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The present study sought to test the hypothesis that the production of speech and the comprehension of speech in the left temporal lobe can be anatomically disassociated. Moreover, it is aimed to show that the standard intraoperative object naming task is not sufficient to test all the functionally essential areas in the left temporal lobe. In the introductory part of the article we described the existing information about the left temporal lobe and the awake surgery procedure. In the course of the study, we collected and analyzed the data from intraoperative brain mapping of 25 patients with brain lesions – gliomas or pharmaco-resistant epilepsy, who underwent awake craniotomy. All the patient went through intraoperative language mapping with the use of direct electrical stimulation. In order to map language production and comprehension modalities, in addition to the classical object naming task we used an additional task, the phonological judgment task. The results showed substantial dissociation between mapping of two tasks. According to these findings, we can conclude that the object naming task alone is not suitable for adequate brain mapping of the left temporal cortex. The same dissociation may be regarded as an argument in favor of the anatomical dissociation of the production and comprehension of speech in the left temporal cortex.

Key words: neurolinguistics, left temporal lobe, production of speech, comprehension of speech, intraoperative brain mapping, direct electrical stimulation, object naming, phonological judgment.

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Introduction

Left Temporal Cortex and its Functions

The question of how language is represented in the brain has been extensively discussed for more than two centuries. It has been a long time since Marc Dax discussed the left hemisphere lateralization of language in 1836 [Buckingham, 2006]. However, in the 21st century, we still do not have an exact answer to the question where language is located in the brain. The question itself has changed throughout history. Nowadays, the majority of scientists do not believe that certain brain regions correspond to specific functions. Language processing is considered to rely on a distributed network. Latest relatively recent model that has the largest explanatory power is the one developed by [Hickok and Poeppel, 2007]. The model proposes two streams of language processing. The ventral stream involves the temporal lobe and sustains mapping phonological representations onto lexical conceptual representations, the conscious perception of visual information, and the perception and recognition of auditory objects such as speech. The dorsal stream involves posterior temporal/ inferior parietal structures and posterior frontal areas. It maps phonological representations onto articulatory motor representations. The model, in particular, implies the multifunctionality of the left temporal cortex, suggesting that it is involved in two different language modalities, comprehension and production.

The first scientist who postulated the role of the temporal lobe in language comprehension was Carl Wernicke. He claimed that the posterior temporal area was devoted to auditory word processing [Wernicke, 1874]. Since then, the temporal cortex has continued to be the focus of scientific investigation. In the seminal study by [Binder, 2000], the processing of speech and non-speech sounds was related to the activation of the temporal lobe, as visualized with functional magnetic resonance imaging (fMRI). The participants performed a listening task, which included two types of stimuli: non-speech and speech sounds. The brain activations in response to different types of stimuli was compared. The superior temporal lobe showed the bilateral activation in response to the both types of stimuli. Critically, word stimuli caused more left than right hemispheric activation. However, [Binder, 2000, p. 521] related this phenomenon not to language specificity of the left temporal lobe; rather, this asymmetry was due to the fact that words stimuli were less effective at the activating of the right temporal lobe in comparison to the activation by other tasks. Overall, the bilateral superior temporal cortex responded more to the speech sounds than to non-speech sounds.

In another important study, [Scott, 2000] carried out the experiment using positron emission tomography, a variant of functional neuroimaging. The participants were presented with sentences,

and after each stimulus were asked about how much they understood it (sentences were in two conditions: intelligible and unintelligible). In contrast with the [Binder, 2000], that study showed that speech-specific response was obtained in the left temporal lobe structures, suggesting different subsystems in the auditory cortex; whereby non-speech audio processing was bilateral, with phonetic processing being mostly carried out by the left superior temporal gyrus. Despite some open discussions about the interaction between speech and non-speech audio stimuli processes, currently there is no doubt that the left temporal cortex is involved in the speech processing circuits of the brain. For instance, [Trimmel, 2018] compared activation during fMRI tasks in a healthy controls group and in patients with temporal lobe epilepsy. A visual naming task (with pictures) and an auditory naming task (with verbal cue) were used. The analysis demonstrated a functional coupling of the left posterior inferior temporal region to other brain regions related to the language network [Trimmel, 2018, p. 2414].

