Optimizing the task selection and direct electrical stimulation during language mapping in epilepsy patients. *A critical in-depth evaluation.*

Master thesis Neuropsychology

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Abstract

To predict the risk-benefit balance of elective epilepsy surgery as accurately as possible, it is essential that the clinical protocol is systematic, reliable, and validated. In clinical practice, the procedures and task selection of language mapping have unfortunately never been standardized. It was assumed that clinicians often develop their own protocols by selecting tasks ad-hoc and based on implicit considerations. Therefore, the aim of this research was to establish a structured, systematic, hypothesis testing approach, based on a language model, in order to achieve a structured rationalized task selection procedure during language mapping. This retrospective explorative intra-individual study was an in-depth case analysis of three characteristic patients intended for elective neurosurgery to treat epilepsy. Data consisted of multiple-day, 24-hour-per-day video registrations. Direct electrical stimulation was used on cortical areas to produce a reversible lesion, simulating the effect of resection of the stimulated site. This study examined the stimulated locations, the performed tasks, the task performances and the clinician's decisions. Results showed that incomplete reports lead to an unstructured and inconsistent working method, causing electrodes and tasks to be over-stimulated and especially under-stimulated based on the 3-out-of-5 paradigm. Given the tasks performed, the clinicians focused more on auditory comprehension and spoken production than on written comprehension and production. As a result, not all the language components were examined and could not be distinguished. New tasks have been advised and included in two newly constructed flowcharts which serve as a structured rationalized hypothesis-oriented task selection during language mapping.

Keywords: epilepsy; elective surgery; language; language mapping; direct electrical stimulation; cognitive neuroscience

Introduction

Epilepsy is one of the most common neurological conditions, with a lifetime prevalence of 0.7-1.0% worldwide (Fiest et al., 2017). Moreover, the World Health Organization ranks epilepsy as the second most burdensome neurologic disorder worldwide in terms of disability-adjusted life years (Murray et al., 2012). Epilepsy is defined as a neurological condition characterized by the occurrence of two or more unprovoked seizures, where a seizure involves the misfiring of neurons and the emittance of abnormal electrical discharge in the brain. this results in muscle spasms, altered consciousness, convulsions, and changes in psychological and socioemotional functioning (Rush, 2020; Shorvon, 2009). Besides the burden due to the seizures, patients also experience burden because of the stigma and social exclusion as a result of negative attitudes of others (De Boer, Mula & Sander, 2008; Reynolds, 2000). Considering the high amount of burden in daily life, it is important to gain a better understanding of the treatment process of epilepsy patients and how this can be optimized.

As a result of the burden they experience, epilepsy patients may decide to follow a treatment program. There are various treatment options, with antiseizure medication being the most commonly used (Picot et al., 2008). Antiepileptic medications are effective in approximately 70% of the patients, but often have side effects and merely suppress seizures rather than modifying the disease course (Perucca et al., 2009; Kwan & Brodie, 2000). Therefore, in patients considered for elective epilepsy surgery, prospective success must be weighed against potential risks (Clusmann & Schramm, 2012). Elective epilepsy surgery includes a variety of operations aimed at eliminating seizures without producing a new neurological deficit (Daroff & Aminoff, 2014). Epilepsy surgery is often performed on refractory epilepsy patients or patients who suffer from unacceptable side effects (Lamberink et al., 2020; Stevelink et al., 2018). Epilepsy surgery is the most effective and often the only way to cure epilepsy in patients and can lead to improvements in cognition, behavior, and quality of life (Ryvlin et al, 2014). Nevertheless, epilepsy surgery is under-utilized due to a lack of factual information regarding epilepsy surgery and uncertainty around treatment outcomes (De Flon et al., 2010; Uijl et al., 2012; Dewar & Pieters, 2015). In addition, unlike in neurology or psychiatry, neurosurgical practice can result in non-reversible disruption of processes in the brain (Ford & Henderson, 2005). Therefore, the risk-benefit balance plays an important role in considering and eventually carrying out epilepsy surgery.

To predict the risk-benefit balance as accurately and reliably as possible, a presurgical evaluation will be performed. The goals of the presurgical neuropsychological evaluation in epilepsy surgery are to delineate eloquent areas and to determine the laterality, localization, and extent of the epileptogenic focus (Pondal-Sordo et al., 2007). To this end, electrocorticography (ECoG) is sometimes performed before cortical resection (Cross et al., 2006; Spencer et al., 2005). Direct electrical stimulation (DES) through ECoG electrodes may be performed for clinical mapping purposes, both intraoperatively and during the patients' clinical observation (Vincent et al., 2016). The use of DES is widespread, as it is easy to use, safe, and increases the precision of the surgery while minimizing permanent postoperative impairments (Sanai et al., 2008; Ilmberger et al., 2008). Clinical mapping involves several seconds of electrical stimulation to the cortical surface to determine the functional role of the cortex beneath the stimulating electrodes (Hamberger, 2007). The combination of mapping and recording by stimulation is used to best inform clinical decisions regarding reducing or eliminating seizures through resection while maintaining cortical function (Caldwell et al., 2019). If stimulation interferes with the ongoing function, e.g., stops intended movements or speech, that particular site is regarded as a functional boundary to avoid during surgery. During the presurgical evaluation, different physical and cognitive functions of the patient will be examined (Duffau, 2016).

Cognitive profiles in epilepsy are as heterogeneous as the epileptic syndromes themselves (Ryvlin et al., 2014). Of the cognitive problems seen in epilepsy, language impairments are particularly important to identify and address. Besides communication problems, language dysfunctions can contribute to academic underachievement and long-term social and psychological problems (Overvliet et al., 2010). By using DES during the presurgical evaluation, critical cortical and subcortical language areas and pathways can be identified (Hamer et al., 2012; Pereira et al., 2009). Unfortunately, linking language to specific brain areas is a complex matter because language is organized in distributed corticosubcortical networks that are sensitive to plasticity mechanisms (Hickok & Poeppel, 2007; Coello et al., 2013). Nevertheless, there are also commonly known language-related hubs such as Broca's area located in the posterior inferior frontal gyrus, Wernicke’s area in the superior temporal gyrus and the basal temporal language area in the fusiform gyrus of the dominant temporal lobe (Schäffler et al., 1996). The locations of these areas can provide useful information for language mapping.

Language tests are performed during the presurgical evaluation to create a baseline for an intraoperative test moment, to detect language disorders, to functional differentiate the language components, and to create a baseline for follow-up test moments (De Witte et al., 2016). The sensitivity of the tasks is important in concluding whether a brain region can be resected. Object naming is one of the most frequently used tasks in epilepsy surgery (Ojemann et al., 2008). It plays a central role in the presurgical evaluation of epilepsy patients because naming is a core component of language abilities and has proven to be a reliable and robust method for identifying widespread essential language sites (Ojemann et al., 2008;

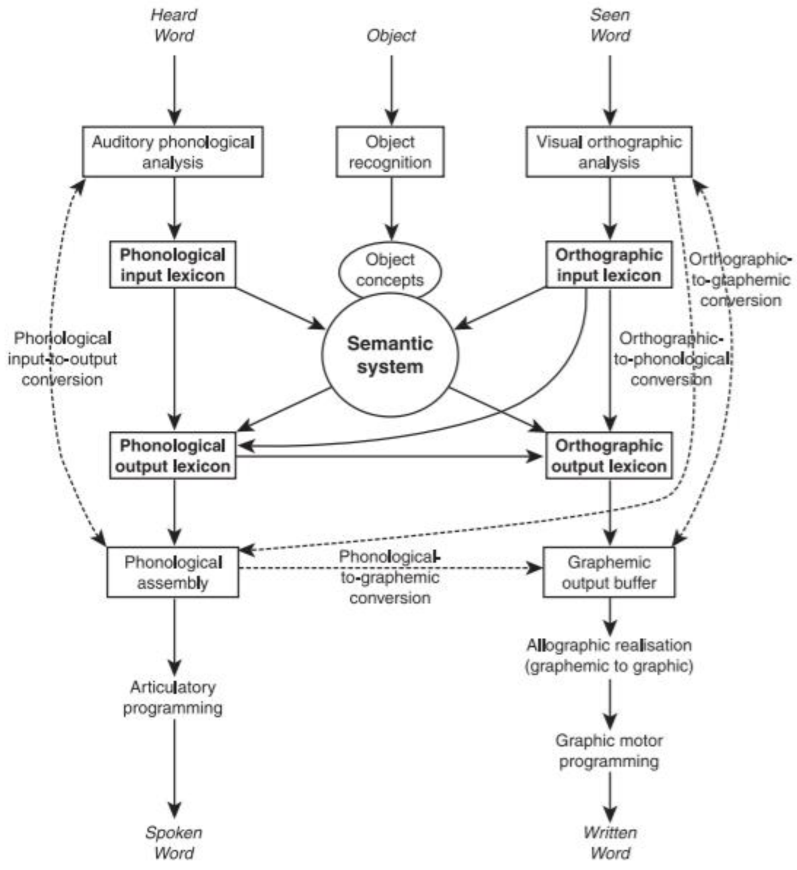
Hermann et al., 1992). Object naming involves a large fronto-temporo-parietal network (Corina et al., 2010; Llorens et al., 2016). Although the naming task has been established as a useful way of mapping language function during surgery, it does not contain all the components of language. Therefore, it is important that a clinical protocol include multiple language tasks to ensure a brain region is considered resectable without significant concern of language decline.

