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The Single Word Auditory Comprehension (SWAC) test: A simple method to identify receptive language areas with electrical stimulation

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ABSTRACT

Objectives: Resective surgery for medically refractory epilepsy in proximity to speech receptive areas requires balancing adequate resection of the epileptogenic zone for optimal seizure control with preservation of function. We develop a simple test (Single Word Auditory Comprehension or SWAC) to localize speech receptive areas by evaluating patients' ability to comprehend a single word.
Methods: Patients were studied during presurgical or intraoperative assessment for epilepsy with intracranial electrodes. They were asked to listen to a common word (target word) and to describe what it meant without saying the target word. Electrical stimulation (trains of biphasic 2-ms pulses, 50 Hz for 3 s) was delivered while the patient listened to the target word, not while the patient explained the meaning of the word. In six patients, SWAC test was carried out during extraoperative chronic recordings, and in one patient in the operating theater under local anesthesia.
Results: Among the 7 patients where the test identified deficits, 6 underwent resection (4 temporal, 1 supramarginal, and 1 occipital). Two patients showed temporary minor speech deficits after resection. No patient showed permanent speech deficits after resection.
Conclusion/significance: The SWAC test is reliable, simple and fast to implement, and suitable for intraoperating mapping. It could be used as a simple initial test to identify receptive language areas where more complex additional tests can be performed.

1. Introduction

Resective surgery for medically refractory epilepsy in proximity to eloquent cortical areas requires a delicate strategy to balance adequate resection of the epileptogenic zone for optimal seizure control with preservation of functional areas to avoid neurological deficits. Whereas limited removal of association cortex does not usually induce permanent or serious deficits, resection of language, primary motor, or sensory areas should be avoided, as their resection can be associated with corresponding permanent deficits.

Given the individual variability in the anatomical location of functional areas, detailed localization in each patient may be required before resection. Identification of responses to trains of electrical pulses applied to the cortex is a standard method to identify functional areas. While cortical stimulation of motor/sensory areas induces clear positive responses (movement, sensations), stimulation of language areas is associated with less clear language interference responses consisting of arrest of specific speech functions or, more rarely, jargon aphasia. Consequently, speech areas cannot be identified unless the subject is engaged in specific tasks. Therefore, the tests used to map language, particularly receptive language, are less standard or reliable than those used for motor/sensory mapping.

Noninvasive functional methods (positron emission tomography [PET], magnetoencephalography [MEG], functional magnetic resonance imaging [fMRI]) seem to implicate larger cortical areas in language function than initially thought [1–5]. For instance, although the superior temporal gyrus appears to be related to the interpretation of speech, other temporoparietal regions may be necessary for language

Abbreviations: SWAC, Single Word Auditory Comprehension test; PET, positron emission tomography; MEG, magnetoencephalography; fMRI, functional magnetic resonance imaging.

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comprehension [6,7]. These regions include the midtemporal gyrus, the inferior temporal gyrus, the fusiform gyrus, and the angular gyrus (Brodmann areas 20, 21, 36, 27, 39) [8]. However, not all areas identified by neuroimaging during language function may be necessary for language, and in the majority of patients, there is poor correlation between language mapping with electrical stimulation and fMRI [4]. As a result, preoperative fMRI cannot reliably be used without electrical stimulation to make critical surgical decisions [9]. Consequently, electrical stimulation is still crucial to identify the areas indispensable for language by simulating the effects of a temporary resection [10]. Electrical stimulation and diffusion tensor imaging can identify the arcuate fasciculus (connecting Broca's and Wernicke's areas), and both techniques colocalize well with anterior language areas, but less so with posterior (receptive) language areas, suggesting that the latter may be more disperse [11].