In addition to the established contribution of the left temporal cortex to language comprehension, it was also found involved in language production. Recently, [Wilson et al., 2015] have explored transient aphasia after left hemisphere resective surgery. Language abilities of patients who underwent resection to the language-dominant hemisphere were evaluated postoperatively using a comprehensive aphasia battery. The study showed that naming deficits were associated with resection of several temporal structures, including the middle temporal, inferior temporal, fusiform, and parahippocampal gyri [Wilson et al., 2015, p. 8]. [Agarwal et al., 2018] analyzed fMRI results of the patients who underwent presurgical scanning. They claimed that sentence completion task, which assesses the production of speech, evoked repeated activation in the left temporal lobe, including Wernicke's area.

In this study, we approached the involvement of the left temporal cortex in the two outlined dichotomies – comprehension/production and phonological processing/lexical processing – from the causal perspective. We used different language tests to assess these aspects of language during intraoperative brain mapping.

Intraoperative mapping of the left temporal cortex

Awake surgery is performed using “asleep-awake-asleep” protocol [Duffau, 2012]. In the first and third stages of a surgery, the patient is asleep under general anaesthesia, while the neurosurgeon exposes the patient's cortex and closes the flat bone. During the second stage of the surgery, the patient is awake and performs linguistic tasks. Awake surgery procedures allow for a tailor-made approach to be developed for every patient, as brain functions can be controlled during brain tumor removal. Direct electrical stimulation (DES) is used to monitor resection in order to

avoid damaging brain areas near or within where the tumor is located, which are essential for the language functions. The DES procedure consists of the application of a monopolar or bipolar electrode on the surface of the exposed cortex. Through such an electrode, electrical pulses are delivered according to safety guidelines - within frequency of 25–60 Hz and with the maximal current of 20mA [Szelényi et al., 2010, p. 2]. The amount of current should be tailored for each patient to avoid epileptic seizure. DES inhibits the small part of the brain tissue, disrupting the ongoing language task. As [Ojemann, 1983, p. 190] put it, the stimulation acts like a temporary lesion. While the neurosurgery team is carrying out DES, the patient is asked to perform language tasks, while the surgeon places an electrode on the cortex. All the stimuli in each test are presented to the patient for four seconds; any longer stimulation might provoke a seizure [Haglund, 1994: 568]. If any disruption (in language, speech, articulation, etc.) occurs, it means that this exact region is engaged in the network responsible for the function tested. This disruption is commonly called “positive”. Each region is tested at least 3 times to ensure that disruption is due to the electrical stimulation and not due to confounding factors. All the regions of disruptions are marked by the neurosurgeon with sterile tags, the linguist or the neuropsychologist who does testing also keeps track of all the tags, and they are fixed in a protocol. After the areas responsible for language have been mapped, the surgeon starts the resection of the tumor while avoiding the tagged regions.

In the intraoperative setting, there are several considerations that should be taken into account when designing linguistic tests. First of all, task complexity should be wisely considered, as the patient has only four seconds to respond. For instance, discourse tasks, presumably, would not make a good choice. Secondly, the fixed position of the patient’s head also influences the level of difficulty of certain tasks (reading, etc.) Thirdly, patient fatigue, which progresses over the course of the surgery, should also be taken into consideration [Mandonnet et al., 2010, p. 136]. Considering all of these factors, relatively simple and well-tolerable tests should be developed to tap into various aspects of language during awake neurosurgeries.

The conventional and standard task for intraoperative language mapping is object naming. The most essential benefit from the task is that it assures that several essential aspects of language (semantic processing, lexical access, basic grammatical encoding, articulation) will not be impaired in an individual after the neurosurgical resection. However, everyday communication obviously relies on a much wider range of language functions. The use of an inappropriate or sub-optimal linguistic test may cause a postoperative deficit, despite excessive testing [Mandonnet, 2010, p. 189]. This is why neurosurgeons and linguists are incorporating different tests into intraoperative brain mapping. For instance, [Malow et al., 1996] compared visual naming and auditory naming tasks using electrical stimulation mapping different brain regions, including

lateral temporal cortex, in patients with temporal lobe epilepsy. They found that stimulation of the anterior and posterior temporal cortex elicited errors in auditory naming but not in the visual naming task [Malow et al., 1996, p. 249]. This confirms the hypothesis that visual object naming might be insufficient for the identification of eloquent language-related brain areas including those in the left temporal lobe.

