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The Wada test or intracarotid amobarbital procedure is commonly used to determine hemisphere dominance for language and memory. This study presents the first standardised Wada protocol for Russian-speaking population. First, we provided the background on the Wada procedure and made the comparison of two most widely accepted standardised protocols, the Montreal and the Seattle ones. Next, the whole procedure of the Wada test according to our protocol was presented. Additionally, the main types of speech errors that may occur during the procedure were analysed. The protocol was first tested in 20 non-brain-damaged participants. Finally, the newly designed protocol was clinically piloted, with resulted in revealing its high reliability. With the new protocol, it was possible to determine for each of the tested patients, which hemisphere was responsible for language, and which - for memory.

JEL Classification: Z.

Key words: language, memory, Wada, fMRI, EEG, the Russian language, Seattle protocol, Montreal protocol

Introduction

The Wada test, named after Juhn Wada, a Japanese Canadian neurologist, is used to identify the language dominant hemisphere of the brain. The initial purpose of the Wada test was to stop the seizure activity of the affected hemisphere. After Paul Broca described the frontal operculum as an area responsible for language, the test has instead become used to determine language dominance – in a variety of neurosurgery patients (with tumours, drug-resistant epilepsy, etc.), when knowledge about functional lateralisation is clinically relevant. The Wada test's modern usage also includes the localisation of potential epileptogenic zones. The test provides information on potential postoperative functional deficits.

The Wada test is a procedure during which a patient performs several cognitive tasks while one hemisphere is anaesthetised at a time. Specifically, an anaesthetic agent is injected into the left or right internal carotid artery, thereby unilaterally inactivating the function of one of the hemispheres for several minutes. When the injection is given into the right carotid artery, the right side of the brain is "asleep" and cannot communicate with the left side and vice versa. Then the patient performs tasks on language and memory to assess the involvement of the active hemisphere for the respective function [Daroff et al., 2014].

Unfortunately, the Wada test is very limited in time. An investigator has a few minutes to test each hemisphere. In addition, the test is invasive, which makes it difficult to repeat on the same individual. Due to the complexity of performing the Wada test and

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the risk to a patient, some authors [Bauer et al., 2014; Papanicolaou et al., 2014; Massot-Tarrús et al., 2019; Massot-Tarrús et al., 2020] have compared the Wada test with non-invasive modern neuroimaging techniques – functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG). The results of language lateralisation obtained with fMRI were 95% consistent with the outcome of the Wada test. A similar comparability was found between the MEG and the Wada test, varying between 87% and 100%. However, despite such a high concordance, the Wada procedure remains the basis for determining hemispheric language and memory lateralisation.

The cognitive and linguistic content of the Wada test differs among clinical centres; a uniform procedure to adapt it to a new language is missing. There are two main standardised protocols, Seattle and Montreal, which were designed to lateralise language and memory. In both, electroencephalography (EEG) recording is set up first, to monitor the suppression of the hemisphere. The Seattle protocol consists of three tasks: object naming, reading phrases, and the recall of previously named objects [Dodrill et al., 1997]. A patient's ability to follow commands during the Wada test provides a measure of auditory language comprehension as well. The Montreal protocol involves the presentation of five objects during the anaesthetic effect, and their recall after the anaesthetic has worn off, to lateralise memory. Eisenman [Eisenman, 2005] compared these two approaches and found that the Seattle protocol predicted postoperative memory deficits with 75% accuracy, while the Montreal protocol did so correctly only in 48% of patients. The Seattle protocol has a lower error rate and a higher sensitivity compared to the Montreal protocol [Dodrill et al., 1997].

The aim of this study was to use the advantages of different parts of both protocols, to design a new optimal protocol for the Wada test in Russian, to standardise it in a cohort of healthy participants, and to test it in clinical settings.

Method

According to our protocol, each hemisphere is tested separately using the same procedure, but with non-identical (though balanced) testing materials. The second hemisphere is tested 12–15 minutes after the first, to make sure the latter fully recovered from the anaesthesia [Połczyńska et al., 2015]. This is often complicated by a patient's consciousness disturbance in the form of confusion, drowsiness or psychomotor agitation, regardless of the type of the anaesthetic agent. Before the start of the test, the patient raises the hand opposite the tested hemisphere, which controls it in a contralateral manner. The surgeon then injects the anaesthetic agent. Nowadays methohexital, propofol and sodium thiopental have replaced amobarbital [Curot et al., 2014; Loddenkemper et al., 2009]. The dose of the second injection matches the first one. The fall of the hand signals that the medicine has begun to act. Additionally, the effect of the anaesthetic agent is verified using the EEG. Language and memory are tested sequentially.

The assessment of language lateralisation occurs at three levels: automatised speech, language comprehension, and language production. Counting from one to ten during the injection of an anaesthetic agent is meant to test automated (well learnt) speech. If a patient stops counting along with the hand falling, the anaesthetised hemisphere is considered dominant even for such non-propositional language (which might also be supported with a language non-dominant hemisphere [Eisenman, 2005]. Language comprehension, which may dissociate from production in terms of brain lateralisation [Połczyńska et al., 2015] is assessed using simple verbal commands. In one hemisphere, the participant is invited to blink twice and then to stick out their tongue; in the other – to close their eyes and then to open their mouth. If automatised speech (counting) is spared, we probe more complex language production – object naming, three items per hemisphere. Table 1 lists the used items: for each hemisphere, Russian words of increasing length (3, 4, and 5 phonemes) were selected, all of middle frequency [19–80 instances per million words (ipm); Lyashevskaya, Sharov 2009]. Real objects the words refer to are shown to the patient one by one, who is asked to name each with one word.