When multiple language components are performed during the presurgical evaluation, the selection of the language tasks is of crucial importance because of its direct effect on the clinical outcome (Hamberger et al, 2005). Even though the language functions of a certain brain area can only be deduced by disturbing it with DES, task selection has not received the attention it deserves (Hamberger, 2007). For instance, in clinical practice, the procedure of task selection has unfortunately never been protocolized. As a result, it is expected that clinicians often develop their own protocols by selecting the tasks ad-hoc and based on implicit thoughts where a structured and evidence-based approach is lacking. This way of working is not necessarily wrong, since clinicians can make many good choices based on their experience. However, new clinicians do not have this experience.

According to Rofes et al. (2019), a good understanding of a cognitive language model is essential to motivate task selection and to tailor surgical procedures, e.g., understanding which functions may be more or less relevant to be tested. Because language tasks consist of different processes, individuals may have trouble with a task for different reasons (DeLeon et al., 2007; Ulvin et al., 2017). Lesions in different brain regions can disrupt different components of language and speech, but all result in the same impairment during language tests (DeLeon et al., 2007). Therefore, a language model can help to differentiate the language components and to understand the language processes from a scientific basis. An underlying premise of a language model is that the cognitive system is composed of functions that can be selectively impaired during DES or after brain damage (Rofes et al., 2019). Figure 1 depicts a model for the comprehension and production of language with a key aspect of the shared lexical-semantic system (Whitworth et al., 2014). The lexical-semantic system plays a central role because damage or interruption of this level will impair performance in both comprehension and production (Rofes et al., 2019). This model is based on DES data and features functions for visual object and picture recognition, written and auditory word comprehension, and written and spoken word production.

Figure 1

Language-processing model, based on Whitworth, Webster and Howard (2014)



In this study, a structured, hypothesis testing approach is going to be established from the language model to achieve rationalized task selection for epilepsy surgery. This new structured, hypothesis-testing approach aims to determine the underlying cause of the impairment due to DES during language tasks. This should specify which component of the language model is temporarily impaired by assessing language components in a structured manner. It prevents information from being overlooked, which can lead to unanticipated postoperative deficits. The analysis of error types narrows down the hypothesis and helps to select the next task (Whitworth et al, 2014). By studying the language errors during DES, it is possible to determine the causes of the errors and which cognitive functions and processes are required (Mandonnet et al., 2017; Whitworth et al., 2014). This makes it possible to determine the risk-benefit balance with more certainty so that we know if the brain area in question is involved in language and if it can be removed or not.

This study fits the learning health care system, which proposes that it is essential to integrate research and practice (Faden et al., 2013). When the language of epilepsy patients can be mapped more accurately and efficiently, it will have positive consequences for the risk-benefit balance and the prognosis of epilepsy patients. To achieve this, an answer must be given to the following research question: How can a language model optimize the direct electrical stimulation of language mapping procedure in epilepsy patients?

Method

Participants

This retrospective explorative intra-individual study was an in-depth case analysis of three characteristic patients intended for elective neurosurgery to treat epilepsy. The three patients needed high-end medical care due to the refractory nature of epilepsy and the complexity of the pathology. Table 1 provides general information about the participants. The data was received from an existing database of the UMC Utrecht hospital. The data consist of multiple-day, 24-hour-per-day video registrations with ECoG at the Intensive Epilepsy Monitoring Unit (IEMU) of the UMC Utrecht. Inclusion criteria consisted of IEMU patients with extra-operative, intracranial grid recording and language functions located in the epileptogenic zone. They also had to be older than eighteen-year, had Dutch as a mother tongue, had normal vision and hearing, and had no (history of) neurological other than the related to the epilepsy, cardiovascular, psychiatric, or developmental language and/or speech disorders. All participants gave explicit permission to give their data to science. The study was approved by the ethical committee of Utrecht University. All patients already underwent a subdural EEG grid implantation. The pre-existing outcomes of the language mapping before the participants were observed for this study are mentioned in Appendix A.

Table 1

General participant information

	Participant 1	Participant 2	Participant 3
Age	37	22	45
Sex	Male	Male	Male
Handedness	Right	Ambidextrous	Right
Language dominance	Left hemisphere	Left hemisphere	Left hemisphere
Epileptogenic focus	Left frontal, left central	Left temporal, left parietal	Left temporal, left parietal, left occipital

Seizure description	Daily seizures with short speech arrest and goosebumps while fully conscious	Comprehension problems, motorically agitated, strange words and buzzes in the right ear, and cramps with a clonic right arm while fully conscious	Aphasic speech, comprehension problems, déjà-entendu feelings with words and smells different scents while fully conscious
Intracranial electrodes	64 (F58 and F59 do not register)	48 (D1-3 and D4-5 do not register)	64
Grid placement	Frontal: 8x8	High temporal: 2x8 Low temporal: 2x8 Subtemporal: 1x8 Depth: 1x8	Temporal: 4x8 Parietal: 2x8 Subtemporal front: 1x8 Subtemporal back: 1x8
Duration grid	4 Days	7 Days	7 Days
Stimulation information	500 µs, 30 Hz, and 9-10 mA for 4-5 s.	300 µs, 30 Hz and 9 mA for 3-4 s	250 µs, 30-50 Hz and 6-7 mA for 4 s
Duration stimulation	14 sessions, 4 hours and 15 minutes including 2 hours and 38 minutes language-related	16 sessions, 4 hours and 20 minutes including 3 hours and 23 minutes language-related	17 sessions, 7 hours and 50 minutes including 5 hours and 41 minutes language-related
Resection	No	Yes	Yes

Electrocorticography

Electrocorticography (ECoG) measure epileptiform activity directly from the cortex, aiming to delineate the epileptogenic tissue (van ’t Klooster et al., 2017). Direct electrical stimulation (DES) is an invasive procedure that uses evenly spaced electrodes embedded in “grids”. Subdural grid arrays are used when seizure activity cannot be located by ictal scalp recordings and when functional cortical mapping is required before surgery (Zhou et al., 2021). Grids come in standard pre-set sizes but can also be trimmed to accommodate the size and shape of the exposed cortical surface. DES has the ability to test discrete cortical areas and essentially produce a reversible lesion, presumably simulating the effect of resection of the stimulated site (Hamberger, 2007). In this study, stimulation was performed with a Micromed stimulator with biphasic block pulses.

Clinical care as usual

Before language mapping, all tests were performed without stimulation to determine the participant's baseline. Determining the baseline was important to consider whether the participant was competent enough to perform the task. If this was not the case, then disruption by stimulation was useless because the errors made by the participant were not reliable. Secondly, the baseline could determine how long it took for the examiner to provide the instruction or how long the participant took to respond to a stimulus. To prevent epileptic seizures, the stimulation may last up to five seconds (Ojemann et al., 2008). Finally, the baseline was used as a global comparison of the responses given during stimulation. All tasks were adjusted to the level of the patient, such that spontaneous errors did not occur. Patients only performed the items that they performed without mistakes during baseline testing, so an error could most likely be considered stimulation-related.