For these reasons, identification of transient speech deficits associated with cortical stimulation remains the gold standard to identify speech areas [12,13]. Arrest of on-going speech production can be induced by stimulation of Broca's area and disturbance in speech understanding can be observed when stimulating Wernicke's area. For localization of Broca's area, the traditional task consists in asking the patient to read, count or recite a known lullaby or song, while checking for pauses in speech associated with stimulation. Identification of the Wernicke's area is more complex, as detecting pauses in speech understanding is more subtle. Hamberger and Tamny [14] highlighted the paradox of patients describing word-finding difficulties in conversational speech without demonstrating deficits on formal confrontation testing, and thus devised the auditory responsive naming test [15] that, in addition to word retrieval, requires sentence comprehension. A number of different paradigms have been designed to identify speech areas with electrical stimulation: visual confrontation naming (visual object naming), picture selection, verbal/semantic fluency, auditory description (responsive) naming, token test, and aphasia batteries. Each method may be more suitable for mapping specific aspects of speech function. The performance of the following three methods was compared by Ojemann and Malow et al. [12,16]:

a) *Auditory responsive naming*: During stimulation, the patient listens to a brief description ("Tell me what is a barking pet….") and should then name the concept described.
b) *Picture selection*: During electrical stimulation, the name of an item is said aloud by the examiner, and the patient has to point at the named item among four drawings of common objects.
c) *Visual confrontation naming*: During stimulation, the examiner says "What is this?" while a drawing of a common object is presented to the patient who has to name it.

Electrical stimulation was delivered during 5 s for each item. Picture selection was only slightly disrupted by stimulation in most areas, possibly because of the randomness factor associated with selecting one picture out of 4, as the authors did not describe factoring in such randomness in the analysis. Auditory responsive naming was the most specific method for mapping lateral temporal (receptive) speech. However, mapping of receptive language appears to be less commonly used, possibly because of difficulties involved in administering the auditory responsive naming test. Whereas most centers (66%) use visual confrontation naming, only 6% use auditory responsive naming [17].

More recently, other language performance tasks have been suggested for assessment of Broca's and Wernicke's areas, including spontaneous speech, word repetition, object description, reading, syntax, comprehension, and verb generation [4,13]. Results from these tasks can point to close, but different brain regions to those identified with more traditional tasks. However, the number of different tasks that a patient can perform should be limited to avoid exhaustion and excessive charge delivery during electrical stimulation. Thus, a selection of the most clinically relevant tasks is required for each individual case.

In the present article, we report and evaluate feasibility and tolerability of a new simple method for functional mapping of receptive speech areas with electrical stimulation. The method was designed for fast implementation while avoiding long stimulation periods and the randomness associated with picture selection. It explores patient's ability to comprehend a single word, the basic unit of speech understanding; therefore, we have named the test "single word auditory comprehension" (SWAC) test. Essentially, patients were asked to listen to a common word (target word) and to explain the meaning of the target word without saying the target word. Electrical stimulation was delivered while the patient listened to the target word but not while the patient explained the meaning of the target word.

2. Methods

2.1. Patients

Between 2009 and 2014, 9 patients with electrodes overlying the left posterior rostral temporal and perisylvian regions were assessed with the SWAC test for functional mapping of Wernicke's area. In the present work, we report results from the 7 patients who showed language deficits during the SWAC test. All patients had epilepsy refractory to medical treatment and were under consideration for resective surgery. The type, number, and location of the electrodes were determined by the suspected location of the ictal onset region, according to noninvasive evaluation: clinical history, scalp electroencephalography (EEG) recordings obtained with the Maudsley system [18–20], neuropsychology [21], and neuroimaging. The selection criteria and electrode implantation procedures have been described elsewhere [22,23].

2.2. Intracranial electrodes

All patients were assessed with intracranial subdural or depth electrodes during presurgical assessment or intraoperative electrocorticography for the treatment of epilepsy. When performed, resections were guided by preoperative chronic intracranial recordings or intraoperative electrocorticography combined with intraoperative neuronavigation (Stealth, Medtronic, Houston, Texas, USA). Surgical outcome with regard to seizure control was classified in four grades according to the following criteria, which are largely based on Engel's classification [24]: grade I, free of disabling seizures; grade II, almost seizure-free (three or fewer diurnal or nocturnal seizures per year); grade III, worthwhile improvement (but more than three diurnal or nocturnal seizures per year); grade IV, no significant improvement.

