal, proactive interference resistance; the SIMPLE model (Brown et al., 2007; Hulme et al., 2006) demonstrates the significance of signal amplification by subtracting specific characteristics of the recalled object; and, finally, Baddeley’s working-memory model (2003) revolves around the control block, the so-called central executive.

We suggest the following psychophysiological model of verbal-information maintenance in working memory. In our opinion, this model, on the one hand, conforms to the results of our study and, on the other hand, is consistent with experimental data from other studies described in the literature. Moreover, our model combines already-existent memory models. Thus, we hypothesize that verbal-information maintenance in working memory is provided by the functioning of five subsystems:
1. Sensory filter: partial blocking out and filtering of extra sensory information at the moment of information maintenance in memory. This blocking function is probably related to the activity of the left caudate nucleus, which slows down the thalamic nuclei (responsible for the entrance of sensory information into the left hemisphere of the brain) through the globus pallidus.

2. Sensory screen: temporary verbal-information storage, from which the information is directed to the other subsystems for processing.

3. Semantic filter: suppression of internal interference, such as other stimuli, thoughts, associations, attention fluctuations. This subsystem functioning is probably related to the activity of the left anterior cingulate cortex.

4. Central executive: voluntary control over incoming information according to the present task. The central executive plays an important part in controlling sensory and semantic filters and the sensory screen. Generally, this block is similar to Baddeley’s working-memory block of the same name. Presumably, its functioning is related to the activity of the left prefrontal cortex.

5. Archiver: information processing (collection, classification, cataloging) for long-term storage. This processing consists of the creation of associative links. The maintained information is transferred to long-term memory from this block. Supposedly, this subsystem functions because of the activity of the left posterior cingulate cortex and left hippocampus.

Figure 1 describes the psychophysiological model suggested above.
Verbal working memory...

It is necessary to point out several limitations of the proposed working memory model. Firstly), it describes only the maintenance of a verbal stimulus in working memory and does not concern information input and primary processing or the retrieval of information in working memory, the role of emotions and functional state, and so forth. Secondly, the present working-memory model was the basis for choosing the data in the verbal working-memory tests in the first place. This sequence probably explains the fact that the results of our study include correlations of working-memory test results only with the left hemisphere brain structures. We can hypothesize that the present model can also be applied to nonverbal stimuli maintenance in working memory, but this statement requires further research.

Acknowledgements

This study was supported by Russian Humanitarian Science Foundation (RHSF) project #13-06-00570.

References


Received: 10 July 2013
Accepted: 22 September 2013
Available Online: 27 November 2013