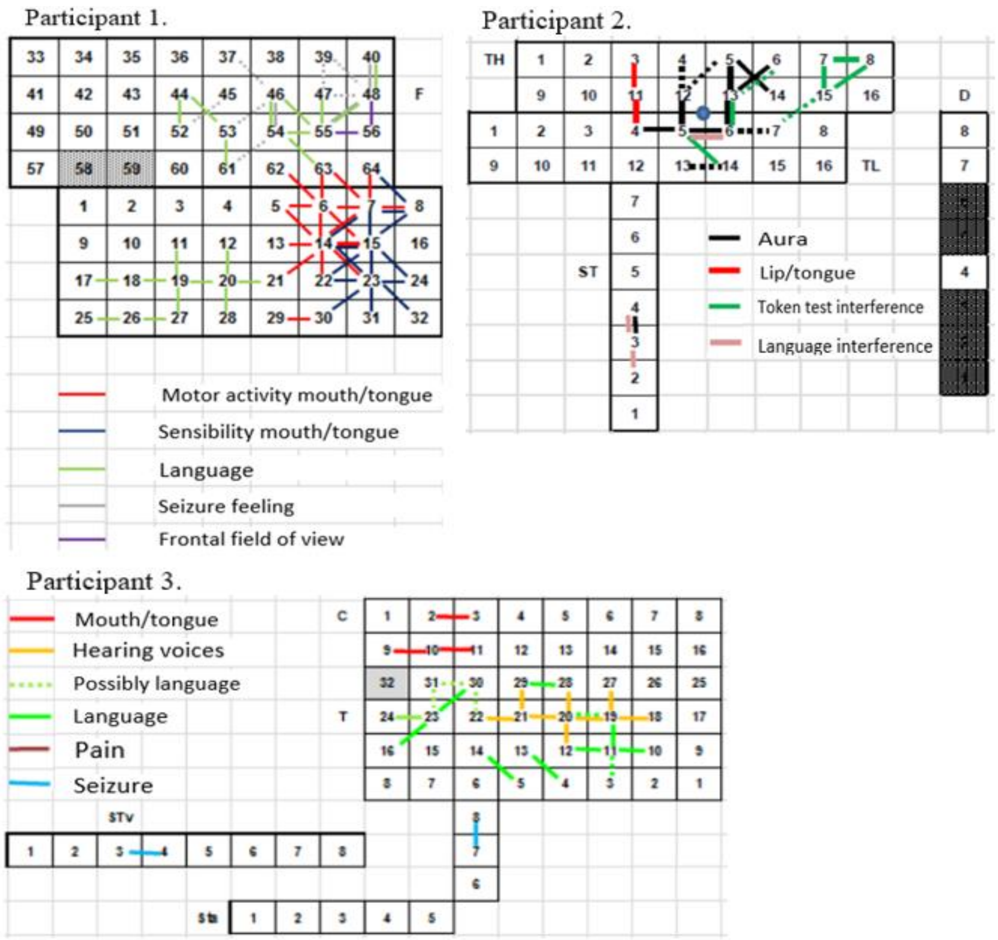
The intensity of DES through ECoG varies across individuals (Pouratian et al., 2004; Gallentine & Mikati, 2009). Therefore, a threshold value was determined in advance, per person. The goal was to use a stimulation amplitude high enough to elicit an effect on a potentially functional cortex, but low enough to avoid a clinical seizure that may confound further mapping and testing (Kuruvilla & Flink, 2003). The stimulation timing depends on the patient's speed and on the goal of the task. Once the threshold and the timing were determined, clinicians intended to begin exploratory stimulating all electrode pairs at least once during object naming. They performed object naming since this has proven to be a reliable and robust method for identifying widespread essential language sites (Ojemann et al., 2008). If an error occurs, they intended to stimulate this electrode pair multiple times to investigate if the DES-induced impairment was reliable or not.

Assessing the reliability of the responses was investigated by using the evidence-based 3-out-of-5 paradigm (De Witte et al., 2016). An impairment was considered reliable when it occurs three out of five times. The impairment does not arise by coincidence but was attributable to the DES. Per a series of five tests, three stimulations were performed without the knowledge of the patient or neuropsychologist. When the impairment during object naming was considered reliable, the stimulated brain area was related to the language components involved during object naming. After object naming, the 3-5 paradigm was used in other tasks to ensure that other language components were involved or not. Besides the affected electrode pair, the clinicians intended to stimulate the surrounded electrodes in four directions (horizontal, vertical, and diagonal).

Clinicians kept an overview of the impairments by indicating them with colored lines in a grid which corresponds to the grids on the brain. The grids of the participants are shown in Figure 2. How these grids were placed on the participants' brains is shown in Appendix B. The impairments could occur due to various reasons. A distinction can be made between three types of errors: stimulation-related errors (e.g., hearing voices or muscle spasms), unrelated errors and other errors (e.g., insufficient attention or fatigue). A correct test performance during DES is called a negative stimulation. A language-related incorrect test performance during DES is called a positive stimulation. A regular line indicates that the impairment was due to a particular reason. With a dotted line, there were usually inconsistent findings. This study will examine the colored stripes to see if the right decisions were made based on explorative stimulations and the 3-5 paradigm.

Figure 2

Participant's grids with colored lines indicating the causes of the disturbances at the electrodes during language mapping



Procedure

Because this was a retrospective study, all participants already underwent the clinical process. The language mapping procedure started after the patients recovered from the subdural EEG grid implantation. The DES-induced language errors of epilepsy patients were observed during the different tasks. A clinical neuropsychologist and clinical neurophysiologist were always present during the administration of the tasks. The patient and the clinicians were observed utilizing video material made at the time. All data from one patient was fully analyzed before another patient was examined. To ensure reliability, all video images were extensively examined a total of four times. The first time, all video footage was viewed without prior knowledge to ascertain how clinicians work and how data could be noted. After consultation and explanation from the clinicians, the video footage was thoroughly examined the second and third times. Here the specifications were noted and the responses transcribed. Finally, the video footage was reviewed one more time to check and improve everything. This study quantitatively examined which electrodes were stimulated, how often and during which task. In addition, the patients' responses were transcribed. To examine the stimulations and responses, they were ordered by electrode pair. The evaluation of the responses was based on the exploratory stimulation and the 3-5 paradigm. If stimulating was performed less or more than five times during one task, so that the 3-5 paradigm could not be used, the tasks were considered incorrect if 50% or more stimulations produced an incorrect response. Subsequently, using the language model in Figure 2, it was possible to determine which language components may be disturbed by the DES. Finally, these findings were compared with the clinicians' decisions. This was done by examining the reports and the colored stripes in Figure 2. Based on the lessons learned from this study, two flow charts were constructed for a rationalized task selection

Results

Tasks

During the pre-operational phase, various tasks were performed to be best informed about the cognitive and motor representation in the participant's brain. This study focused only on the tasks that provide insight into the language and speech ability of the participant. The performed tasks are briefly explained below.

Repeating words, non-words and sentences

Here the participant needed to repeat the heard word, sentence and non-words (“birthday”, “he wears green shoes”, “ramalast”). The response was considered incorrect when the participant did not repeat the word, sentence or non-word exactly the same or if the response was given after the stimulation. Repetition requires hearing and vocal production but not comprehension. The aim of the word repetition task was to assess word production according to the phonological input- and output route.

Object description

During object description, the participant was offered three pictures. The clinician gave a vocal description which describes one of the pictures. For example, "the kids are playing outside". After the description was given, the participant had to point to the correct picture. The aim of this task is primarily to test verbal comprehension with the semantic system.

Digit span backwards

The Digit Span Task is the most commonly used test in clinical neuropsychology to assess working memory capacity (Hilbert et al., 2014). On each trial, participants were presented with a series of spoken digits. At the end of each series, participants must recall the digits in the reverse order they appeared. By first performing the test without stimulation, it was possible to determine how many digits will be used. There must be enough digits to load the working memory (minimum of 3). On the other hand, it should not be too difficult since the error must arise from the stimulation. The length of the sequence must also be considered as it cannot be stimulated for more than 5 seconds. The test was also administered in the same way with letters instead of digits.

Token test

The Token Test is a part of the Akense Afasie Test (Bleser et al., 1991). The token test is, among others, a measure of verbal comprehension in which the subject manipulates a set of tokens in response to spoken instructions. The test evaluates higher-level comprehension deficits, as well as memory and attention deficits. The original version of this test consists of 62 items, but in this study, a 21-item short-form was used (De Renzi & Faglioni 1978). The materials consist of tokens that differ in color, shape (squares and circles) and size (large and small). The participant must follow verbal instructions which increase in complexity from simple commands (e.g. ‘Touch a square; ‘Touch the yellow circle’) to commands such as ‘Before touching the red circle, pick up the blue square’.

Object naming

In this task, a participant was shown a picture of an object and was asked to name the object (for a picture of a cow, a participant was asked to say “this is a cow” or “cow”). The pictures represented objects from several semantic categories and were taken from the well-known and often-used Snodgrass and Van der Wart's (1980) set. The response was considered incorrect when it did not match the picture or if the response was given after the stimulation. Object naming requires both comprehension and production (Kim & Thompson, 2000). Retrieving a word for production during object naming requires a combination of functions occurring at the semantic and lexical levels (Whitworth et al., 2014). During object naming, the patient's response could begin with "this is a" so that speech was already initiated while naming the object. Specific object naming sites are mainly localized in Broca’s area and the temporal cortex (Lubrano et al., 2014).

Object writing

During this task, a participant was shown a picture of an object and the participant was asked to write down the name of the object. The same pictures were used for object naming. The response was considered incorrect when it does not match the picture or if the response was given after the stimulation. Object writing requires both comprehension and production (Kim & Thompson, 2000).

Action naming

The participant was shown a picture and, on each slide, a short introduction phrase (“the man …”) was presented that must be completed with a finite verb in the third person singular depicted by black and white drawings of an action. Reading the introduction phase aloud was performed to ensure that disturbed verb naming was not due to seizures induced by the stimulation. To produce the correct response, the patient must retrieve the correct verb and integrate the verb into the sentence by inflecting it for the correct person, number, and tense. Including grammatical factors, allows for testing the patient’s language skills more thoroughly than an object naming task alone. Action naming aims to assess syntactic and semantic processing. Action naming is part of the Dutch Linguistic Intraoperative Protocol (DuLIP) (De Witte et al., 2015).