The characteristics of the electrodes used were as follows:

Subdural electrodes: Subdural electrodes consisted of strips and mats (AdTech Medical Instruments Corp., WI, USA). Each strip consisted of a single row of 4 to 8 platinum disk electrodes spaced at 10 mm between centers. The disks were embedded in a 0.7-mm thick polyurethane strip that overlapped the edges leaving a diameter of 2.3 mm exposed, and recessed approximately 0.1 mm from the surface plane. Mats contained rectangular arrays of 12, 16, 20, 32, or 64 similar platinum electrodes with 10-mm center-to-center distances within rows.

Intracerebral (depth) electrodes: Multicontact flexible bundles of depth electrodes (AdTech Medical Instruments Corp., WI, USA) were implanted stereotactically under MRI guidance. The electrode bundles contained 8 or 10 cylindrical 2.3-mm long platinum contacts separated by 5 mm between centers of adjacent electrodes of the same bundle.

2.3. Procedure for language mapping (SWAC test)

Prior to functional mapping with electrical stimulation, patients were informed about the purpose of the test and the type of clinical responses that could be expected during electrical stimulation, such as speech arrest or comprehension difficulties, and the risk of stimulation-induced seizures, which could prove distressing. All patients understood the extent of the medical procedure and gave consent to proceed prior to testing.

Cortical electrical stimulation for functional mapping was induced by trains of biphasic 2-ms pulses at 50 Hz lasting for 3 s delivered between contiguous electrodes. Simultaneous EEG was recorded with the electrodes not used for stimulation in order to monitor for afterdischarges and seizure activity. Functional mapping was carried out during extraoperative chronic recordings in six patients, and in the operating theater during a craniotomy under local anesthesia in one.

One second after the onset of the train of electrical pulses, an assistant with English as mother tongue vocalized the target word from a list of randomly ordered common nouns and adjectives (such as car, bank, dog, wall). After the train of electrical pulses ended, the patient had to explain the meaning of the target word without saying the target word. Preferably, the assistant saying the target word was a relative of the patient in order to eliminate potential language misunderstandings due to accents or individual differences in pronunciation.

For each pair of stimulating electrodes, the test was repeated at stimulating intensities (1, 2.5, 5, or 7.5 mA) that were progressively increased unless one of the following occurred:

a) Intensity of 7.5 mA for subdural electrodes or 5 mA for depth electrodes was reached.
b) Afterdischarges occurred.
c) A language interference response (see below) occurred suggesting that Wernicke's area had been stimulated.

Localization was provided by “language interference responses”, consisting of the patient stating that the target word had not been understood, a word had not been said, the patient asking if the target word could be repeated. If a language interference response occurred, identical electrical stimulation was repeated with a new target word. Language interference responses were considered as localizing if they occurred on three successive identical stimulations with different target words. On occasions, the patient did not initially understand the word but was able to repeat it, and understand the word thereafter. As the patients were able to repeat the word after stimulation, the findings suggest that language interference responses were due to a deficit in receptive language rather than to an auditory deficit. This method involved only minor modifications to the standard methods used for functional mapping with electrical stimulation and therefore required no formal ethical approval.

Postsurgical language evaluation occurred in the surgical ward during postsurgical recovery and at the follow-up clinic visits that took place every 6 months after surgery during the first year and once a year thereafter. The clinician would observe and specifically ask the patient and family about postoperative language difficulties.

3. Results

As the study implied a relatively minor adjustment of a variable and personalised assessment method during a standard clinical procedure, the protocol did not require King's College Hospital Ethics Committee review.