Recently, some research teams have started developing more sensitive test batteries for intraoperative mapping. The most comprehensive battery is the Dutch Linguistic Intraoperative Protocol (DuLIP) [De Witte et al., 2015]. It offers a wide range of tests for mapping temporal lobe regions, namely the posterior superior temporal gyrus, the middle and posterior superior temporal sulcus, the middle inferior temporal gyrus, and the anterior middle temporal gyrus. The tests include semantic picture out, semantic judgment, object naming, phonological odd word out, phonological judgment, and semantic judgment. Despite the existence of the tasks that test the comprehension of the speech, they all use visual stimuli, i.e. they are not able to test the lower auditory processing at the same time. According to [Hickok and Poeppel, 2007], phonological analysis is performed in the dorsal superior temporal gyrus and posterior superior temporal sulcus separately from lexical analysis, and it is important to have a task specifically for the assessment of a phonological processing pathway. Our study continues [De Witte et al, 2015] research line and tests sensitivity of a newly developed linguistic task for mapping language in the temporal cortex. Following their suggestion about the necessity to compare additional tasks to the gold standard object naming, we contrasted the two tests. Our newly developed task, the phonological judgement [Dragoy et al. 2017], allows us to track the speech comprehension and auditory processing at the same time. This saves time during intraoperative language mapping, and allows us to test several functions using only one task.

The previous data and the [Hickok and Poeppel, 2007] model supposed that the left temporal lobe participates in both modalities, production and comprehension of speech. The goal of our study was to show the clear disassociation between the processes of production and comprehension in the left temporal lobe.

Methods

Participants

The participants were 25 patients who underwent the awake surgical procedure for treatment for glioma (13 patients) or drug-resistant epilepsy (12 patients) in the left frontal-parietal-temporal region (16 females; mean age 36, SD 10.6, range 17 - 59 years) between 2017 and 2020 in several hospitals: National Medical - Surgical Center named after N.I. Pirogov (Moscow), Medical and

Rehabilitation Center (Moscow), Federal Center for Neurosurgery (Novosibirsk), and Privolzhskii Research Medical University (Nizhniy Novgorod). All the patients were self-reportedly right-handed, native speakers of Russian (five of them were balanced bilinguals).

Tasks

We used two tasks in our study: the classical object naming and the phonological judgement task. Both tasks were standardized for Russian and adopted for the awake surgery settings. These tasks were developed at the Center for Language and Brain NRU HSE.

(1) Object naming

Object naming is considered to be the “gold standard” for the brain mapping procedure [Talacchi et al., 2013]. One of the classical object naming tests is *The Boston Naming Test* [Kaplan et al., 1983]. Object naming is discussed in detail elsewhere (see [Dragoy et al., 2016]; [Ojemann, 1979]). During the task, the patient is presented with a set of black-and-white slides with a line drawing of a common object, and they have 4 seconds to name it. Every nomination should start with the word “*Eto*” (“This is”) for the neurologist to differentiate between anomia (retrieval failure) and speech arrest (inability to speak), in other words, between language and speech errors. The task consisted of 50 object pictures. Example of the stimulus:



Figure 1. Object naming stimulus example

The answer here should be: “*Eto kolyaska*” (“This is a baby carriage”).

(2) Phonological judgement task

In the task, the patient should determine whether the pair of the auditorily presented pseudowords are different or identical. For instance, “*py-pi*” (different) or “*tosh-tosh*” (identical). The stimuli are played on a tablet, the audio track having been recorded beforehand. The phonemes

are distributed into the pairs on the basis of their softness/hardness, permutations of sounds, a place of formation, deafness-sonority, and the method of word formation [Zhirnova, 2019]. The standardized Russian test consists of 100 pseudoword pairs, half different and half identical.