Picture story

During this task, the participant was given a paper with different pictures (cartoons) on it. The participant must create a story by using the given pictures. The response was considered incorrect when it does not match the pictures, grammatical errors were made, or if the response was given after the stimulation. The pictures are from the Taaltoets Allochtone Kinderen Bovenbouw (TAK-BB) of Verhoeven and Vermeer (1993).

Reading

During the reading task, the participant must read stories aloud. The response was considered incorrect when it does not match the word or if the response was given after the stimulation.

Three stages are involved in reading comprehension: visual orthographic analysis, the orthographic input lexicon and the semantic system. As illustrated in Figure 1. Three routes could be used to read words aloud: the semantic lexical route, the sub-lexical route (orthographic-to-phonological conversion) and the direct lexical route (Whitworth et al., 2014). Comparing the reading aloud of regular and irregular words or non-words allows the clinician to hypothesize to what extent the three reading routines could be impaired or preserved.

Spontaneous speech

There are different tasks you can choose to investigate spontaneous speech. In this study, it was important that the story, which the participant needs to tell, was also verifiable. Therefore, the participant had to tell a familiar story, such as a fairy tale or the 10 commandments from the Bible. It was important that the story was told by heart and without any effort. Reduction of spontaneous speech was found after stimulation of Broca's area, the supplementary motor area, the insula and the subcallosal fascicle (Fontaine et al., 2002; Bello et al., 2007).

Counting, days of the week, phone number

Counting, naming the days of the week and telling their phone number were performed to start an automatic process which are self-generated. They performed these commonly known task in order that the clinicians could verify the responses of the participants.

Oral Trailmaking Test

Here the participant was asked to alternate between saying 25 numbers and letters in a progressive sequential order (1, A, 2, B, 3, C, …). The oral TMT-B is not specifically a language test. Successful completion of the oral TMT-B requires cognitive set-shifting.

Corsi block span test backwards

The Corsi block-tapping test backwards is not a language test but it measures visuospatial short-term and working memory. It involves mimicking a researcher backwards as they tap a sequence of up to nine identical spatially separated blocks. The sequence starts out simple, usually using two blocks, but becomes more complex until the subject's performance suffers. By first performing the test without stimulation, it was possible to determine how many blocks will be used. The participant must touch enough blocks to load the working memory. On the other hand, it should not be too difficult, since the error must arise from the stimulation.

Sound naming

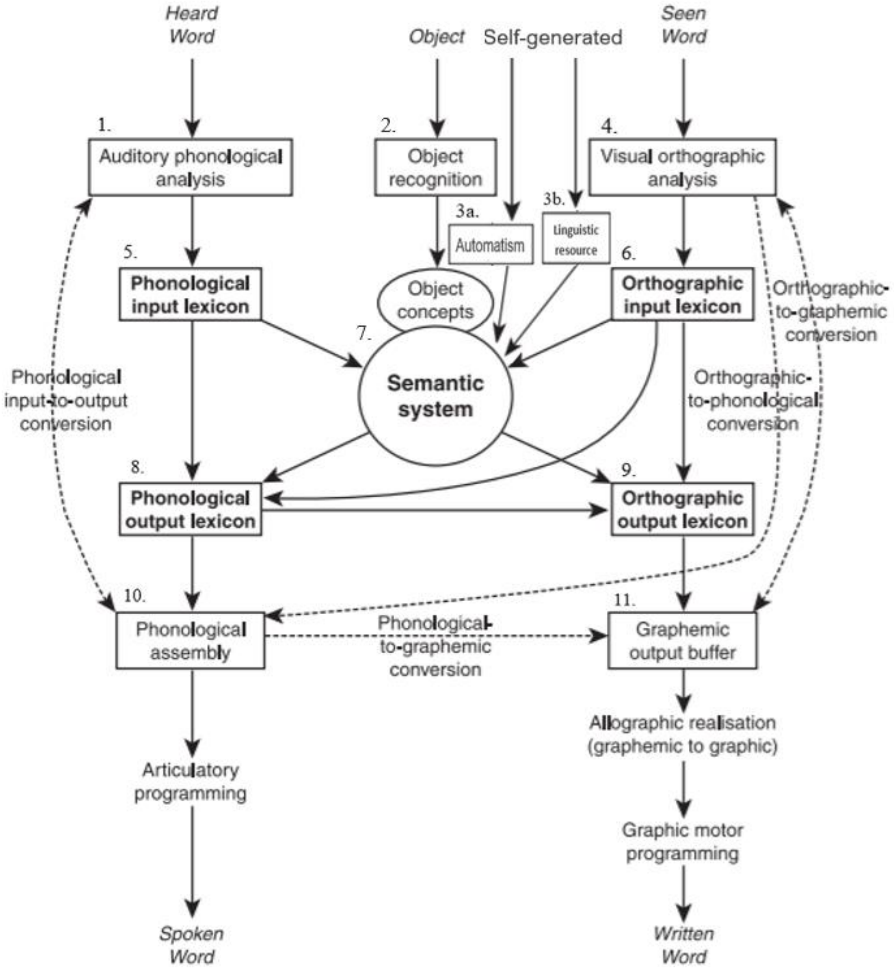
During sound naming, the participant was asked to name the sound he hears. The sounds were common everyday sounds such as the sound of a telephone, alarm clock or a church bell. Sound naming requires hearing processes, the semantic system and verbal production.

Extended language model

In Figure 1, the language model starts from three different modalities from which language can start. From a heard word, seen object and seen word. However, people may also start talking from their own concepts or thoughts. This was also the reason why spontaneous speech tasks were performed on the participants. Spontaneous speech is the most common way in contemporary life and therefore an important concept of this language model. For this reason, an additional modality was added to the language model in Figure 1. This new modality was called “self-generated”, see Figure 3. Spontaneous speech may occur automatically where the syntactic, morphological and phonological elements are not newly or individually generated (Code, 2005). In addition, linguistic resources are often needed to produce normal language. Therefore, “Automatism” and “linguistic resources” were added to Figure 3. In addition, the different components of the language model are numbered.

Figure 3

Extended language-processing model, based on Whitworth, Webster and Howard (2014)



Evaluation of the tasks performed

In Table 2, the language tasks were categorized into the begin modalities of the language model of Figure. The tasks contain a series of numbers representing the components of the language model which are related to the language task. By dissociating the different components of the language model, it was possible to investigate whether language was involved in the particular brain region and the cause of the DES-induced language error during language tasks. Furthermore, Table 2 provides an overview of the tasks performed by the participants. It also indicates whether there was a positive stimulation during the task. When only a few electrodes were tested, this is indicated in the table. The baseline was considered incorrect if the task could not be performed correctly even without stimulation

Table 2

The tasks performed by the participants along with the associated language components

Category	Task	Language components	Participant 1	Participant 2	Participant 3
Heard word	Repeating words	1,10 or 1,5,8,10 or 1,5,7,8,10	✓ 3 elec	✓	✓
	Repeating non-words	1,10		X 1 elec	✓ 4 elec
	Repeating sentences	1,10 or 1,5,8,10 or 1,5,7,8,10 + syntax		X 1 elec	
	Object description	1,5,7		✓	
	Digit span backwards	1,10 or 1,5,8,10 or 1,5,7,8,10	X 1 elec, Baseline incorrect	X 5 elec	X Baseline incorrect
	Token Test	1,5,7		✓	X 3 elec
Object	Object naming	2,7,8,10	X	X	X
	Object writing	2,7,9,11	✓ 1 elec		

	Action naming	2,7,8,10 + syntax	X 2 elec		
	Picture story	2,3ab,7,8,10 + syntax	X 3 elec		
Seen word	Reading	4,6,7,8,10 or 4,6,8,10 or 4,10	✓	X	
Self-generated	Spontaneous speech	3ab,7,8,10 + syntax		X	X
	Counting	3a,7,8,10	✓		
	Days of the week	3a,7,8,10	✓ 2 elec	X	
	Phone number	3a,7,8,10	✓ 1 elec		
	Oral TMT-B	3ab,7,8,10	X 2 elec, Baseline incorrect		
Others	Corsi block tapping			✓ 4 elec	
	Sound naming	7,8,10		✓ 3 elec	

Note. X = Positive stimulation present, ✓ = Negative stimulation only, Nothing = Task not performed, 1 elec = Task performed on only 1 electrode pair, Baseline incorrect = Incorrect task performance without stimulation

Given the tasks performed, the clinicians focused more on auditory comprehension and spoken production than on written comprehension and production. Furthermore, according to Table 2, tasks could involve different language components based on how the tasks were performed. In Figure 2, the dashed lines are the non-semantic routes which contribute to different language processes. Therefore, repeating words, repeating sentences, digit span backwards test and reading had different options in terms of the affected language components. Specifically focusing on the reading task, participants only read a story where comprehension was not tested. When testing reading, it was important to consider both reading comprehension and reading aloud. Therefore, it is recommended to improve the reading task into a reading picture out loud task. This task consists of two parts, reading a word aloud and pointing to the corresponding picture. While reading aloud, different language components could be involved because it was unclear whether the semantic system was involved, or the pronunciation may be impaired. While pointing to the correct picture, the word has been read correctly, and the semantic system is involved. Finally, both reading aloud and pointing could be performed correctly, to ensure the semantic system is involved.