3.1. Patients (Table 1)

The range of patients' age at the time of functional mapping was 17–45 years (Mean = 32.57, SD = 12.1). Four females and three males were studied. All patients were native English speakers. Intelligence and memory neuropsychological testing (Wechsler Adult Intelligence Scale Revised, Wechsler Memory Scale and delayed recall form of the Rey–Osterrieth figure) revealed normal intelligence quotient scores, language function, attention, and memory functions in all patients, i.e., no significant cognitive deficits were present prior to functional mapping. More specifically, no patient had major language impairments or demonstrated comprehension difficulties prior to mapping. Six patients were right-handed and one was ambidextrous. Patients 4 and 5 had a particularly early age of onset of their epilepsy, which may have been responsible for mixed dominance in patient 5 and somewhat anterior location of speech area in patient 4 (Fig. 1). Hemispheric speech dominance was

Table 1
Patient data. Abbreviations: f/u = follow up; y = years; L = left; R = right; −ve = negative; +ve = positive; TCS = tonic–clonic seizures; BA = behavioral arrest; A = automatisms with impaired awareness; SMG = supramarginal gyrus; DNET = dysembryoplastic neuroepithelial tumor; VNS = vagus nerve stimulation; MST = multiple subpial transection; FCD = focal cortical dysplasia; lat = lateral; T = temporal; F = frontal; P = parietal; O = occipital; Post = posterior; Sup = superior; AG = angular gyrus; N/A = not applicable.

Patient	1	2	3	4	5	6	7
Age	17	19	27	32	42	45	43
Sex	F	M	F	F	M	M	F
Handedness	R	Ambidextrous	R	R	R	R	R
Primary language	English	English	English	English	English	English	English
Age of epilepsy onset	8	17	19	Early childhood	4	28	12
Seizure type	A with aura & dysphasia	BA, A, and TCS	TCS and A	A	TCS and A	TCS and A	TCS and A with postictal dysphasia
MRI	+ve	+ve	+ve	+ve	+ve	−ve	+ve
Estimated epileptogenic zone	Occipital	Temporal	Temporal	SMG	Temporal	Temporal	Temporal
Implanted electrodes	L depth T O	L Subdural lateral T	L depth T	L Subdural lateral T F	L subdural T F P	L subdural T F P O	L subdural T F P O
Lateral temporal coverage	Post sup T gyrus	Post 80% of sup and mid T gyri	Post sup T gyrus	Sup T gyrus	Post half of sup and mid T gyrus + AG	Post half of sup and mid T gyrus + AG	Most lat T cortex + AG
Surgery	Cortical resection	cortical resection & MST	1. Temporal lobectomy 2. VNS	Cortical resection SMG	Neocortical resection posterior temporal	Left temporal lobectomy	No
Histopathology	Ischemia	Left temporal DNET	MTS	FCD IIB	DNET	Normal	N/A
Hemisphere dominance	Left	Left	Left	Left	Mixed L > R	Left	Left
Mapping findings in relation to epileptic lesion	Speech areas remote	Speech areas overlapping	Speech areas remote	Speech areas adjacent	Speech areas adjacent	Speech areas remote	Speech areas overlapping
Postoperative deficits	No	Yes (expected), resolved	No	No	Yes (2y receptive aphasia)	No	N/A
Seizure outcome	II	I	IV (VNS,1 year seizure free)	IB (auras)	I	III	N/A
	(1 y f/u)	(6 y f/u)	(2 y f/u)	(2.5 y f/u)	(3 y f/u)	(2 y f/u)	