Tab. 1. List of objects

Hemisphere	Object for naming	Object for recognition	Correct answer for recognition
1	*myach* ‘ball’ (3 phonemes, 26.4 ipm)	*myach*	yes
	kljuch ‘key’ (4 phonemes, 78 ipm)	*kljuch*	yes
	lozhka ‘spoon’ (5 phonemes, 40.5 ipm)	*wilka* ‘fork’ (5 phonemes, 16 ipm)	no
2	*syr* ‘cheese’ (3 phonemes, 19.5 ipm)	*syr*	yes
	ochki ‘glasses’ (4 phonemes, 56 ipm)	*chasy* ‘clock’ (4 phonemes, 72.5 ipm)	no
	ruchka ‘pen’ (5 phonemes, 57.6 ipm)	*ruchka*	yes

At the end of the language tests, the patient is asked simple questions (e.g., “What is your name?”, “Where do you live?”) to monitor the washout of the anaesthetic agent and functional restoration. The recovery is also verified with the EEG. When the recovery is confirmed, memory is formally tested: the patient is shown two objects that were presented during anaesthesia and one, which was not presented, but is a semantic distractor to the remaining presented object, and asked which of those they saw, responding with "yes" or "no".

The results of the language lateralisation assessment can vary. If the anaesthetised hemisphere is dominant for all aspects of language, speech arrest and complete inability to understand speech occurs, which lasts for several minutes until the hemisphere recovers from anaesthesia. Rarer cases include dissociation between different aspects of language: for example, naming (language production) can be negatively affected, but counting (automatised speech) or execution of commands (language comprehension) might remain. That would mean that only language production is unilaterally lateralised, while other aspects of language are represented either bilaterally or in the contralateral hemisphere. If a hemisphere is anaesthetised, but all language tasks are, in principle, performed well, it is considered non-dominant for language; in this case dysarthria is still possible due to the motor inhibition of half of the articulation apparatus.

As for the results of memory testing, if the anaesthetised hemisphere is dominant for memory, the patient, after return to the neurologic baseline, as demonstrated by normal language and correct answers for questions, has memory deficit; it manifests itself through the inability to remember objects that were presented under anaesthetic. If a hemisphere is anaesthetised, but a patient answers questions correctly and remembers all the objects, it means that the hemisphere is non-dominant for memory.

Standardisation

The protocol was first tested in non-brain damaged participants. All participants reported normal or corrected to normal vision and no hearing problems or history of neurological disorders. The group included 20 individuals (14 women, mean age = 36.9, SD = 11.7, age range 20–52).

Participants were tested individually with both equivalent versions of the protocol, with a 12–15 min break between the versions, to mimic the clinical presentation timing. The order of the versions was randomised among participants. 95% (19 out of 20) of the participants had no errors passing both versions of the test. One participant (female, 41 years old) had difficulty passing the first version of the test: she made an error recognising an object that was shown earlier. She stated that she had been shown the fork earlier, but this was wrong. She later explained it by inattention.

Clinical testing

We also tested the protocol in the clinical settings. The participant was a 37-year-old, right-handed, male patient who suffered from epileptic seizures from the age of 14. His seizures originated from the left parietal-frontal-temporal cortical region, as shown by a previously conducted video EEG monitoring. High-resolution structural MRI also confirmed a left cerebral hypoplasia with heterotopia. The patient was a candidate for neurosurgery to resect the epileptogenic locus. To identify his individual language and memory lateralisation patterns and avoid potential postoperative deficit, he underwent the Wada test following our new proposed protocol.

We first tested the right hemisphere. Under the angiography control, the catheters placement and the lack of interhemispheric vascular bifurcation were confirmed. 45 mg thiopental sodium was injected into the right internal carotid artery while the patient counted. Thirty seconds after the start of the agent injection, the contralateral (left) arm fell; yet in ten seconds, the EEG indicated anesthetisation. Then language comprehension and naming was tested, according to the first version of the protocol. The patient performed testing well, with no errors. In two minutes, the EEG indicated recovery. Three minutes later, the patient showed restoration of the left-hand motor function. Eight minutes after that (that is, 13 minutes after the start of the procedure), a recognition test was performed. The patient could not recognise any object presented to him during anaesthesia, replying “no” in all three trials. He further reported that he could not recall which objects were previously shown to him and which were not.

In 15 minutes, after the start of the right hemisphere testing, the procedure was repeated on the left hemisphere; 37.5 mg thiopental sodium was injected into the left internal carotid artery while the patient again began counting. Thirty seconds after the injection started, the contralateral (right) arm fell, and the anaesthesia result was confirmed by the EEG. The patient was again offered a language test consisting of verbal commands and naming objects, according to the second version of the protocol. The patient did not follow any command, nor was he able to name any object, he stayed completely mute. In 6 minutes, after the patient recovered from anaesthesia, the recognition test was performed. The patient correctly recognised the two previously presented objects and replied that he did not see the one, which was not shown.

The result of the test clearly indicates that the right hemisphere of the patient was dominant for memory, while his left hemisphere was dominant for language.

Conclusions

Despite recent efforts to replace it with non-invasive methods, the Wada test remains the gold standard for testing language and memory localisation. The result of the present study shows the reliability of the newly developed protocol. Using this protocol, we determined that the patient's left hemisphere is dominant for language and his right hemisphere - for memory. This protocol is the first attempt to standardise the procedure of determining a hemispheric dominance among the Russian-speaking population. The overall design of this protocol combining the best components of other existing protocols makes it useful for adaptation to other languages.

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