Additionally, the results showed that not all the language components in Figure 3 were examined. As a result, the language components could not be properly distinguished. Therefore, in Table 3, new tasks are recommended as they are more suitable for dissociating the language components of the language model. The heard word picture out test and the semantic picture out test are recommended since spoken production and written production are the only language-related forms of production. These tasks will dissociate the semantic system and the spoken or written production more easily. During the heard word picture out test, the participant sees three different pictures and hears a word in which the correct picture must be pointed out. During the semantic picture out test, the participant sees three different pictures and based on the semantic information they had to point out the picture that does not fit between them. Furthermore, the origin of written words comes from three main modalities, i.e., either copying a text, spontaneous production, or writing from dictation. To include every modality, it is advisable to perform writing from dictation. Here, participants must write down a heard word or sentence. Roux et al. (2014) results showed that comprehension of the dictated sentences involved lexico-semantic retrieval and phonological processing. Writing from dictation includes a new route of the language model, which allows other language components to be tested simultaneously.

Table 3

New recommended tasks

Category	Task	Language components
Heard word	Writing from dictation	1,5,7,9,11
	Heard word picture out test	1,5,7
Object	Semantic picture out test	2,7
Seen word	Reading picture out loud test	2,4,6,7,8,10
	(Reading)	(4,(6,7,8,),10)
	(Picture pointing)	(2,4,6,7)

Case evaluation

During language mapping, many electrodes were stimulated. To maintain an overview, only those electrodes that provide sufficient information based on the language model in Figure 3 were included in this study. Therefore, only the electrode pairs that were stimulated more than six times in total during at least two different tasks are used in Table 4. Table 4 lists the tasks administered to each electrode pair, if the task is considered impaired, and which language components of Figure 3 were impaired. It indicates whether this was consistent with the clinicians' decision based on Figure 2.

Table 4.1

The test performances, impaired language components and clinical decision of participant 1 on different electrodes

Electrodes	Test performance correct	Test performance incorrect	Impaired language component	Consistent decision?	Clarification
F54-55	Counting, Days of the week, Repeating words	Object naming, Action naming,	2, syntax	Yes	
F18-19	Counting	Object naming	2	Yes	
F40-48	Counting, Mobile number	Object naming	2, syntax	Yes	
F47-55	Counting, Object writing, Repeating words	Object naming, Picture story	2, syntax	Yes	
F54-46	Counting	Object naming	2	Yes	
F61-62	Picture story, Repeating words	Object naming		Yes	
F44-52	Counting	Object naming	2	Yes	
F61-54	Repeating words	Object naming, Picture story	2,3a,(7,8), syntax	No*	Dotted line “feeling” instead of language

* The decision of the clinicians was understandable, as test performance could also be disturbed due to the effect of the stimulation. For example, due to hearing voices, muscle spasms or aura interferences.

Table 4.2

The test performances, impaired language components and clinical decision of participant 2 on different electrodes

Electrode	Test performance correct	Test performance incorrect	Impaired language component	Consistent decision?	Clarification
TH16-8	Reading, Token test, Digit backwards, Object naming, Object description			Yes	
TL13-TL6	Object naming, Spontaneous speech, Reading, Days of the week, Token test			Yes	
TL6-5	Token test, Object description	Object naming, Reading, Days of the week, Spontaneous speech	2,3a,4,(6),8,10	Yes	
TH15-8	Spontaneous speech, Corsi test, Object description	Token test, Digit backwards	Verbal comprehension, Linguistic working memory	Yes	

TH7-15	Object naming, Reading, Token test, Days of the week, Digit backwards, Corsi test, Object description			No	Token interference instead of nothing
TH7-8	Object naming, Digit backwards	Reading, Token test,	4,5,(6), verbal comprehension	No	Nothing instead of language
TH15-16	Reading, Object naming, Digit backwards, Corsi test	Token test	5, verbal comprehension	No	Nothing instead of language and token interference
TL14-5	Spontaneous speech, Token test	Object naming	2	No	Token interference instead of language
TL13-5	Spontaneous speech, Object description	Object naming, Reading, Token test	2,4,(6), verbal comprehension	No	Nothing instead of language and token interference
TL6-TH13	Object description, Token test, Repeating non-words	Object naming, Repeating words, Repeating sentence,	2,8,10, syntax	No	Token interference instead of language

Table 4.3

The test performances, impaired language components and clinical decision of participant 3 on different electrodes

Electrode	Test performance correct	Test performance incorrect	Impaired language component	Consistent decision?	Clarification
T23-22	Object naming, Spontaneous speech, Repeating words, Repeating non-words			Yes	
T11-12	Digit backwards	Object naming, Token test	2,5,7,8, verbal comprehension	Yes	
T6-7	Object naming, Spontaneous speech, Token test, Repeating words			Yes	
T23-32	Object naming, Digit backwards, Repeating words			Yes	
T21-22	Spontaneous speech, Token test	Object naming	2	No*	Voices instead of language
T14-15	Spontaneous speech	Object naming	2	No	Nothing instead of language
T23-24	Object naming, Spontaneous speech, Repeating words, Digit backwards,			No	Language instead of nothing

T23-16	Object naming, Repeating words, Repeating non-words		No	Language instead of nothing

* The decision of the clinicians was understandable, as test performance could also be disturbed due to the effect of the stimulation. For example, due to hearing voices, muscle spasms or aura interferences.

Lessons learned:

Lessons were learned from the literature, the language model, and the three participants. Clinicians intend to start exploratory stimulating all electrodes with object naming to investigate whether language may be involved in the stimulated brain region. However, this study showed that this was not consistently performed. Several electrodes were never stimulated during object naming (e.g., participant 2 TH15-8) and some only after other tasks were performed (e.g., participant 2 TH16-8 and TH15-16). In addition, the electrode should always be re-stimulated if an error occurs during the first stimulation. This is, in fact, the purpose of exploratory stimulation. Unfortunately, this was often not correctly performed since electrodes were stimulated only once regardless of a positive stimulation. As a result, controversial conclusions and decisions were made which are not verifiable.

In addition to exploratory stimulation, the 3-5 paradigm was not consistently performed causing electrodes to be over-stimulated and especially under-stimulated. Electrode pairs were often stimulated only a few times, which means that no conclusion could be formed based on the 3-5 paradigm. For example, if an electrode pair was stimulated a total of four times, with two negative and two positive stimulations. According to the 3-5 paradigm, it should be stimulated one more time to give a decisive decision whether language was involved or not. Unfortunately, this was rarely performed. On the other hand, some electrode pairs were also stimulated too often. For example, with participant 3, electrode T23-24 was stimulated twenty-eight times during object naming. This was done to determine with certainty whether a brain region was involved in language or not. However, it appears that similar situations were handled differently and led to different conclusions. Based on the data and the clinicians' reporting, it was unclear when a positive stimulation was considered reliable.

Besides the quantity of stimulation, some test performances were also misinterpreted. This is shown in Table 4. For example, with participant 2, it was concluded that only a token test interference occurs at TL14-5 while there was no error at all during the token task. The token task was also only tested once. In addition, during object naming, six out of seven test performances were incorrect. Based on the 3-5 paradigm and the language model in Figure 3 we concluded that there was language interference instead of token test interference. Thus, this conclusion was different from the clinicians' conclusion. Consequently, from this example, it was concluded that some electrodes were not stimulated enough but also incorrect conclusions based on the test performances were present. However, this is based on the available data from this study where clinicians have more information and knowledge about the situation. Lastly, in Figure 2, there were dotted and normal lines, and it is still unclear how these were distinguished by the clinicians. There seems to be no systematic and consistency in reporting this either.

Based on the tasks performed, many language components could be examined during language mapping. However, many different language components were under-stimulated because some tasks were hardly used and often on a few electrodes. For example, written production was only performed on one electrode pair with one participant. This also indicates that many tasks, which were also performed more frequently, test verbal production. It is advisable to use more different tasks so that multiple language components could be examined. This could lead to better and more reliable conclusions about whether the brain area was involved with language or not.

Many tasks in this study were evidence-based and provide sufficient information. However, it is advisable to perform new tasks which allow dissociating of language components easily. In addition, by improving the reading task, it can be concluded with certainty which language components were involved while performing the task. The tasks recommended were explained earlier and were shown in Table 3.

Additionally, this research showed that simpler tasks were performed first and when the response was incorrect, they performed a comparable complex task as well. For example, first repeating words and later repeating sentences. It is advisable to start with a more complex task. With a negative stimulation, it is not necessary to perform the simpler tasks. With a positive stimulation, a simpler task can specify which language components might be disrupted. For example, first repeating words and after that repeating non-words can provide clarification about language components 1 and 10.