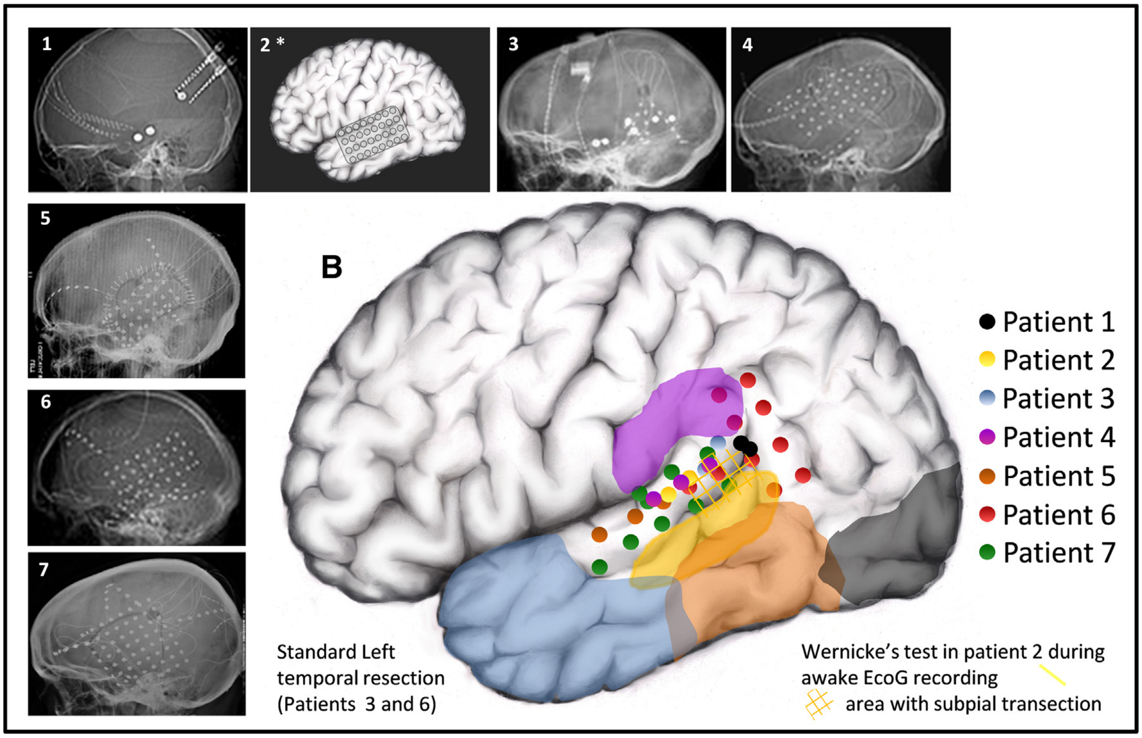

Fig. 1. Location of Wernicke's areas. X-rays showing the positions of depth and subdural electrodes (note that patient 2 has an estimated position from a drawing made during awake electrocorticography). B) Composite map of all Wernicke's areas and resections for the 7 patients (different color for each patient). Patent 7 had no surgery. Coregistration of electrode position on image was carried out manually.

confirmed by the Sodium Amobarbital Test in patients 3, 5, and 6, who were left-hemisphere dominant. The remaining patients were right-handed and therefore assumed to be left dominant. All patients had normal development and schooling. No patient had history of status epilepticus, additional neurological disorders, family history of epilepsy, or history of psychiatric disorders including periictal psychosis. Six patients were assessed with one subdural mat and several subdural strips. One patient was assessed with a combination of temporal subdural strips and depth electrodes. Fig. 1 shows the electrodes used in each patient.

3.2. Language mapping

As expected by the inclusion criteria, electrical stimulation with the SWAC test elicited language interference responses in all 7 patients. Areas showing language interference responses suggested that receptive speech areas were located around the left perisylvian area and the left posterior temporal lobe. Receptive speech areas identified in each patient are shown in Fig. 1. In six patients, the SWAC test was carried out in the telemetry ward during chronic recordings without anesthesia. In one patient, the SWAC test was performed in the operating theater at the time of surgery under local anesthesia.

3.3. Surgery and speech outcome

Among the 7 patients, 6 (85.7%) had resections (all resections were left-sided; 4 temporal, 1 supplementary motor, and 1 occipital) and 1 patient (14.3%) did not have surgery because the SWAC test revealed that the epileptic focus was intimately associated with receptive speech areas. In addition to the resection, one patient had multiple subpial transections over the speech areas. Regarding seizure control after surgery, two patients became seizure-free, one only had simple partial seizures ("auras", Engel IB); one had two seizures in one year (Engel II); one had three seizures in one year (Engel III), and one had seizures recurring one year after surgery (vagus nerve stimulator implanted). The reasons for seizure recurrence after surgery are unclear but may be because of incomplete resection or reactivation of the focus.

Among the 6 operated patients, no patient showed permanent speech deficits. Two patients (33.3%) had temporary deficits. Patient 2, who had resection and multiple subpial transections, showed mild temporary speech difficulties, which were resolved in two weeks. Patient 5, with resection close to speech areas, had some minor difficulties (expected), which were resolved. He resumed work 6 weeks after surgery, and speech completely recovered after 24 months with occasional visits to the occupational health therapist. There were no other postoperative deficits in any patient.

In summary, none of the 3 patients (patients 1, 3, and 6) with resections remote to the identified speech areas showed postoperative speech deficits. Among the 3 patients (patients 2, 4, and 5) with resections adjacent or overlapping speech areas, 2 (66.7%) showed transitory deficits (patients 2 and 5), and 1 (33.3%) showed no deficits (patient 4).

4. Discussion

4.1. The SWAC test

We describe a method to localize speech receptive areas by evaluating patients' ability to comprehend a single word. Six of the 7 patients who showed speech deficits during stimulation underwent surgery (among which, 4 had temporal resections). None of the 3 patients with resections remote to the identified speech areas showed postoperative speech deficits whereas among the three patients with resections adjacent or overlapping speech areas, two showed transitory deficits. This suggests that distance between resection and language areas identified by the SWAC test is a predictor of deficits, providing some validation for the test.

The SWAC test is simple and fast to administer, and reliably produced auditory language comprehension deficits. The method is suitable for implementation in the operating theater under local anesthesia, which appears highly relevant to the growing field of speech mapping during tumor surgery. However, the SWAC test only explores the comprehension of single words, the simplest units of speech understanding. Natural speech comprehension requires the listener to integrate groups of words that are presented in sentences [25,26]. Therefore, the SWAC test should perhaps be used as an initial test in conjunction with other tasks to identify the networks involved in more complex functions of speech understanding. The SWAC test induced comprehension deficits when stimulating areas located around the left perisylvian region and left posterior temporal regions, in regions broadly corresponding to Wernicke's area. Compared with findings from previous literature, these areas correspond with the traditional location of receptive language areas, in keeping, for instance, with the figure 2 of shown in the article of De Witte et al. [4]. The SWAC test was specifically designed to map receptive speech. Consequently, while the SWAC test might be reasonable for identifying superior temporal areas (i.e., Wernicke's area), this task may fail to identify critical naming sites, which tend to be scattered across the perisylvian region [13,27–29]. This further stresses the use of the SWAC test in conjunction with other tasks, as discussed above.

On occasions, patients did not initially understand the target word, but if they repeated the word sounds, they would then understand the meaning of the word. This suggests that language interference responses are due to a deficit in receptive language rather than an auditory deficit, further suggesting that receptive language areas and primary auditory areas are distinctly different [30]. Both areas show nevertheless very intimate cooperation, as indicated by the topographic distribution of distinct phonetic features in the superior temporal gyrus, which suggests an integrated acoustic and phonetic representation of speech in humans [31].

Modern neuroimaging research has questioned the standard views about localization and connectivity of language areas, particularly those involved in receptive speech. First, it appears that the traditional Broca's and Wernicke's areas show more profuse and wider connectivity than initially thought, including parietal and sensorimotor networks [32,33]. Second, there appears to be a much more distributed language network involved in more complex language functions such as syntactic function and multisensory speech recognition [2,34,35]. Third, the unilateral representation of receptive language areas has also been questioned [36,37]. In general, the language areas identified by electrical stimulation may be more localized than those defined by functional imaging. This may be because of two factors:

a) The tasks used during electrical stimulation tend to be simpler than those used in imaging because their time course is necessarily limited to a few seconds for safety reasons.
b) The purpose of functional mapping with functional imaging and with electrical stimulation is different. Whereas imaging tends to identify those areas "activated" by function, the objective of mapping with electrical stimulation is to identify those areas "essential" for function. Thus, imaging may identify additional areas connected or coupled to those carrying out the function. Such secondarily activated areas may not be essential for function, and their activation may be considered as an epiphenomenon of function.

In particular, our task was aimed at localizing the understanding of single words. We found that this function was lateralized, since deficits were induced by unilateral stimulation, a view also supported by the Wada test [38]. Furthermore, the areas stimulated to induce deficits in word understanding were located around the posterior aspect of the superior temporal gyrus, broadly at the origin of the dorsal and ventral tracks of speech processing [10].

4.2. Advantages and limitations

The SWAC is reliable, simple and fast to implement, and therefore suitable for the operating theater. It avoids the randomness associated with picture selection, consequently requiring less stimulation trials. There is no need for additional equipment, such as, computers or touch screens. These features make the test ideal for intraoperative mapping. When explaining the test to patients, it is very important to emphasize that the purpose is not to obtain a high score of correct responses and not to over explain the method. Otherwise, in their eagerness to describe target words correctly, patients may learn to rehearse the sounds in their head after stimulation, allowing them to understand the word when rehearsing, thus defeating the purpose of the test. This phenomenon has never been reported and may be a potential source of false negatives for the SWAC and other auditory tasks. In addition, this phenomenon suggests that stimulation can block receptive speech areas without blocking primary auditory areas.

For these reasons, it is important to stress that finding reliable deficits during stimulation does not necessarily provide evidence for validity of the test. Because of ethical reasons, it would be very difficult, if not impossible, to empirically validate a test for stimulation mapping. Promising validity stems from the absence of permanent deficits among the 4 patients who underwent temporal resections and from the fact that deficits were only seen in patients where resection was overlapping or adjacent to the identified speech areas. When resection margin is close to the identified speech areas, there may be subtle short-lived deficits even when the resection does not include the speech areas (Fig. 1, patients 2 and 5). Nevertheless, the population is too small to draw definite conclusions.

The findings show that words behave as semantic units with distinct receptive language areas. However, although the proposed single word test is reasonable for the identification of single word comprehension, this is also its limitation, as it does not test for more complex sentence understanding. The SWAC test could be used as an initial test to identify the areas where more complex additional tests can be performed in order to preserve higher language postoperative function.

The study has the limitations common to any study in which the clinical team is not blinded to the results of the test at the time of the surgical decision. The test cannot define whether the area identified as language relevant is necessary, sufficient, or both, and therefore, the results of the study cannot be generalized.

4.3. Future directions

This is a feasibility study that demonstrates that the SWAC test can be used for functional mapping. Comparison with surgical results obtained with other paradigms would be desirable. Since randomization may raise ethical issues, comparisons with results between and within centers using different paradigms might proof the best approach. The method described could easily be used for noninvasive speech mapping with transcranial magnetic stimulation, a presently growing field [39,40].

5. Conclusion

The SWAC test elicited reliable deficits in comprehension of single words in 7 out of 9 patients in this series. The findings suggest that words behave as semantic units with distinct receptive language areas. Responses helped identify lateral temporal receptive language areas. Their anatomical locations were in line with findings from previous methods. The SWAC test is similar but shorter and easier to implement than other methods, suggesting it could be used as a simple initial test to identify the receptive language areas, where more complex additional tests can be performed to preserve higher language postoperative function. Our findings suggest that stimulation can block receptive speech areas without blocking primary auditory areas.

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Appendix A. List of target words used

1. Car
2. Wheel
3. Shelves
4. Bank
5. River
6. Skirt
7. Pen
8. Hello
9. January
10. Shelves
11. Skirt
12. Book
13. Horse
14. Skirt
15. Window
16. Short
17. Wall
18. Shop
19. Shirt
20. Knife
21. Red
22. Hello
23. Shelves
24. Book
25. Door
26. Bank
27. Wall
28. Thirsty
29. Hungry
30. Sky
31. Telephone
32. Letter
33. Window
34. Spoon
35. Wall
36. Hungry
37. Skirt
38. Table
39. Letter
40. Monday
41. Hello
42. Road
43. Tall
44. Grass
45. Shirt
46. Bread
47. Grass
48. Table
49. Red
50. Floor

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