Procedure

To formally assess language outcome of a surgery, perioperative language assessment was performed. We used the Russian Aphasia Test (RAT) [Ivanova et al., 2016] and Token Test [Akinina et al., 2017]. Preoperative assessment was compared to the postoperative assessment in order to elicit the postoperative language deficit that was caused by the resection. Structural MRI was also conducted. For each patient, we used one (only object naming) or two tasks. No tasks or stimuli that the patient was unfamiliar with were used intraoperatively. To ensure that any speech deficit during the DES was the consequence of the stimulation itself, and not due to the preoperative deficit, all intraoperative tasks were carried out twice preoperatively. The trials, where the patient failed, were excluded from the intraoperative presentation to avoid false-positives.

At the second stage of asleep-awake-asleep craniotomy, after the patient was awakened, the neurosurgical team made an effort to lead the patient to an awakened state that could be evaluated by a “2” on the Ramsey scale (meaning that the patient is co-operative, oriented, and tranquil) [Society of Critical Care Medicine, 2002, p. 158]. Following this procedure, neurolinguists conducted a baseline for each of the two tasks without stimulation. When the patient was ready, DES was started during linguistic testing. The probes were separated by a 500-millisecond sound 400 Hz, which signaled the surgeon that the stimulator can be put on the next region. Stimuli were automatically presented on a tablet. A bipolar electrode with 5mm spaced tips delivering a biphasic current of 2 to 12 mA amplitude was applied to the brain. The intensity was adapted to each patient by progressively increasing the amplitude until a sensorimotor response was elicited in order to avoid general seizures. The whole area of the individually exposed cortex was mapped. During mapping, the neurolinguist recorded in the protocol how many times a positive result was obtained on each stimulation spot. Each site was stimulated at least 3 times. If there was a $\geq 50\%$ positive result, the neurosurgeon marked the spot with the sterile tag.

Postoperatively, MRI was carried out again. The neurolinguist assessed the patient’s language status with RAT and Token Test before the patient was released from the hospital.

Data Analysis

The positive sites elicited by DES during surgery were verified according to the neurolinguistic mapping protocol. The anatomical location of these positive sites was identified based on intraoperative neuronavigation (the neurosurgeon marked the sites on a patient's MRI in the navigation system and recorded the results) and/or an intraoperative photo of tags on the surface of the patient's brain.

Further procedures depended on the availability of the neuronavigation screenshots. If there were not any, spots were defined anatomically by visualizing presurgical MR-scan in 3D-space with MRICroGL [MRICroGL, 2012], and defining corresponding gyri and fissures near the positive site on the intraoperative photo and MRICroGL visualization, respectively. After that, we segmented the 5 mm spherical 3D spot using ITK-SNAP [ITK-SNAP, 2019]. If there were neuronavigation screenshots, we proceeded straight to the ITK-SNAP. After that, the segmentation was normalized, MR-segmentation option from Clinical Toolbox [Clinical Toolbox, 2014] for spm12 in MATLAB was used. The Figures in the article were obtained from the visualization made with SurfIce [SurfIce 2015]. All positive sites were laid over the normalized brain MNI152_T1_1mm template. During the process of normalization, the 5 mm spheres that represented positive sites might have moved slightly. We assume that such a shift was permissible for the resulting analysis, having a negligible effect on the results.

Results

Overall, we identified 39 positive sites in 25 patients: 27 using the object naming task and 12 using the phonological judgment task. Object naming positive sites were found in 19 patients, and phonological judgement positive sites - in 7 patients. The difference in numbers does not necessarily allow us to draw any conclusions about the sensitivity of a task. There were several extralinguistic factors that influenced this unbalanced state of affairs. We obtained a greater number of positive sites in the object naming task because this task was used during every surgery. Consequently, there were more opportunities for the elicitation of positive sites for object naming. At the same time, the phonological judgement task was used during every second temporal lobe craniotomy (it was alternated with a different task that will not be discussed here). However, there were situations where for the sake of time the neurosurgeon decided to perform only one task. In such cases, the object naming task was performed. The number of positive sites per patient ranged from 1 to 3. It is important to note that sometimes during surgery, the frontal and/or parietal sites were also elicited. These sites, however, were not included in the analysis.

The distribution of the positive sites elicited in the two tasks are shown in Figure 2. Although some of the spheres seem to be located in the frontal cortex, this is in fact the result of normalization correction. In the intraoperative photos, all of the sites presented below were located in the left temporal lobe.

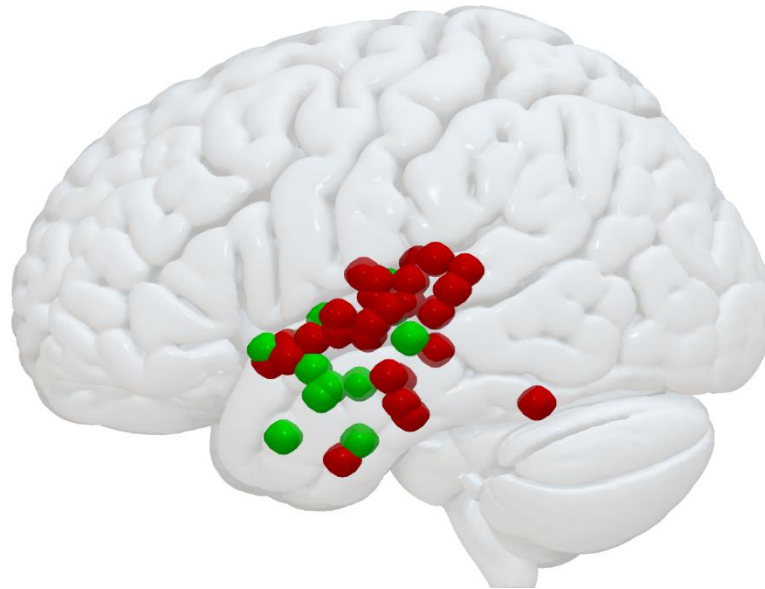


Figure 2. Distribution of the positive sites elicited in different tasks: (1) red – the object naming task, (2) green – the phonological judgment task.

Although some of the sites overlap, the dissociation between different tasks results can be clearly seen.

For object naming, the majority of the sites are concentrated in the superior temporal gyrus, with some of them located in the middle temporal gyrus. Two outliers are located in the temporal pole and posterior part of the inferior temporal gyrus. For the phonological judgment task, there is a different pattern: positive sites are located in the anterior and middle parts of the superior and middle temporal gyri.

From 14 patients who performed both tasks in the course of the surgery, 2 patients had positive sites in the two tasks, and they both had a clear dissociation. Their mapping results are presented in Figure 3.

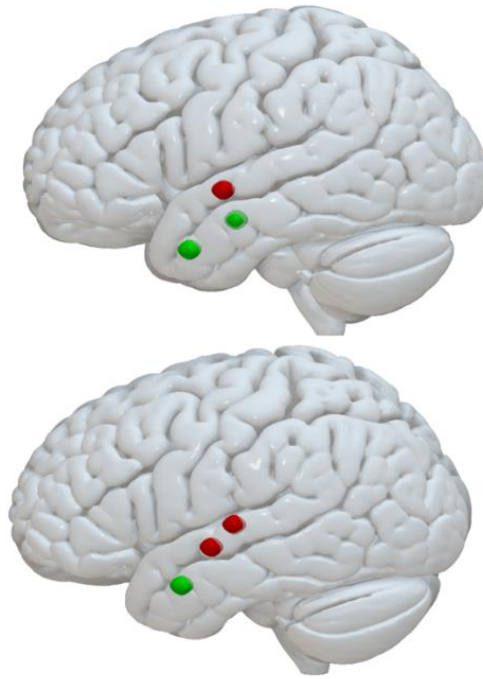


Figure 3. Dissociation between the positive sites elicited the object naming task (red) and the phonological judgement task (green) in two patients.

Discussion

Since the time when the first model of language anatomy proposed by P. Broca and C. Wernicke was accepted by the scientific community, the debate about its adequacy has continued. Scientists have developed new models that have brought us closer to understanding language processing in the brain. However, these models still need to be improved. Intraoperative brain mapping with the use of DES can provide us with insight on how language is processed in the brain. These findings have undoubtedly broadened our knowledge about language and contribute to the improvement of language models.

The goal of the current study was to show that two modalities, speech production and speech comprehension, are anatomically separated in the left temporal lobe. For that, in addition to the classical object naming task (assesses speech production), an additional task, the phonological judgment task (assesses speech comprehension), was used. In our results (Figure 2 to Figure 3), the disassociation between the two tasks is clearly seen, although some positive sites are located in the same places. The cluster of positive sites elicited by the object naming task is located along the middle part of the superior temporal gyrus, while positive sites from the phonological judgement task are mostly located in the anterior part of the superior and middle temporal gyri. In Figure 3, where we depicted the results from individual patients, the dissociations can be seen even

more clearly. From this result we can conclude that the two modalities can be differentiated in the left temporal cortex. Moreover, we can conclude that a classical object naming task is not enough to perform comprehensive intraoperative brain mapping. The overall picture indicates that performing only one task during the surgery is insufficient: we risk to miss the areas that are essential for the language processing if only the object naming task is used. Let us compare our results with several previous studies. [Haglund et al., 1994] discussed the cortical localization of language sites in the temporal lobe. They analyzed the data collected from the intraoperative brain mapping of 44 tumor patients and 83 temporal epilepsy patients, who underwent craniotomies for the tumor or epileptic foci resection while awake. The task chosen was the object naming only. [Haglund et al., 1994, p. 567] concluded that there were significantly more language sites in the superior temporal gyrus than in the middle temporal gyrus. There were no sites found in the inferior temporal gyrus. Our findings do correspond to their results (Figure 2). The majority of sites found in the object naming task were located in the superior temporal gyrus and less in the middle temporal gyrus. Moreover, we did not locate any sites in the inferior temporal gyrus. Several sites are distributed along the middle temporal sulcus; they may be attributed to the middle temporal gyrus. The only positive site on the posterior part of the inferior temporal gyrus may be considered an outlier.

It is also interesting to compare our results with the studies that used other methods in their experiments, for instance, fMRI studies. [Hickok et al., 2000] attempted to prove the hypothesis that the left posterior superior temporal gyrus activates during object naming tasks. The authors performed an experiment in healthy subjects, who carried out object naming tasks during scanning. The results showed that five of seven participants had activation either in the dorsal or ventral portion of the posterior superior temporal gyrus, or both [Hickok et al., 2000, p. 159]. The authors concluded that the area of the left posterior superior temporal gyrus is activated in a language production task. In our study, several clusters of positive sites elicited during object naming were located along the superior temporal sulcus, but in its anterior and middle parts. Another fMRI study found an activation in the middle temporal gyrus. In [Ashtari et al., 2004] healthy volunteers were presented with the phonological judgement task, which was similar to ours, while undergoing scanning. Individual subject analysis showed consistent activations in the left middle temporal gyrus. These findings allowed the researchers to conclude that the middle temporal gyrus plays a key role in the discrimination of the phonemes, suggesting that this region may be specialized for the processing of phonological information and comprehension [Ashtari et al., 2004, p. 391]. The study results correspond to the pattern of the positive sites localization elicited in our phonological judgement task. The greatest number of the positives were located in the middle temporal gyrus.

Some findings in the articles listed above are in agreement with the results of our research. All aforementioned studies identified the involvement of the superior temporal and the middle temporal gyri (as well as our). However, the exact pattern of the production and comprehension networks do not correspond entirely. [Sarubbo et al., 2020] intraoperative brain mapping study found activations in the middle and posterior portions of the superior and middle temporal gyri, but we did only in middle portions. Moreover, inconsistency can be spotted in fMRI studies: [Hickok et al., 2000] claims that the superior temporal gyrus plays the crucial role in comprehension, while [Ashtari et al., 2004] attributes the activation mostly to the middle temporal gyrus. It is worth noting that these differences do not mean that one idea is right and other is wrong. As we claimed before, the language function is considered to be the representation of the network in the brain. In other words, all these regions might be involved in the comprehension and/or the production of speech. We can put all existing data together to compute the networks of both processes. As for now, we do not have enough data to strictly accept or reject our theoretical hypothesis that the comprehension of speech and the production of speech can be anatomically differentiated in the left temporal lobe. Furthermore, the results of our study show foremost that the common task for the intraoperative brain mapping, the object naming task, is on its own inadequate for comprehensive assessment during surgery and does not allow for mapping language comprehension. The anatomical dissociation between positive stimulation sites elicited by the two different tasks we used (object naming and phonological judgment) prove the necessity for a more complex intraoperative test battery covering both modalities of language.

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