Finally, DES-induced impairment does not necessarily arise from language errors. In this study, participant 2 suffered from buzzes in the right ear, which made it impossible for him to perform tasks correctly. If the participant had not mentioned this, wrong conclusions could be drawn and could lead to major consequences. Therefore, it was important to ask questions to the participant when a task was performed incorrectly. For example, it was helpful to know if the feeling was comparable to a seizure and if the participant was aware of the error. These questions provide more clarification and information regarding the cause of the DES-induced impairment. Clinicians already regularly ask these types of questions to the participant, but this could certainly be done more frequently. The questions and responses should also be reported.

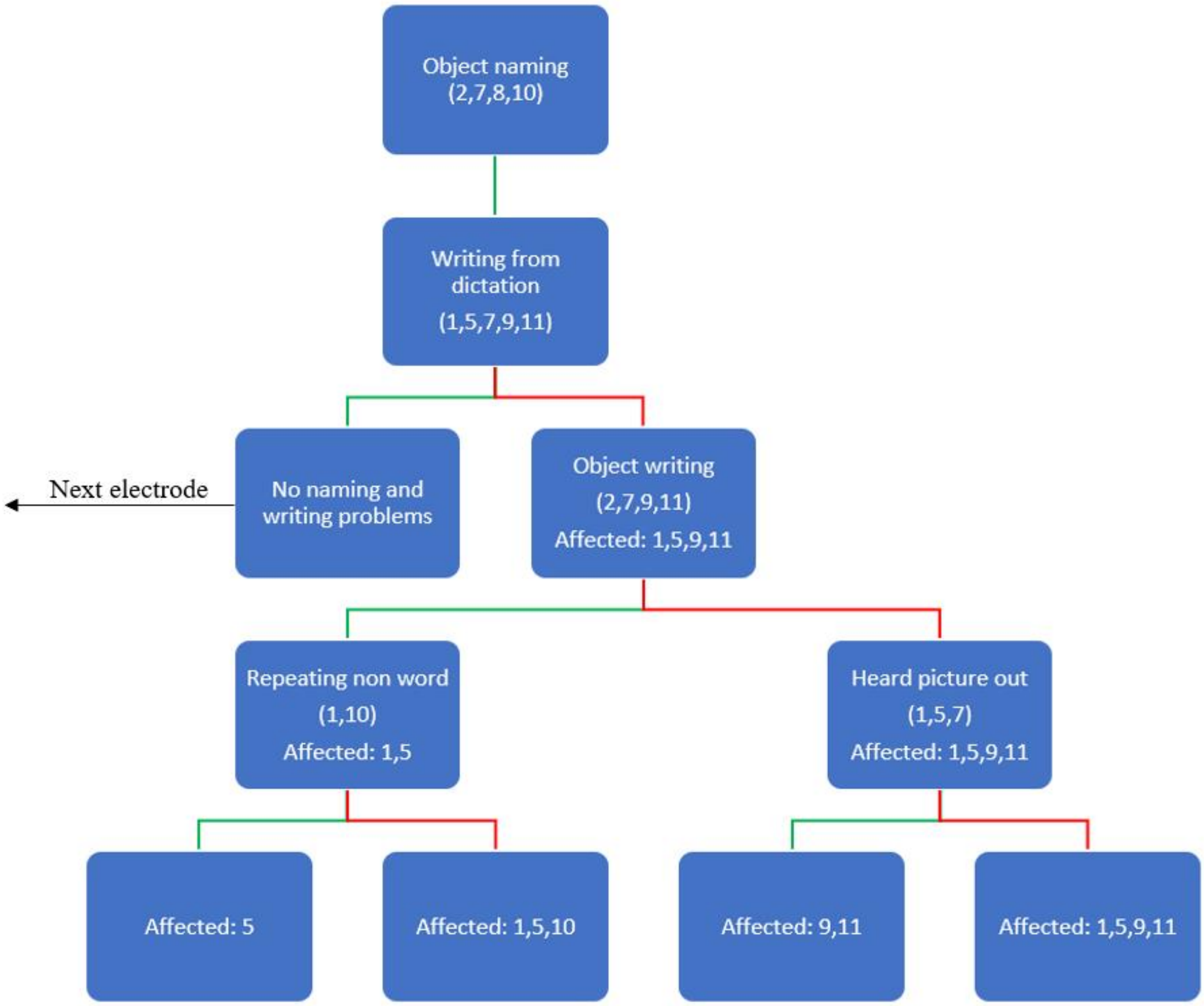
Flowchart

Based on the lessons learned from this study, a flowchart could be formed to indicate which tasks are advisable to perform in order to dissociate the language components of Figure 3. Of course, every situation and every patient is different, yet the flowchart can serve as a guide in task selecting during language mapping. A structured, hypothesis-testing approach based on the language model will result in rationalized task selection for epilepsy surgery. The goal was to exclude the language components that were not involved with language in a specific brain region, in order to predict the risk-benefit balance as accurately and reliably as possible.

Two flowcharts were formed based on the 3-5 paradigm during object naming. It is essential to take into account that the next task only can be performed following the correct use of the 3-5 paradigm. When, based on the 3-5 paradigm, the language components of a task are not involved in language, you should follow the green line. When, based on the 3-5 paradigm, the language components of a task could be involved in language, you should follow the red line. Figure 4 starts with a green line after object naming and examines whether other language components can be disturbed due to the DES. It is important here to examine whether other language components are involved. Since verbal production was not impaired, the flowchart focuses on written production. Figure 5 starts with a red line after object naming and examines which language components are also involved. After the flowchart in Figure 5, the flowchart in Figure 4 can always be used to examine the other language components. In Figure 5, object naming was impaired showing that the brain region was involved in language. However, further testing may be useful to determine exactly which components are impaired. In this way, the clinicians can determine whether the consequences of resection may be minimal and perhaps possible to rehabilitate.

Figure 4

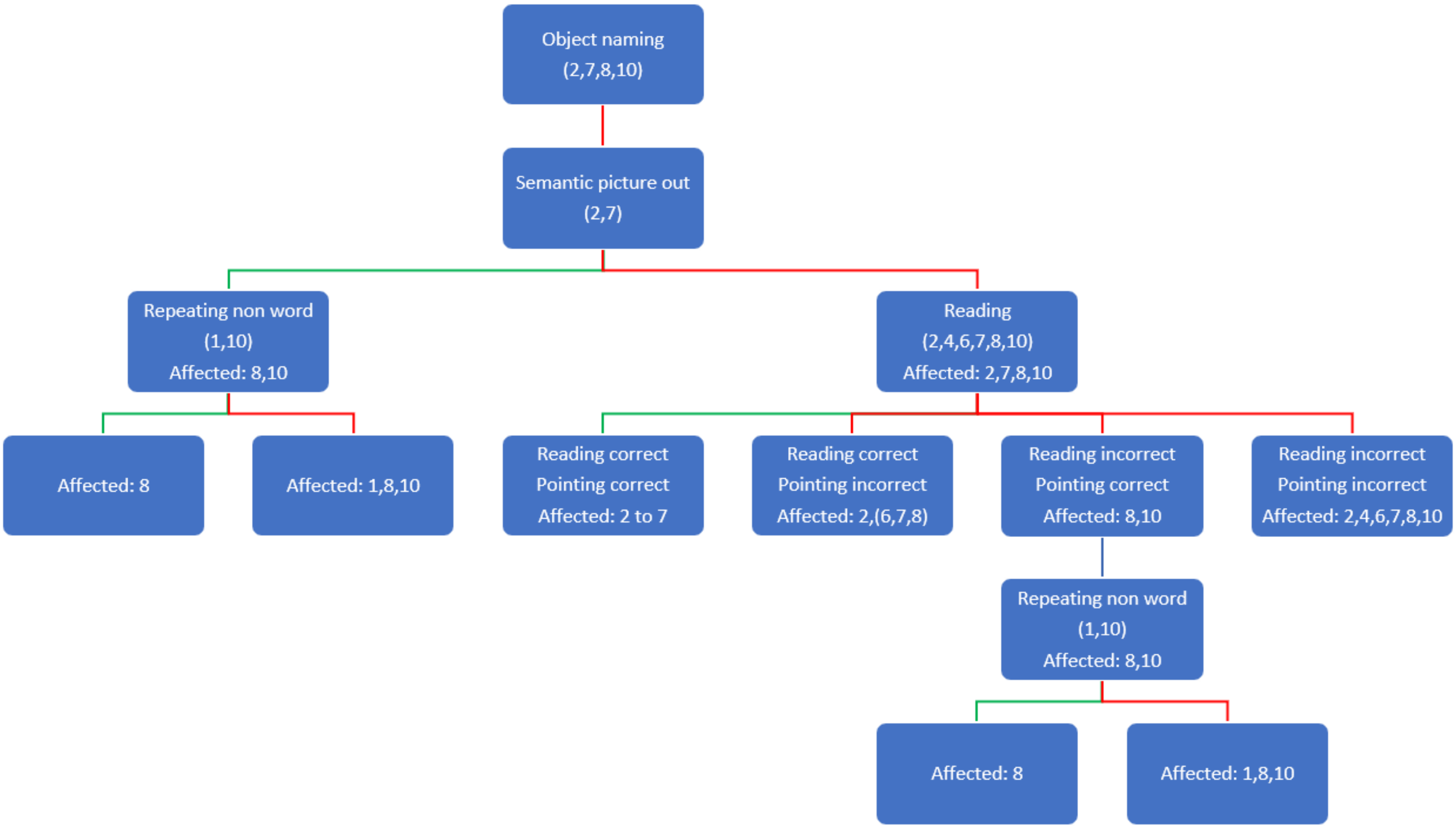
Flowchart for task selection when the test performance during object naming is considered correct



Note. The numbers refer to the numbers in Figure 3. The numbers in parentheses indicate the language components involved during the task. The affected numbers indicate which language components are potentially disrupted by the stimulation of the brain.

Figure 5

Flowchart for task selection when the test performance during object naming is considered incorrect



Note. The numbers refer to the numbers in Figure 3. The numbers in parentheses indicate the language components involved during the task. The affected numbers indicate which language components are potentially disrupted by the stimulation of the brain.

Discussion

In this retrospective intra-individual study, we conducted an in-depth case analysis of three characteristic patients coming from elective neurosurgery to treat epilepsy in order to optimize the language mapping procedure. The study revealed that it was difficult to follow and thereby understand the decisions made by clinicians. Many decisions were based on implicit thoughts and previous experiences where not all actions, thoughts, and outcomes could be traced from the information given. Incomplete reports led to an unstructured and inconsistent working method, causing insufficient argumentation why electrodes and tasks were over-stimulated and especially under-stimulated. The study showed that clinicians occasionally selected tasks ad-hoc and based on implicit thoughts where a structured, systematic and evidence-based approach was lacking. Implicit thinking can lead to ad hoc decisions, making it difficult to retrace these decisions and to pass on the knowledge to successors. The lessons learned, and the recommendations are further explained below.

The literature, the language model and the three participants showed that the direct electrical stimulation of language mapping in epilepsy patients could be optimized in several aspects. Since this study was based on clinicians' reports and video footage, this was an important component of the study. However, it appears that the clinicians' report was often incomplete, making it impossible to ascertain particular decisions. First, despite the use of multiple cameras from different angles, not all the important information was filmed. For example, there was no camera focused on the stimuli offered to the participant. As a result, it was sometimes unclear when the participant was offered the stimuli and whether the patient performed the test correct or incorrect. When analyzing the video footage, the stimuli were present and therefore did not cause any problems or misconceptions. Nevertheless, it took a lot of unnecessary time. Secondly, some discussions among clinicians took place off-camera. These important conversations were also not documented in the reports. Besides the incomplete video footage, there was no record of how often an electrode was stimulated during a task. In a short period of time, a huge number of electrodes were stimulated during different tasks. It was therefore conceivable that the clinicians were not able to keep track of this and therefore under- and overstimulated the electrodes. Lastly, in Figure 2, it was unclear how dotted lines and normal lines were distinguished. As a result of the incomplete report, while analyzing the video footage, it was unclear why they made certain decisions and deviated from standard operating procedures such as exploratory stimulation and the 3-5 paradigm. For follow-up studies, it is recommended that the stimuli offered to the participants be specifically filmed. In this way, it is clear to the researcher what the stimulus is, when it is offered, and whether the response is appropriate to the stimulus. Furthermore, a complete overview of clinicians' decisions and actions will promote a structured, consistent and reliable working approach that prevents electrodes from being under-stimulated and from making the wrong decisions. This also allows for more lessons to be learned from the experiences of the cases in retrospect.

A consequence of incomplete reporting was the inconsistent working method. For instance, during exploratory stimulation, object naming was not performed at all electrodes (at first). In addition, not all electrodes were re-stimulated in case there was a positive stimulation. As indicated above, this may be due to an incomplete overview of the stimulations. However, the location of the epileptogenic brain region was not considered in this study and may affect the number of stimulations. The effectiveness of epilepsy surgery depends on the underlying pathology, the epilepsy type, and the accurate localization of the epileptogenic brain region (Ryvlin et al., 2014). Therefore, it was conceivable that clinicians, based on their knowledge, experience and previous stimulations on the patient, might deliberately stimulate electrodes less often or not at all. As mentioned before, there are commonly known language-related hubs such as Broca's area, Wernicke’s area and the BTLA (Schäffler et al., 1996). Brain regions can be related to specific tasks and provide additional information. For example, the middle temporal gyrus and some of its subcortical pathways have been reported as relevant for reading, object naming, and word repetition (Sarubbo et al., 2015). The involved cortical and subcortical areas may have an effect on the number of stimulations and the task selection in combination with the place of the electrodes. For example, if the area of an electrode was not involved in the epileptogenic zone, then it was not necessary to examine this because removing the area will not reduce seizures. Therefore, the location of the epileptogenic zone, the functions of brain regions, and the experience of clinicians can provide additional information which ensures them to deviate from standard operating procedures such as exploratory stimulation and the 3-5 paradigm. To map the functional boundary for possible surgery as good as possible, it is particularly important to stimulate around the epileptogenic zone. From the 3-5 paradigm, positive and negative stimulations can provide clarification.

Although the above statements should be taken into account, it is important to mention that these examples are suggestions because, based on the information given, we cannot explain why clinicians made certain decisions. Moreover, it also entails risks when decisions were made based on the epileptogenic zone. According to Ryvlin et al. (2014), it is difficult to conclude where the epileptogenic zone exactly is since the epileptogenic zone cannot be defined solely by the areas of onset because of the restricted temporal or spatial resolution of available methods. Further, in three out of the four cases of the study by De Witte et al. (2015), intraoperative results did not correlate with preoperative fMRI results. The absence of a strong correlation between fMRI and DES results highlights the importance of intraoperative stimulation and testing. Furthermore, with epileptic seizures, it is important to consider not only the origin of epileptic activity but also the propagation of abnormal dischargers. Spreading epileptiform activity can disrupt cortical association areas (Mula et al., 2009). Besides the epileptogenic zone, linking language to specific brain areas also contains limitations. Linking this is a complex matter because language is organized in distributed cortico-subcortical networks that are sensitive to plasticity mechanisms (Hickok & Poeppel, 2007; Coello et al., 2013). Furthermore, there is a higher percentage of epilepsy patients with atypical language representation (Möddel et al., 2009). As a result, it is unreliable to compare the brain and the associated functions of epileptic patients to “normal brains”. In summary, although the epileptogenic zone can provide useful information, it was not a reliable stand-alone way to draw conclusions about whether a brain region was involved with language.

Therefore, it is advisable to always use the structured evidence-based 3-5 paradigm that enables to determine the risk-benefit balance in a reliable and safe way.

Thus, the atypical language representation of epilepsy patients results in an unreliable comparison of the functional localization of epileptic patients and “normal brains”. However, the functional differentiation of language is the same in people with or without epilepsy. Therefore, this study focused on the functional differentiation of language and the language model from Figure 3 is an adequate model to use. Nevertheless, it was useful to include the differences in functional localization in the study since the atypical language representation of epilepsy patients leads to unfavorable language abilities (Goldmann & Golby, 2005). Because epilepsy patients are more likely to make errors during language tasks, it was also more difficult to ascertain the reliability of a positive stimulation. It was more difficult to distinguish a positive stimulation/language related-error from a negative stimulation or a stimulated-related error. To remain as sensitive as possible, it is important to continually check the baseline. The baseline changes constantly due to the patient's attention, fatigue, and concentration. After all, a lot was asked of the patients during language mapping. To ensure the validity, it is important to constantly check whether the error that occurs was attributable to the stimulation or to something else.

The results from this in-depth analysis also made us realize that the language model of Figure 1 does not fully represent all the language aspects. For this reason, the spontaneous speech was already added to the language model. However, besides automatism and linguistic resources, the spontaneous speech also consists of other aspects such as context, language preference, and language capabilities (Le, Licata & Provost, 2018). Besides spontaneous speech, the syntax was not taken into account, while syntactic capabilities are important for language during daily life (Jeong et al., 2007). When certain language components are not included in a language model, it can lead to under-testing of these components in practice. However, it is important to mention that language is a complex adaptive system, making it difficult to develop an all-encompassing language model. Therefore, many language models focus on specific components of language, e.g., Levelt's model of language production (1999) and the neurocognitive model of language comprehension of Friederici (2002). Although the language model in this study does not highlight all language components, it contains sufficient information to determine the risk-benefit balance of elective epilepsy surgery. Follow-up studies can take syntax and spontaneous speech into account by using separate evidence-based language models.

In this study, it appeared that the clinicians used object naming for exploratory stimulation in order to determine whether language was involved or not. This was in line with other studies where object naming (Ojemann et al., 2008), sometimes combined with counting (Bertani et al., 2009, Duffau, 2007), was commonly used as a language paradigm. However, this approach does not cover the integral variety of expressive and receptive language functions necessary for adequate communication (De Witte et al., 2016). This was in line with the language model of Whitworth et al. (2014). After a negative stimulation during object naming, language-related errors can still occur in other tasks by the disruption of other language components. During language mapping, it is important to determine the risk-benefit balance as accurate as possible to ensure that language ability remains adequate during daily life. However, this process can take several days and is also considered a very exhausting and heckling period for the patient. Therefore, retrospective follow-up studies could examine whether the test performance of object naming can function as a stand-alone paradigm. In case of uncertainties, additional tasks can still be performed. If it turns out that this method provides the same result as when multiple language components are examined, then it was unnecessary to use additional tasks. Language mapping will be much faster and less intensive with this method.

As indicated in the introduction, studies mention that the analysis of error types during DES helps to narrow down the hypothesis, select the next task, determine the causes of the errors and which cognitive functions and processes are required (Mandonnet et al., 2017; Whitworth et al., 2014). For example, in the case of a semantic paraphrase, you expect it to occur because of an error in the semantic system. However, in this study, the type of error did not directly reflect the cause of the impairment. For example, participant 1 and participant 3 had multiple semantic paraphrases during object naming, but after analyzing all responses from the tasks, it appeared that the semantic system was not affected by the stimulation. It is possible that this happens because another part of the semantic system was affected. Research by Caramazza et al. (2000) also showed that naming errors that are classified as semantic paraphasia can result either from damage to modality-specific lexical nodes or from damage to the semantic system. These results showed that it was more important to know during which task an error occurs than what exactly the error type is. It is therefore desirable that tasks are sensitive enough whereby the disturbances in the brain, caused by the stimulation, are also reflected in the responses of the patients.

Lastly, all the lessons learned from this study results in structured flowcharts for a rationalized hypothesis-oriented task selection during language mapping. The flowcharts act as a guide and provide support if clinicians are unsure about the next task selection. Despite the fact that spontaneous speech is the most natural form of speech in daily life and therefore important during language mapping, no spontaneous speech tasks were implemented in the flowcharts. This was because, as mentioned earlier, it is advisable to examine spontaneous speech from a stand-alone language model since it is a very complex process due to the many variables. Nevertheless, it is advisable to perform spontaneous speech tasks when there was uncertainty about whether an area was involved in language or not. It is important to include spontaneous speech during language mapping because spontaneous speech allows the integration of all language modalities (semantics, phonology, prosody, syntax), but also other cognitive functions (e.g., working memory, attention) (Cummings, 2016). During spontaneous speech tasks, it should be taken into account that participants can compensate for language problems because of strategic language behavior. Follow-up studies may focus on a stand-alone language model of spontaneous speech in order to implement spontaneous speech into the current flowcharts of this study.

Conclusion

This critical in-depth analysis showed that a complete overview of clinicians' decisions and actions promotes a structured, consistent and reliable working approach that prevents deviating from standard operating procedures, electrodes from being under-stimulated and from making the wrong decisions during language mapping. The use of a cognitive language model facilitated the understanding of which language components were assessed with each task and how to best combine language tasks to tailor surgeries to the risk-benefit balance of each patient. This research led to several recommendations, including two constructed flowcharts serving as a rationalized hypothesis-oriented task selection during language mapping.

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Appendix A

The summarized pre-existing reports of the participants' language mapping

Participant 1:

This is the first implantation. During this language mapping, the classical Broca area is found with speech arrest and not being able to pronounce words without a motor block. A second language area is found on the gyrus frontalis medius with speech arrest and not being able to come up with words during naming tasks and storytelling. The participant experiences this differently from the disorder during stimulation in Broca. After stimulation, it is concluded that there is no good sampling of the epileptogenic zone and that it may be located in-depth in a sulcus of the posterior gyrus frontalis medius and/or superior. There is an accessory language area in the posterior gyrus frontalis medius that severely limits resection possibilities. Therefore, no surgical strategy can be devised with the present findings.

Participant 2:

This was the second implantation attempt since seizures were still present after the frist resection. During this language mapping, language interference was detected posterior to the lesion, probably interfering with his hearing. Furthermore, there is interference in a small area directly under the lesion and subtemporo-occipital. The idea is that the true Wernicke area has not been found and is located in a place where there has been no sampling, probably lower in the gyrus temporalis medius. Everything points toward a focal cortical dysplasia. A surgical strategy is devised. The proposal is to do a lesionectomy in the gyrus temporalis superior around the depth electrode. It is uncertain whether this will bring all epilepsy to a halt, as there is a second active circuit formed by subtemporo-occipital and parietal gyrus supramarginalis.

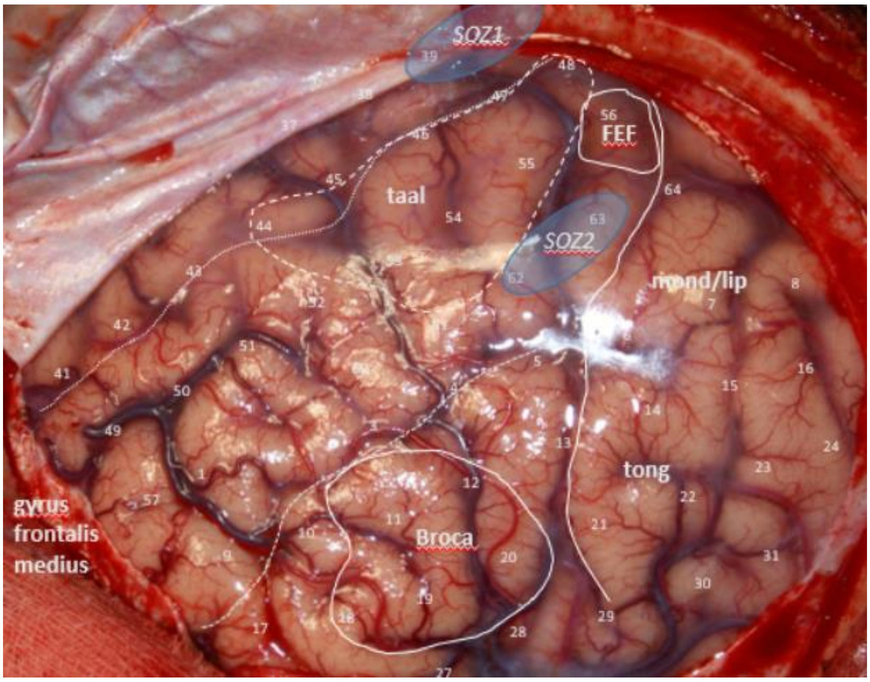
Participant 3:

This was the second implantation attempt because in 1998 they could not detect the Wernicke area properly during awake surgery. They have done a small parietal resection. During this language mapping, an extensive language network is detected in the temporo-occipital interface, especially in the gyrus temporalis medius, behind the resection cavity. There is also an extensive area at the back of the gyrus temporalis superior where he hears voices during DES. Given the functional anatomy, it was decided to leave the gyrus temporalis superior intact. A resection is proposed for an extension of the existing resection cavity to the median and anterior to the pia of the gyrus temporalis superior.

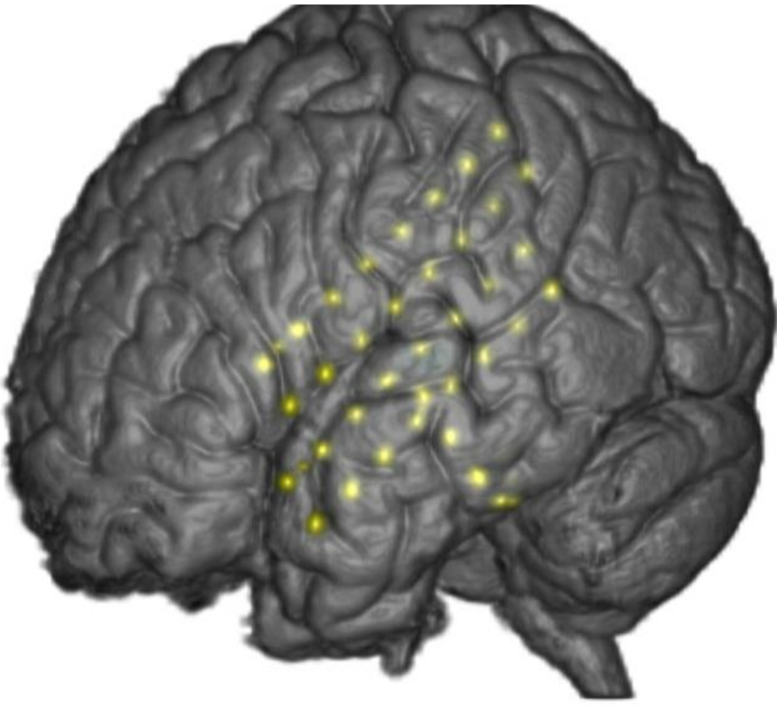
Appendix B

Grid placement on the brain

Participant 1:



Participant 2:



Participant 3: