MASTERARBEIT / MASTER’S THESIS

Titel der Masterarbeit / Title of the Master‘s Thesis

Language Impairments in Individuals with Brain Tumors. Characteristics and Diagnostic Methods

verfasst von / submitted by

Aylin Calleja-Dincer, BA, BSc

angestrebter akademischer Grad / in partial fulfilment of the requirements for the degree of

Master of Science (MSc)

Wien, 2021 / Vienna 2021

Studienkennzahl lt. Studienblatt / degree programme code as it appears on the student record sheet:	A066 013
Studienrichtung lt. Studienblatt / degree programme as it appears on the student record sheet:	Joint Degree Programme MEi:CogSci Cognitive Science
Betreut von / Supervisor:	Dr. Robert Darkow

“[…] theorists are enthusiastic in their quest to solve the puzzle of the dissociation between intact language structures and impaired communication demonstrated by the […] clinical populations. How is it that people who have sufficient and sophisticated words at their fingertips can fail to be able to use these words to describe a simple task, or to understand a joke? This question is intriguing, and points to the very heart of what characterises ‘human’ communication. We do not only communicate symbolically, but inferentially. We read beyond the symbol, to infer the desires, intentions and beliefs of another person in conversation“ (Martin & McDonald, 2003, p. 462).

Acknowledgements

I would like to thank the following persons, alphabetically by last name: my husband Nicolas Calleja-Dincer who always supports me in what I do, my supervisor Dr. Robert Darkow for his guidance along the process of writing this thesis, and Simon Sollereder, a MEi:CogSci alumnus and friend, who was the principal investigator of the experiment that forms the foundation of this master's thesis.

Table of Contents

List of Abbreviations

ACL	Aphasie-Check-Liste [Aphasia-Check-List]
ASHA	American Speech-Language-Hearing Association
CNS	Central Nervous System
CT	Computer Tomography
EEG	Electroencephalography
EHI	Edinburgh Handedness Inventory
fMRI	functional Magnetic Resonance Imaging
FOP	Fragebogen zur Orientierungsprüfung [Questionnaire about Orientation]
ICD-O	International Classification of Diseases for Oncology
MEC	Protocole Montréal d' Evaluation de la Communication / MEC-Testverfahren [Montreal Evaluation of Communication]
MEG	Magnetoencephalography
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
NBV	N-Back Verbal
NET	Neglect-Test
PET	Positron Emission Tomography
RWT	Regensburger Wortflüssigkeits-Test [Regensburger Word Fluency Task]
WHO	World Health Organization

1. Introduction

Language is based on a distributed brain network (Tremblay & Dick, 2016) involving cortical, subcortical and cerebellar structures (Fedorenko, 2014). The role of structural networks in the form of fiber tracts is ever more discussed in language processes (Gierhan, 2013) and it is assumed that a high-level linguistic system is engaged in specific linguistic processes while a domain-general cognitive control system supports these processes with mnestic, attentional and inhibitory mechanisms (Fedorenko, 2014). Amongst other reasons, language abilities can be disturbed by stroke, traumatic brain injury or brain tumors (Schneider et al., 2012).

A brain tumor is a heterogenous disease (Nabors et al., 2020) which can affect cognition negatively due to the tumor's characteristics, medical treatment or a combination of these factors (Taphoorn & Klein, 2004). Language impairments are common in brain tumors of the temporal (Noll et al., 2016) or frontal lobes (Habets et al., 2019). The language impairments caused by brain tumors are described to be rather mild (Davie et al., 2009) and may affect various aspects of language (Brownsett et al., 2019).

Pre- and postsurgical language testing are essential to diagnose these impairments, assess treatment success and to plan neurorehabilitation. However, diagnostic tools are usually borrowed from stroke research, even though it remains unclear whether the language assessment of brain tumor patients requires different tests (Miceli et al., 2012). First research about test validity in the field has revealed that the language impairment pattern may not be adequately reflected by use of language tests from stroke research (Wacker et al., 2002). Additionally, it is still debated whether impairment severity is associated with larger brain tumor size (Talacchi et al., 2011) and higher brain tumor grade (Yuan et al., 2020).

Apart from the missing information on language impairment patterns as well as difficulties with available test batteries (Wacker et al., 2002), the recovery of language seems to follow a specific pattern in brain tumor patients. Due to inter- and intrahemispheric functional reorganization of the brain, language impairments can remain subtle even if the tumor is located in language-relevant areas and a surgical tumor resection can transitorily lead to a deterioration of language abilities immediately after surgery before further reorganization takes place (Duffau et al., 2003; Heiss et al., 2003).

The objective of this master's thesis is to study the characteristics and diagnostic methods of language impairments in individuals with primary and secondary brain tumors which are predominantly located in the frontal or temporal lobes of either the left or the right hemisphere. More specifically, the aim is to find out whether communication differs between brain tumor patients and healthy individuals, before and after surgical resection, and between those with a tumor of the right or left hemisphere. Furthermore, it is researched whether tumor size and tumor grade affect language impairment severity.

To answer these questions, the communicative abilities of 15 individuals with left or right mostly frontal or temporal lobe tumors are evaluated by analyzing parts of the standardized language tests *Aphasie-Check-Liste (ACL)* (Kalbe et al., 2002), *Regensburger Wortflüssigkeits-Test (RWT)* (Aschenbrenner et al., 2000) and *MEC-Testverfahren (MEC)* (Scherrer et al., 2016) before and after tumor resection as well as *magnetic resonance imaging (MRI)* data.

The first part of this document entails the theoretical background with an introduction to brain tumors and the neuroanatomy of language. In addition, characteristics of language impairments in brain tumor patients as well as the available diagnostic tools are introduced and discussed. The introductory part of this thesis precedes the methods section, in which research questions and hypotheses, as well as the details on the conduction of the underlying experiment are described. In this section, the relevance of the topic for cognitive science and research in general is addressed as well. Further chapters present the data analysis and the discussion of results in view of the current state of research. Here, additional exploratory observations are described as well. The results are then also interpreted in the face of several frameworks of cognitive science, most notably in reference to embodiment (Barsalou, 2008). Finally, limitations of the current study and consequences for future research are addressed.

2. Theoretical Background

2.1 Brain Tumors

A tumor or neoplasm is a disease which is defined by an abnormal growth of cells in the body. Primary tumors are located and remain in their original location of growth, while secondary or so-called metastatic tumors encompass those tumors which arise when neoplastic cells spread to other parts of the body (Liu, 2018). Accordingly, primary brain tumors emerge from the brain tissue or neighboring tissues such as the meninges, while secondary brain tumors are diagnosed when primary tumor cells migrate from parts of the body to the brain (Mattle & Mumenthaler, 2017). Any primary tumor can be the origin of a secondary brain tumor, but the majority of secondary brain tumors can be traced back to lung tumors in 50-60% and breast tumors in 15-20% of cases. In 5-10%, skin tumors are identified as the primary site of a subsequent secondary brain tumor (Netwon, 2016).

The most recent classification of tumors of the *central nervous system (CNS)* by the *World Health Organization (WHO)* is based on histological and molecular parameters and identifies 17 groups of CNS tumors such as diffuse astrocytic and oligodendroglial, ependymal, neuronal and neuroglial tumors, meningiomas or lymphomas (Louis et al., 2016)[1]. Beyond the classification into tumor types, the WHO histologically grades tumors from I (benign) to IV (malign) to assign the grade of malignancy and indicate the prognosis. WHO grade I points to a minimal proliferative CNS tumor which may be removed by neurosurgery. WHO grade II indicates that the tumor has a rather low growth rate, but tends to reoccur after resection. WHO grade III refers to CNS tumors with a higher growth and reoccurrence rate, and WHO grade IV CNS tumors are characterized by very fast growth (Reifenberg et al., 2006). However, the assignment of malignancy is only partially suitable in the field of CNS tumors, as some of them may fall under the definition of being benign, but may still cause severe impairments or death and may be difficult to surgically resect (Weller & Schlegel, 2012). The *International Classification of Diseases for Oncology (ICD-O)* provided by the WHO offers an additional tumor grading system based on the histological differentiation of malignant brain tumors. The six-digit code ranges from digit one (well differentiated) over digit four (undifferentiated) to digit nine (differentiation undetermined) (World Health Organization, 2013).

Approximately 400.000 Austrians fall ill with malignant tumors per year. In 2017, the incidence rate amounted to 41.389 individuals and the mortality rate was 20.148. A quarter of all deaths in Austria are attributable to malignant tumors. The most common cancer types are tumors of the bowels, breast or prostate. Brain tumors constituted to 2% of all newly diagnosed malignant tumors and were responsible for 3% of deaths following cancer in Austria in 2017. Malign brain tumors occur more frequently than benign brain tumors. Both brain

[1] For in-depth information about the WHO CNS tumors classification consult Louis et al. (2016).

tumor incidence and mortality rate have been relatively stable between 2007 and 2017, and the relative survival rate of malignant brain tumors has risen from 55% to 59% between the periods of 2000 to 2004 and 2015 to 2017 (Statistik Austria, 2020).

Brain tumors are heterogenous in their frequency of occurrence, preferred therapy, prognosis and outcome (Nabors et al., 2020). The most common intracranial brain tumors are neuroepithelial tumors (30-40%), brain metastases (20-30%) and meningiomas (approximately 25%) (Wiestler & Reifenberger, 2003). Gliomas are also the most common group of brain tumors arising from the neuroepithelial tissue (Zanella, 2002). Gliomas form from glial cells such as astrocytes, oligodendrocytes or ependymal cells (Abrey & Mason, 2003). The glioblastoma multiforme is most common (50%) and the most aggressive glioma. It usually grows in the deep white matter of the temporal and frontal lobes. Meningiomas are derived from the meninges, which cover the brain and the spinal cord (Abrey & Mason, 2003). Meningiomas commonly grow slowly and mostly in the spinal cord, or in an intradural or extramedullary location (Westphal et al., 2003). In the case of brain metastases, the tumor cells reach the brain via the hematogenic pathway, leading to secondary brain tumors along the blood flow, most commonly in the cerebral hemispheres and less frequently in the cerebellum or brain stem (Netwon, 2016). Tumor growth and metastatic progression are tissue-specific, meaning that the tissue of tumor origin is influential on how the tumor progresses (Oliver et al., 2018). The three mentioned as well as the remaining tumor types of the total 17 brain tumor types will not be discussed in further detail, as it would go beyond the scope of this work.

Neuroimaging plays an essential role in the diagnosis of brain tumors, helps to plan the treatment, and allows for an assessment thereof (Cha, 2009). *Computer tomography (CT)* and *magnetic resonance imaging (MRI)* are employed when a tumor is suspected, but the diagnosis needs to be further ensured by use of histology (Liu, 2018). CT is suitable as a first screening method but is inferior to MRI in its resolution of details, especially of subtle or infiltrative changes. Since classical MRI is restricted to depicting morphological abnormalities, physiology-based methods which cover functional, physiological, and anatomic aspects, are ever more used. Examples of these advanced imaging methods are *diffusion-weighed MRI*, *perfusion MRI*, and *proton magnetic resonance spectroscopic (MRS)*. Diffusion-weighed MRI is critical to evaluate the integrity of white matter for brain tumors affecting this structure. Perfusion MRI is applied to assess tumor vascularity and to evaluate treatment response to antiangiogenic substances. MRS is recommended for image-guided surgical biopsy and the grading of glioma (Cha, 2009). *Positron emission tomography (PET)* is another essential imaging tool for tumor grade prediction, recurrent tumor discovery and the evaluation of treatment response (Nandu et al., 2018). In awake surgery, peri- or intra-operative language assessment can help to monitor and persevere functioning. Before surgery, diffusion tensor imaging can be employed to differ between essential, or so-called eloquent, language regions which should be spared by resection, and modulatory language regions which can be resected, because their functions will most probably be taken over by other regions. During awake surgery, cortical mapping in form of direct electrical stimulation can be used for the designation of essential language regions (de Witte & Mariën, 2012).

Symptoms in brain tumors are caused by the infiltration of tumor cells into healthy brain tissue as well as by the tumor cells forcing the non-tumoral tissue to adapt to their expansion. Apart from these local changes, the overall cerebral network can be disturbed by the brain tumor and its treatment (Heimans & Reijneveld, 2012). Tumor cells also have the ability to change cell metabolism in favor of their own transformation and progress. In other words, a reprogramming of metabolic activities takes place to ensure that the tumorous cells can start or continue to grow (Vander Heiden & DeBerardinis, 2017). The heterogeneity of brain tumors can be observed in the variety of symptoms arising from them, such as symptoms ranging from fatigue or motor problems over memory decline to impaired language (Nabors et al., 2020). Symptoms can be either focal or generalized. Focal symptoms are neurological symptoms caused by the tumor’s compression or ischemia of a certain area relevant to a specific motor, sensory or other cortical function. To allege an example, a glioma of the occipital lobe may result in hemianopsia or other visual disturbances due to the brain area’s involvement in vision. Generalized symptoms, on the other hand, are usually less specific signs such as headaches or sleepiness. Oftentimes, these symptoms are a consequence of increased intracranial pressure due to the tumor’s size (Schlegel et al., 2003). Since the cranium is a closed space, tumor growth or associated edema can harm the homeostatic environment within the cranium by taking up more space and thereby increasing pressure (Sorribes et al., 2019). The core set of symptoms in persons with newly diagnosed primary brain tumor is fatigue in 34% of cases, 25% reporting sleepiness, 25% describing memory dysfunction, 24% suffering from sleeping problems, followed by symptoms such as feeling distressed, irritability, dry mouth and a not further specified difficulty with speaking (Armstrong et al., 2016). Epileptic seizure is identified as the most frequent initial symptom in 33% of cases (Alther et al., 2020). Brain tumor-related epilepsy is multifactorial, some initiating causes being the changed brain tissue itself, edema, changes in metabolism or disturbance of neuronal connectivity (Shamji et al., 2009). The duration from symptom to diagnosis, the symptom-to-diagnosis interval, varies between one and 96 days with a median of 39 days. The shortest interval is described for headaches, closely followed by cognitive symptoms, nausea and epileptic seizure. By contrast, visual impairments or headaches exhibited a longer symptom-to-diagnosis interval (Alther et al., 2020). Language impairments will be discussed in chapter 2.3.

Possible treatments of brain tumors are surgical intervention, chemo- or radiation therapy, the latter of the tumor itself, the surrounded region or the whole brain (Weller, 2003). Surgical intervention is the most frequent therapeutic measure for primary brain tumors and aims at tumor removal, seizure control and the reduction or reversal of neurological symptoms. It is either employed as a curative method for the resection of a benign tumor as a whole, or in form of a non-curative malign tumor resection for life prolongation and enhancement of neurological functioning. Radiation therapy is the recommended measure for high-grade gliomas, low-grade primary brain tumors which proceed to grow after resection, or which are not easily accessible via surgery. Chemotherapy is usually administered as an additional treatment for high-grade primary brain tumors or for low-grade primary brain tumors which progress after surgical intervention (Newton, 2016). Secondary brain tumors are surgically resected in the case that they are solitary and accessible metastases, while this type of therapy is usually not performed for multiple brain metastases. Radiation therapy is the first-line treatment for accessible, large or multiple brain metastases. Chemotherapy is indicated for secondary brain tumors of recurrent nature, especially when they originate from primary tumor types which are very sensitive to chemotherapy such as breast cancer (Netwon, 2016).

2.2 Neuroanatomy of Language

Historically, the left posterior inferior frontal gyrus was identified by Pierre Paul Broca as an area essential for language production. A lesion to Broca's area was described to lead to *nonfluent* or *expressive aphasia* (*Broca's aphasia*). Carl Wernicke then described a center of language comprehension, located in the left posterior part of the superior temporal gyrus. A lesion to Wernicke's region was found to cause *fluent* or *expressive aphasia* (*Wernicke's aphasia*) (Tremblay & Dick, 2016). Aphasia will be defined and further addressed in chapter 2.3. Due to advances in neuroscience, this historical or classical model of the neurobiology of language has been challenged (Tremblay & Dick, 2016):

> "While the importance of the inferior frontal and posterior temporal regions for expressive and receptive language functions is not disputed […], evidence that the network supporting language functions is vastly distributed across the brain is now overwhelming" (Tremblay & Dick, 2016, p. 62).

In other words, it is accepted that these core regions are significant for language processing, but it is argued that a larger number of brain regions is involved, including parts of the basal ganglia, cerebellum and thalamus. An additional problem with the historical approach is that no consensus has been reached over the precise definition and concise location of Broca's and Wernicke's area (Tremblay & Dick, 2016). Newer research has shown that Broca's area is not exclusively involved in articulation but also takes over a supervisory role in coordinating sensory information across a larger network for word production before articulation (Flinker et al., 2015), and that it is involved in syntactically complex sentence processing as part of a more general cognitive control system (Novick et al., 2005). Further, the classical model is criticized for its exclusive focus on cortical structures and the missing integration of white matter connectivity in language processes (Tremblay & Dick, 2016).

In contrast to this outdated localist approach, novel clinical data and diffusion tensor magnetic resonance imaging tractography propose a complex *perisylvian network* essential for language processing (Catani et al., 2005). The initially described perisylvian cortex is located in the left hemisphere around the Sylvian fissure in the majority of right-handers and most left-handers. It entails structures of the inferior frontal, inferior parietal and superior temporal lobes (Pulvermüller, 2013). More recent evidence suggests a perisylvian network with three segments of direct and indirect pathways. The long segment forms a direct pathway and its location corresponds to the *arcuate fascicle* between frontal and temporal lobes. The posterior segment connects temporal with parietal regions, while the anterior segment runs between parietal and frontal regions, together forming an indirect pathway (Catani et al., 2005). The white matter connectivity in the perisylvian area is sometimes called *perisylvian long association fiber pathway* or *language connectome* (Tremblay & Dick, 2016). The more general term *human connectome* refers to a complex network of interconnected neurons and brain regions which enables the generation and distribution of information

(Sporns, 2012). It is assumed that "neuronal interactions represent dynamics on a fixed structural connectivity that underlie cognition and behavior" (Park & Friston, 2013, p. 579). In other words, a relatively fixed, but connected anatomical structure is assumed as a base which gives rise to more dynamic, functional connections which enable complex brain functions (Park & Friston, 2013). Such structural networks in form of fiber tracts in the white matter are ever more discussed as essential to language production and comprehension. By definition,

> "anatomical connections between the cortical areas […] materialize as bundles of white matter, i.e. projections of nerve cells that proceed under the surface from one cortex to another. The cellular projections bundle during their course, and form so-called *fiber tracts*" (Gierhan, 2013, p. 205).

Fiber tracts make it possible for cortical areas to exchange information, but the exact course of the fiber tracts, their nomenclature and their involvement in specific language processes are still discussed (Gierhan, 2013). Fiber tracts for language processing form a number of association pathways which can be divided into fronto-temporal, parieto-temporal, occipito-temporal, and fronto-frontal connections. In addition, thalamic association pathways and cortico-bulbar, cortico-striatal and cortico-cerebellar loops, establishing a link between the cortex and the midbrain, basal ganglia, and cerebellum, exist (Tremblay & Dick, 2016). Furthermore, language fiber tracts can be divided into dorsal and ventral as well as direct and indirect pathways (see *Figure 1*). The *arcuate fascicle (AF)* is a dorsal pathway which directly connects the frontal with the temporal lobe. Also dorsally, an indirect superior pathway, the *superior longitudinal fascicle (SLF)* links the supervisory frontal regions with the temporal cortex, and an indirect inferior pathway ties the inferior frontal regions with the temporal cortex. The SLF can further be subdivided into three bundles, the SLF I, II and III. The SLF I is described to run medially and does not seem to be involved in language processing, while the SLF II stretches from the dorsal premotor and prefrontal cortex to the caudal *inferior longitudinal fascicle (ILF)*, and the SLF III travels from the ventral premotor and prefrontal cortex to the rostral *inferior parietal lobule (IPL).* The parieto-temporal part of the SLF II is sometimes also named SLF-tp. Secondly, the inferior direct tracts forms the second indirect dorsal pathway. Ventrally, two major pathways connecting the frontal with the temporal lobe by passing through the extreme capsule can be identified. The first is the *uncinate fascicle (UF)* which connects the inferior frontal cortex with both the prefrontal and the anterior temporal cortex. The second is the so-called *inferior fronto-occipital fascicle (IFOF)* which is a link between the frontal cortex, the posterior temporal cortex and the occipital cortex, travelling through the extreme capsule. Finally, the ILF and the *middle longitudinal fascicle (MdLF)* are additional ventral pathways, but seem to play only a minor role in language processes (Gierhan, 2013).

With regard to specific language processes (also see *Figure 1*), the AF and the SLF as dorsal fiber tracts are described to be in charge of phonological processing. Especially the parieto-temporal part of the superior longitudinal fascicle is assumed to be essential for phonological comprehension and production. For articulation, the superior precentral gyrus as part of the insular cortex, together with the dorsal tract, seem to be important. In detail, the SLF III is described to be essential for articulation, while the role of the SLF II and the SLF-p for articulation have not been extensively studied yet. Controversial findings have been reported for the role of the AF in speech repetition. The evidence suggests that the SLF-tp and the SLF III are crucial for repetition. Semantic processing involves the anterior and middle parts of the IFOF. Additionally, other ventral fiber tracts but no dorsal fiber tracts may be involved. For the processing of complex syntax, the dorsal fiber tracts appear to essential, while the ventral pathway seems to be important for more simple syntactic processes (Gierhan, 2013).

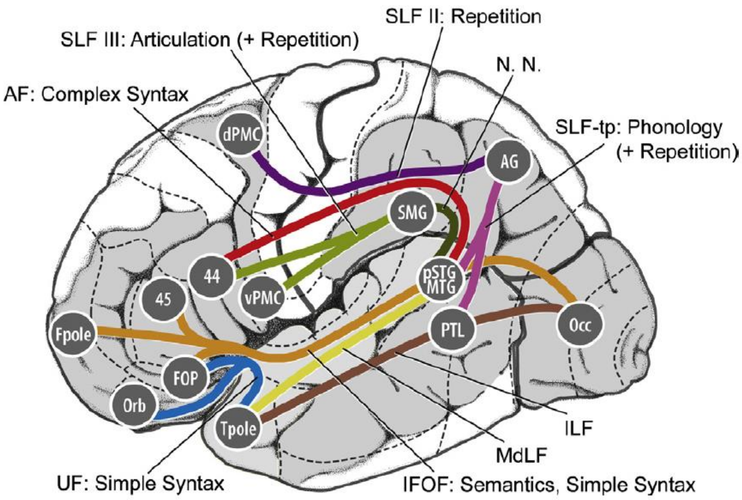


Figure 1: Neurocognitive Model of Language-relevant Fiber Tracts (Gierhan, 2013, p.218)

According to the dual-stream model of speech processing, structures of superior and middle temporal lobe form a ventral stream which is in charge of speech comprehension or recognition. More specifically, the ventral part of the model maps representations of sensory or phonological nature onto lexical conceptual representations. On the other side, a dorsal stream is represented by structures in the posterior frontal lobe, posterior dorsal temporal lobe and parietal operculum and is responsible for the integration of auditory information with the motor system for articulation, by mapping representations with a sensory or phonological character onto articulatory representations. The ventral stream is described to be bilaterally organized, while the dorsal stream is left-dominantly organized (Hickok & Poeppel, 2007).

While subcortical structures such as the thalamus and the basal ganglia are assumed to contribute to language processing too, their exact role remains unclear. The basal ganglia are associated with motor processing in language, the thalamus is involved in an integration of language-relevant cortical areas (Radanovic & Scaff, 2003). As for the cerebellum, a motor speech stream is described with cortico-cerebellar loops which are rather involved in speech- but not so much language-related aspects such as coarticulation (Dick et al., 2014).

In addition to this up-to-now presented high-level linguistic processing system, a domain-general cognitive control system is believed to be engaged in language processing too. The high-level linguistic language system is mainly involved in linguistic processes, and the domain-general cognitive control system is engaged in mnestic, attentional and inhibitory mechanisms. However, the latter also supports language processes. The high-level linguistic processing system, as mentioned in the previous paragraphs, is distributed along the left frontal, temporal and parietal cortices as well as in subcortical and cerebellar regions, while the domain-general system resides dorsolateral prefrontal cortex, insular cortex, precentral gyrus, pre-supplementary and supplementary motor regions, and parts of both the anterior cingulate and intraparietal sulcus (Fedorenko, 2014). A dorsolateral circuit of the frontal cortex is engaged in verbal fluency, inhibition, working memory, problem-solving and abstract thinking. A ventromedial circuit is associated with motivation and the orbitofrontal circuit is involved in social behavior (Alvarez & Emory, 2006).

Generally speaking, the frontal lobes are described to be involved in controlling and integrating information from other brain regions (Rojkova et al., 2016). To be more precise, the frontal lobes are engaged in executive functioning, self-awareness, consciousness, attentional processes, affective responsiveness, decision-making and language processing (Fang et al., 2016; Stuss, 2011). Executive functions are sometimes also described as higher-level functions which are in charge of organizing, supervising and conducting complex thinking and behaving (Alvarez & Emory, 2006). Executive functions thereby encompass inhibitory control, working memory and cognitive flexibility, the three of which enable the higher-order executive functions of reasoning, problem-solving and planning. Attention, behavior, thoughts and emotions are controlled by the first core executive function, which is inhibitory control. The second core executive function, working memory, is divided into verbal and nonverbal or visual-spatial working memory and is necessary for mentally handling information (Diamond, 2013). Working memory is believed to mainly reside in the dorsolateral and ventrolateral prefrontal cortex (Narayanan et al., 2005). Cognitive flexibility as the third core function, allows quick and flexible changes of perspective at a spatial or interpersonal level and supports creativity (Diamond, 2013). The definition of executive functions and what they entail is still highly discussed and a variety of models exists. It is essential to mention that it is an umbrella term, referring to a large number of different cognitive and behavioral functions that are summarized under one term but whose dysfunction can manifest very differently (Chan et al., 2008). Examples of language processes with an involvement of the domain-general network or executive functions are the selection of appropriate words in language production by inhibiting competing alternatives or the language comprehension of competing interpretations according to a communicative situation or goal (Ye & Zhou, 2009). It is also assumed that pragmatic language, which integrates structural aspects of language such as syntax and semantics with social, context-dependent information, depends on executive functions (Martin & McDonald, 2003).

The lateralization of pragmatic language in the brain has been a matter of discussion for a long time, and pragmatic language disabilities have traditionally been described in clinical populations with lesions to the right hemisphere. However, the empirical evidence of this association appears to be inconsistent or at least less clear-cut (Stemmer, 2015). In a meta-analysis of the neural substrates of figurative language processing, the findings of 22 fMRI or PET experiments including 354 subjects point towards a "bilateral fronto-temporal network with a bias to the left in figurative language processing" (Bohrn et al., 2012, p. 2676). More particularly, irony and sarcasm seem to correlate with activation in the medial prefrontal and right fronto-temporal cortex, whereas metaphors and idioms are mainly associated with the left inferior frontal gyrus (Bohrn et al., 2012). In the case of text comprehension, the importance of the right hemisphere has equally been discussed, but a meta-analysis of 23 neuro-imaging experiments concludes that a bilateral fronto-temporal network is involved and no special role goes to the right hemisphere (Ferstl et al., 2008). At this point, it is vital to point towards the individual variability of neuronal correlates, where cognitive function and its underlying anatomy vary between individuals, and both single case studies but also group studies can result in wrong theoretical conclusions (de Schotten & Shallice, 2016).

Cognitive functions are defined as mental processes which play a vital role in the information acquisition and manipulation. Examples of these processes are language, memory, attention and perception (Kiely, 2004). The contribution of mnestic, attentional and perceptual processes to language has been mentioned in this chapter and will now be addressed in more detail. Long-term memory is involved in language processes in the form of a declarative and a procedural mnestic system. Declarative or explicit memory stores and enables the use of knowledge about facts and events and is located in the medial temporal lobes, more specifically it relies on hippocampal regions. Declarative mnestic processes are believed to be involved in the mental lexicon which holds word-specific knowledge. Procedural or implicit memory, on the other hand, allows for the acquisition and use of sensori-motor or cognitive skills and is distributed along the basal ganglia, cerebellum as well as frontal and parietal structures. The mental grammar which holds rules for the formation and interpretation of complex linguistic structures is based on procedural memory (Ullman, 2004). Working memory as a short-term memory enables the temporary storing and manipulating of information and is further divided into the phonological loop (for holding and rehearsing information such as heard letters), the visuospatial sketchpad (for storing and repeating visual and spatial information such as the lines of a book) and episodic buffer (for the storage of multi-modal information as one), all of which rely on the executive system (Baddeley, 2003). Attention is a prerequisite for linguistic processes such as "the use of grammar and lexicon in human discourse" (Myachykov & Posner, 2005, p. 324). In discourse grammar, attention is directed at a visual cue for the assignment of syntactic roles, or attentional mechanisms are exerted at references in a text or speech to be able to resolve ambiguity. In semantics, attention is involved in the processing of the meaning of visually displayed words or in reading (Myachykov & Posner, 2005). Visual perception and language are linked in a complex and bi-directional manner. Visual object perception and recognition are involved in learning object labels, visual contexts help interpret the meaning of linguistic input, and gestures support linguistic output as well as comprehension (Vulchanova et al., 2019)

.

2.3 Language Impairments Following Brain Tumors

Aphasia is defined as an acquired language disorder caused by brain injury at a point in time when language was already fully acquired. Causes of aphasia are ischemic or hemorrhagic stroke (80%), traumatic brain injury (10%), brain tumors (7%), cerebral atrophy (1%), inflammatory diseases of the CNS (1%) or hypoxia (1%). Lesions to the perisylvian area of the language-dominant, mostly the left hemisphere, are described to be the main cause of aphasia. Aphasia may affect the four modalities language comprehension, production, reading and writing (Schneider et al., 2012). It is still a subject of debate whether the modalities are affected in a supramodal (comparable impairment for all four modalities together), multimodal (majority of modalities disordered) or in some cases unimodal (negative effect on one modality only) manner (Tesak, 2006)[2].

The *American Speech-Language-Hearing Association (ASHA)* introduced an additional term for an acquired language disorder, namely *cognitive-communication disorders* which are defined as disrupted verbal or nonverbal communication owing to impaired cognitive processes such as attention, executive function, orientation or memory. All language domains can be affected, namely phonology, morphology, syntax, semantics, and pragmatics. The impairment can be either congenital or acquired. The causes of an acquired cognitive-communication disorder include but are not limited to stroke, traumatic brain injury, (non-) degenerative neurological diseases, brain tumors or toxic encephalopathy (American Speech-Language-Hearing Association, 2005).

The difference between aphasia and cognitive-communication disorders may be equated to the terms *primary* and *secondary aphasia*. Primary aphasia designates language impairments that result from deficits of high-level linguistic language-processing mechanisms and secondary aphasia denominates language disorders caused by including but not limited to impaired memory, attention or perception (Caplan, 1996). According to Büttner and Glindemann (2019) who introduced the term cognitive-communication disorders to German-speaking countries as *Kognitive Kommunikationsstörungen*, the concept fits the idea of a disorder of integrative language functions. In the *International Classification of Functioning, Disability and Health (ICF)*, a common framework for the description of health-related issues, *integrative language functions* are coded as *b1672* and denoted as

> "mental functions that organize semantic and symbolic meaning, grammatical structure and ideas for the production of messages in spoken, written or other forms of language" (World Health Organization, 2001, p. 62).

Recently, the term *Kognitive Dysphasie* (*cognitive dysphasia*) was introduced as well and refers to a secondary language disorder following a primary neuropsychological disorder in the attentional, mnestic, demential or psychotic area, induced by acquired brain damage after the completion of language acquisition. Examples for cognitive dysphasia are language

[2] See Tesak (2006) for an overview of the controversy about aphasia definitions.

impairments caused by dementia, psychosis, lesions to the right hemisphere or the frontal lobes (Heidler, 2005). It is supposed to substitute the non-specific term *nicht-aphasische zentrale Sprachstörung* (*non-aphasic language disorder*) (Prigatano et al., 1985) by referring to etiology and primary symptoms, for instance in the case of the diagnosis *cognitive dysphasia of dysexecutive genesis in traumatic brain injury with a prefrontal lesion* (Heidler, 2005). It should again be contrasted to aphasia which encompasses only primary, language systematic, standard syndromes such as global, Broca's, Wernicke's and amnestic aphasia (Heidler, 2005, 2007). Nevertheless, the term cognitive dysphasia has been the subject of criticism because the proposed diagnosis, as in the example above, suggests a clear pathomechanism (Regenbrecht & Guthke, 2017).

It becomes clear that over the course of time, the precise etiology and definition of aphasia (Berg et al., 2020; McNeil & Pratt, 2001) as well as the terminology and distinction of aphasia from cognitive-communication disorders (Büttner & Glindemann, 2019; Heidler, 2005) have been discussed. Some authors argue that non-linguistic cognitive deficits as part of a certain neuropsychological disorder should not be defined as a possible cause of aphasia, while others assume a broader underlying etiology (McNeil & Pratt, 2001). To address this issue, other concepts and terms of distinction between aphasia and cognitive-communication disorders have been established. Some of the terms emphasize a distinction based on etiology, while others focus on the laterality or the linguistic and communicative symptoms (Büttner & Glindemann, 2019). In addition to these considerations, an exact anatomic distinction between aphasia and cognitive-communication disorders seems to complicate under the assumption of a distributed language system of cortical and subcortical structures (Tremblay & Dick, 2016). Accordingly, language impairments could be defined as a neuronal network disorder which cannot simply be traced back to the negative effect of a unitary local lesion, but to a whole region and its associated networks (Stockert & Saur, 2017).

The definitions described up to this point of this thesis illustrate the vast number of sometimes contradictory definitions of neurogenic language impairments. In this master's thesis, the more general term of language impairments will be preferred over other terms, as most authors researching language disorders in brain tumor patients do not distinguish between aphasia and cognitive-communication disorders and the distinction cannot be made based on the available information in articles. Moreover, contrasting aphasia with cognitive-communication disorders is not feasible in the study group of this master's thesis, because non-linguistic cognitive abilities were not routinely assessed.

Following this definition of aphasia and cognitive-communication disorders, the evidence regarding the causes, type and severity of language impairments in individuals with brain tumors both before and after neurosurgery will now be discussed. Generally, cognitive functioning can be negatively affected by the brain tumor itself, tumor regrowth, tumor-related epilepsy, the tumor treatment by means of surgery, radiotherapy, chemotherapy or other medication, by psychological factors or a combination of some or all of these aspects (Taphoorn & Klein, 2004). In addition to tumor-specific treatment, cognition can be influenced by other medication such as anti-epileptic drugs or antidepressants (Heimans & Reijneveld, 2012). The described percentage and type of cognitive and language impairment before and after treatment differs from study to study. Before surgery, cognitive functioning was impaired in 75% of 103 patients with either left frontal or right frontal localized gliomas. More specifically, those with a tumor of the left frontal region were significantly more impaired in attention, expressive and receptive language and verbal learning (Noll et al., 2016). In a similar study, pre-surgical neurocognitive impairment compromised attention (30%), working memory (20%), visual memory (14%), verbal memory (13%), information processing speed (11%) and executive dysfunctioning (8%) in 72 patients with glioma of the right or left hemisphere (Habets et al., 2019). In 139 patients with tumors of the frontal or temporal lobes, it was found that 91% had an impairment of at least one, and 71% of three or more of the tested cognitive faculties. Executive functioning was the most common impairment with 78% of patients affected, while language impairments were seen in only 22% of cases (Tucha et al., 2000). After surgery, a significant amelioration of memory and executive functioning was reported in 49 persons with supratentorial low-grade gliomas three to 28 months after surgery (Barzilai et al., 2018). However, immediately after surgery, a significant deterioration of cognitive functions such as executive functioning may be observed, as in 28 left hemisphere glioma patients (Satoer et al., 2012). Possible reasons for an immediate pre-operative decline and further long-term improvement will be addressed in response to language functions in the following paragraphs.

A systematic review by Finch and Copland (2014) of 1449 articles between 1990 and 2012 with a final number of nine articles meeting study criteria looked at language abilities before and after brain tumor surgery. The results of the review indicate that a decline in language functions is frequently observed immediately post-surgically. The pattern of the language disorders in the reviewed articles was very heterogenous, but most improved or even resolved by three months after the tumor resection. Post-operative language impairments were predicted by the presence of pre-operative language disabilities and the involvement of not further specified subcortical language tracts, but not by tumor histology or its location (Finch & Copland, 2014).

In order to display the more recent scientific evidence of brain tumors and their influence on language before and after resection as well as the used diagnostic methods, a literature review was conducted on *PubMed, PsycINFO*, and *Cochrane* for this master's thesis. Studies between 2012 and 2021 were reviewed. The following search items were used: *brain tumor AND language OR aphasia OR communication OR cognition OR cognitive functioning*. The results' titles were scanned for their relevance. If they were yielded relevant, the abstract was read. If the abstract did not exhibit essential information to the topic, it was discarded. Exclusion criteria were pediatric brain tumors, studies comparing pre- and post-rehabilitative language abilities, studies looking at brain tumors with the presence of other types of neurological diseases, and comparisons of the effect of treatment other than brain surgery. The results of the review are now shortly summarized here together with results of other articles to display language impairments in brain tumor patients before and after surgical intervention according to language modality. Also, the role of the hemispheres will be addressed. For a short and comprehensive overview of the conduction of the literature research as well as language impairments following brain tumors, consult the *Appendix Part 1 and 2*.

The communicative pattern of persons undergoing brain tumor surgery is described to be very heterogenous (Brownsett et al., 2019) and mostly very mild (Davie et al., 2009). For instance, picture-naming was shown to be impaired in correctness and reaction times before and after surgery in brain tumors of different kind and location (Amoruso et al., 2021; Faulkner et al., 2017) with more severe impairments in left hemisphere tumors before (Chakraborty et al., 2012; Papagno et al., 2012) and after tumor resection (Davie et al., 2009). Piai et al. (2020) did not find significant differences to healthy controls.

Spontaneous speech was described to be impaired before, shortly after and up to one year after surgery in patients with gliomas in eloquent language areas. These impairments were incomplete sentences at all points in time as well as a more frequent use of self-corrections and decreased type token ratio shortly after and up to one year after surgery. Only in the long run, mean length of utterance was significantly impaired (Satoer et al., 2018). Other types of errors were phonological errors and word-finding difficulties in the spontaneous speech of left-hemisphere tumor patients especially shortly after surgery (McCarron et al., 2017) and phonological paraphasia in left frontal glioma patients (Rofes et al., 2018). Interestingly, it was also found that some subjects reported word-finding difficulties in everyday life even though their spontaneous speech was described as unimpaired. The authors of the study explain this result with the possibility that word-finding difficulties may be more difficult to diagnose than other symptoms when using a standardized language test (Satoer et al., 2012). However, it must be pointed out that the tests used in the study were not specifically developed for identifying word-finding deficits and that spontaneous speech was rated with a very general scale without clear criteria for the scores.

Word generation as well as lexical and semantical fluency were significantly impaired in mainly left- and right-hemisphere patients before treatment (Faulkner et al., 2017) and after surgery in patients with gliomas of either hemisphere (Papagno et al., 2012). However, other studies report specifically reduced semantic fluency in left hemisphere glioma patients before surgery (Bartha et al., 2000). A reduction of lexical fluency was found in left and right hemisphere glioma patients before operation (Morrison et al., 2016). A decline in both was reported for left hemisphere glioma subjects three to four months after surgery (Satoer et

al., 2012). Lexical and semantic task-switching in left and right frontal and temporal lobe tumors was negatively affected up to two months post-operatively (Bette et al., 2020).
Less correct rhyming before the operation was found in left or right hemisphere glioma patients (Morrison et al., 2016).
In writing, paragraphias were produced only by a single person with left hemisphere glioma 24 hours before surgery (Bartha et al., 2000). Also in other studies, reading and writing was mostly unimpaired in left-, right- or bi-hemispheric brain tumor patients before surgery (Tucha et al., 2000), immediately after and three to four months post-surgically in left hemisphere tumors (Satoer et al., 2012).
Repetition and auditory comprehension were also mostly unaffected by left hemisphere tumors before surgery (Bartha et al., 2000; Satoer et al., 2012). Auditory comprehension and repetition seemed to deteriorate in left hemisphere glioma patients shortly after resection but were similar to the pre-operative assessment after three months (Teixidor et al., 2007). The *Token Test* (Huber et al., 1982) was unimpaired preoperatively, and non-significantly impaired three to four months postoperatively in left hemisphere brain tumors (Satoer et al., 2012).
Problems with non-word repetition were less frequently reported and only described for left-hemisphere patients pre-operatively (Faulkner et al., 2017). The reading comprehension of complex words was significantly impaired before surgery in brain tumors of different lobes (Brownsett et al., 2019). Reading comprehension was not assessed on a text level in any of the mentioned studies.
A difference in pragmatic disabilities could not be selectively identified for either hemisphere, but all left or right hemisphere tumor patients showed an impairment in figurative language before treatment in a test which entails metaphors (Arcara et al., 2018).
The functional reorganization of language after brain tumor removal seems to follow a specific pattern. Pre-surgically, language can be unimpaired even if the tumor is located in an eloquent area of the brain because of compensation. In other words, perilesional sites are recruited and at least partially compensate for the deficit a tumor causes. Shortly after surgery, language can be impaired because these compensating structures are (transitorily) damaged by the resection (Duffau et al., 2003) as well as due to edema (van Kessel et al., 2020) or transitory inflammation processes (Vaidya et al., 2019). Some types of tumor such as high-grade glioma require extensive surgical resection because it significantly contributes to a higher life expectancy. Even low-grade glioma are sometimes resected in a more extensive manner, as the risk of transforming into a malignant type decreases thereby (Sanai & Berger, 2008). Finally, post-operative functional compensation takes place, meaning that due to neuroplasticity a secondary recovery of language functions occurs (Duffau et al., 2003). In addition to the mentioned intrahemispheric recruitment of areas close to the brain tumor site, an interhemispheric recruitment takes place too, where homologous brain areas

of the other hemisphere compensate for the lesion in the other (Heiss et al., 2003). As for the reorganization of language abilities after left middle cerebral artery territory infarction, a different three-step pattern of recovery was identified. In the acute phase after stroke, the activity of remaining language areas in the left hemisphere was reduced. In the following phase after approximately two weeks, an upregulation of the whole bilateral language network was described, with peak activity in right hemisphere areas. This pattern was correlated with an improvement of language abilities. Thirdly, activity shifted back from the right to the left hemisphere, which also correlated with language improvement. It is yet unknown whether the increased activation of the right frontal hemisphere is to be understood as a so-called maladaptive strategy or a proof of the functional role of the right hemisphere in language recovery. Persons with severe aphasia caused by a severe lesion to the left hemisphere might stay in the described second phase (Saur et al., 2006). A difference between the pattern in stroke and in tumor language recovery seems to be that language recovers faster in individuals with brain tumors (Satoer et al., 2018). However, long-term effects of brain tumors on language are scarcely researched. Another difference is that anomic aphasia is the most frequent form of aphasia caused by brain tumors, while global aphasia is much less common in brain tumors compared to stroke (Davie et al., 2009).

After this overview of pre- and postoperative language, the role of tumor size and grade will be discussed. Evidence regarding the influence of tumor size and grade on language is contradictory. Pre-surgically in one study, patients with smaller lesions (mass lesion volume of 1.6-17.4 cm^3) had a significantly lower number of cognitive impairments in comparison to patients with larger lesions (mass lesion volume of 106.0-399.2 cm^3) (Tucha et al., 2000). (Talacchi et al., 2011) also showed that greater tumor size and grade were significantly associated with worse cognitive functions both before and after surgery in glioma patients of the left or right frontal, temporal or parieto-occipital lobes. However, in another study language subtype and severity were independent of tumor location, grade and the number of craniotomies (Davie et al., 2009). With respect to specific cognitive functions, those with larger tumor volumes had significantly worse scores in verbal memory and verbal fluency (Tucha et al., 2000). In individuals with either high- or low-grade glioma of the left hemisphere, language was tested with the *Standard Aphasia Battery of Chinese (ABC)* (Gao et al., 1992), an adaptation of the *Western Aphasia Battery (WAB)* (Shewan & Kertesz, 1980), and the results show that spontaneous speech, comprehension, naming and repetition were significantly worse in high- (WHO grade III and IV) than in low-grade (WHO grade I and II) glioma patients (Yuan et al., 2020). Apart from the influence of tumor size and grade, it has been tested whether the speed of tumor growth affects cognitive functions in a similar way. In was shown that the performance subtests of the *Wechsler-Bellevue Intelligence Scale* (Wechsler, 1941) were significantly more impaired in individuals with fast in comparison to slowly growing tumors (Hom & Reitan, 1984).

2.4 Diagnostic Methods of Language Impairments in Brain Tumors

According to the *Standards for Educational and Psychological Testing* by the *American Educational Research Association (AERA), the American Psychological Association (APA)* and the *National Council on Measurement in Education (NCME)*, well-developed tests should meet the criteria of validity, reliability and fairness (AERA et al., 2014). Validity indicates "the degree to which evidence and theory support the interpretations of test scores for proposed uses of tests" (AERA et al., 2014, p. 11). This criterion includes that the population the test is intended for should be clearly defined. Reliability or precision refers to the consistency of measurements across various instances of testing. Standards such as interrater reliability, indicating that two different testers would come to a similar results, or ecological validity, referring to the relevance of the test's outcome to the person's life, should be met (Turkstra et al., 2005). Amongst other aspects, fairness includes accessibility, meaning that all persons tested should be equally able to demonstrate their competence, regardless of factors such as their educational or cultural background (AERA et al., 2014)[3].

Language and other cognitive resources should be routinely assessed before and after the treatment to be able to identify language impairments, to measure the negative effect of some treatments such as radio- or chemotherapy, to be able to rule out pre-existing cognitive dysfunctioning and also to quantify spontaneous recovery, treatment success (Tucha et al., 2000).

In a review by de Witte & Mariën (2012) it was found that language testing is usually performed up to ten days before surgery, and post-operatively immediately up to one week after surgery, followed by later testing after three and six months and in only a few cases after a year. Further, the authors summarize that the most frequently used language test batteries in studies are the *Boston Diagnostic Aphasia Examination (BDAE)* (Goodglass & Kaplan, 1972)*, Aachener Aphasie Test (AAT)* (Huber et al., 1982*), Boston Naming Test (BNT)* (Kaplan et al., 2001) and various verbal fluency tasks (de Witte & Mariën, 2012). The small number of research with German speaking brain tumor patients used the already mentioned AAT in two studies by (Bartha et al., 2000; Wacker et al., 2002), the *Aachener Aphasie-Bedside-Test (AABT)* (Biniek et al., 1991b) again in the study by (Wacker et al., 2002b) and the *Regensburger Wortflüssigkeits-Test (RWT)* (Aschenbrenner et al., 2000a) in the aforementioned study by (Bartha et al., 2000). Owing to the fact that the participants of the study are German speaking, this master's thesis will not further elaborate on the available and used standardized language tests in English language[4]. Moreover, non-standardized tests and questionnaires for patients and relatives will not be addressed.

Unfortunately, most standardized language tests were developed for and evaluated with stroke patients and not specifically with brain tumor patients. Accordingly, it is not known

[3] Consult AERA et al. (2014) for in-depth information about test standards.

[4] For details on language tests used in studies with brain tumor patients, see De Witte & Marien (2012).

whether these language assessments are suitable for brain tumor patients (Miceli et al., 2012). Prior research indicates that stroke and brain tumor patients with lesions to the same structure should be treated as separate subject groups for several reasons. First, stroke causes more direct neuronal lesions while brain tumors often gradually infiltrate and replace existing structures without immediately damaging it. Secondly, a small stroke can affect language more severely than a small brain tumor of the same location. Thirdly, the correlation of brain tumor location and occurrence of language impairments is inconsistent in comparison to stroke patients (Anderson et al., 1990). At the time of writing this master's thesis, there is no language test specifically based on and tailored to brain tumor patients in German language. In English language, only one language test was developed for and tested with brain tumor patients, namely the *Brief Language Assessment for Surgical Tumor Patients (BLAST)* (Faulkner et al., 2017). It entails nine subtests, picture-naming, verb generation, picture-word verification, real and non-word repetition, a Stroop task, letter and category fluency as well as a test for articulatory agility. These tests are supposed to evaluate cognitive skills which are essential for language. These so-called core cognitive skills encompass auditory word recognition, semantic knowledge access, lexical selection, phonological encoding, verbal short-term memory, goal-driven language selection, verbal retrieval and articulatory motor planning (Faulkner et al., 2017).

Brownsett et al. (2019) argue that the incidence of a post-surgical language impairment is underestimated and underreported due to inconsistent or inappropriate testing. They continue their critique with the argument that some diagnostic tools such as the *Boston Naming Test* (Kaplan et al., 2001) use high frequency words in picture-naming only, thereby omitting the diagnosis of more subtle language impairments. Another problematic aspect of the use of diagnostic methods of aphasia designed for and standardized with stroke patients is that they are based on the historical language model and its syndrome classification. Oftentimes, these classifications rely on an overall aphasia score and normative data for single language functions and subtests are not provided. Accordingly, it is more likely that less severe language impairments affecting only one function are overseen. Additionally, many diagnostic methods were only normed on the healthy cohort, but lack a standardization based on a clinical population, in this case of brain tumor patients. For persons with left-hemisphere glioma of low and high grade, mainly of the frontal and temporal, but some also of the parietal and occipital lobes, it was shown that six to 12 months after tumor resection the *Comprehensive Aphasia Test (CAT)* (Swinburn et al., 2005) was more successful in identifying language impairments than the *Western Aphasia Battery- Revised (WAB-R)* (Kertesz, 2006) with its classification into post-stroke aphasia syndromes (Brownsett et al., 2019). Similarly, in a study with patients with a primary brain tumor or one brain metastasis, the *Aachener Aphasie-Test (AAT)* (Huber et al., 1982), a clinical examination and the *Aachener Aphasie-*

Bedside-Test (AABT) (Biniek et al., 1991) were compared for their diagnostic value in diagnosing language impairments in brain tumor patients (Wacker et al., 2002). In the experiment, the AAT was shown to be more effective in diagnosing language impairments in brain tumor patients than the AABT and the clinical assessment, also with a higher sensitivity and specificity for left- than right hemisphere brain tumors. The results may be explained by the clinician's approach not to expect a language impairment in patients with a right-hemisphere lesion or the different characteristics of a language impairment following a lesion of the right hemisphere. It can be followed that it is not sufficient to rely on the clinician's assessment regarding language impairments in brain tumor patients (Wacker et al., 2002).

Here, it should be mentioned that one study found that only 21% of 25 patients with a primary malignant glioma suffering from a speech-, language- or swallowing disorder were transferred to see a speech therapist (Faithfull et al., 2005). The authors do not put this result into further context, but it could be explained by the study's focus on palliative care, where other services might be more essential. The small percentage of transferal to speech therapists may also be distorted, given that a retrospective case review was performed, and documentation may not always be complete. In another study, 68% of subjects reported a language impairment in a subjective questionnaire, most frequently a word-finding difficulty, followed by reduced processing speed, the occurrence of problems under time-pressure or fatigue. Interestingly, the percentage of self-reported language impairment was higher than the objectively diagnosed language disorder (Brownsett et al., 2019). Also, spontaneous speech analysis has been found to be a sensitive indicator of language impairments in brain tumor patients, possibly more reliable than standardized language tests, because it is more similar to daily communication which incorporates all linguistic levels (Satoer et al., 2018). Other reasons could be that spontaneous speech testing is less structured than most standardized language tests or that the study observed linguistic variables of spontaneous speech which are simply not included in other tests.

Even though the treatment of language disorders in brain tumor patients is not the subject of this master's thesis, it will now shortly be addressed to point out how the topic requires further research. First studies suggest that individuals with primary brain tumors significantly benefit from early cognitive training after tumor resection (Zucchella et al., 2013). Unfortunately, language impairments are often defined as exclusion criteria in studies such as the one by (Zucchella et al., 2013). A single-case study with a glioblastoma patient found a significant improvement of spontaneous speech after eight weeks of treatment (Milman et al., 2020). Another study looked at the advantage of multidisciplinary rehabilitation in 106 primary brain tumor patients and found a significant improvement in communication at three- and six-months follow up (Khan et al., 2014). However, it is not explained how language impairments were diagnosed and how communicative disabilities were treated or measured.

3. Methodology

3.1 Research Relevance & Relation to Cognitive Science

As brain tumors are heterogenous in their symptomology (Nabors et al., 2020), further research may shed light on specific patters of symptoms. Such knowledge may help reduce the symptom-to-diagnosis interval (Alther et al., 2020) in a potentially life-threatening disease (Statistik Austria, 2020). As the exact incidence of language impairments in brain tumor patients remains unclear (Noll et al., 2016; Tucha et al., 2000), and is described to potentially affect all areas of language (Brownsett et al., 2019), studying the characteristics of language in this clinical population in the course of this master's thesis project can provide novel insight to language impairment patterns in this clinical population.

Since the master's thesis does not only rely on behavioral but also MRI data, insights may help contribute to the ongoing discourse about the neuroanatomy of language (Tremblay & Dick, 2016). On a more general note, the results of this thesis may be beneficial to understanding the exact role of certain anatomic structures in cognitive processes (Park & Friston, 2013). In addition to shedding light on the linguistic function of certain brain structures, studying individuals with frontal brain tumors may support the assumption that executive functions play an essential role in language (Fedorenko, 2014). Due to the fact that the topic touches upon the discussion of the role of the right hemisphere in language, especially for pragmatics (Stemmer, 2015), insight of this thesis may help untangle the contradicting evidence of the role of the right hemisphere in language.

Even though it was already pointed out long ago that brain tumor patients should be treated as a separate subject group in comparison to stroke patients (Anderson et al., 1990), standardized language tests for this population are still lacking (Miceli et al., 2012). As first studies suggest that certain language test batteries are not useful for this patient group (Brownsett et al., 2019; Wacker et al., 2002), the master's thesis is clearly relevant for giving more evidence in favor of or against using known diagnostic tools from stroke research. The *Aphasie-Check-Liste* (Kalbe et al., 2002) has not been used with brain tumor patients in any study before, at least at the point of writing this thesis. Owing to the fact that spontaneous speech has been shown to be useful for the diagnosis of language impairments in this group (Satoer et al., 2018), it is further of relevance to analyze spontaneous speech in this experiment. Moreover, text comprehension has not been studied in brain tumor patients yet.

Last but not least, the topic is clearly important, because appropriate diagnosis is necessary for consecutive neurorehabilitation (Tucha et al., 2000b). Due to the negative effect of aphasia on quality of life in stroke patients (Spaccavento et al., 2014), a similar negative impact of language impairments on individual well-being may be assumed in brain tumor patients. As such, it could be argued that it is necessary to facilitate the best possible diagnosis and treatment for the patients' further life.

In addition to the already mentioned aspects of research relevance in general, the topic is interdisciplinary and resides within the scope of cognitive science, because it is thematically embedded in contributing disciplines such as linguistics, psychology and neuroscience (Thagard, 2010). Secondly, it has long been debated whether language and cognition should be treated separately or not (Harris, 2006). Studying the role of the frontal lobes and the relevance of executive functions for linguistic processes (Fedorenko, 2014) may contribute to this discussion and may lead to insights in not only the area of language, but other aspects of cognition too. In detail, the debate could be enriched by contrasting primary aphasia to cognitive-communication disorders. Furthermore, the topic is related to cognitive science as lesion studies and research tackling the topic of neuroplasticity can provide insight into the functioning of the brain and the human body and thereby improve recovery after brain lesions (Mateos-Aparicio & Rodríguez-Moreno, 2019; Vaidya et al., 2019). Given the reorganization of language different to stroke (Duffau et al., 2003; Heiss et al., 2003), the findings of the master's thesis may also underline the neuroplasticity of the brain.

With respect to certain paradigms of cognitive science, it could be argued that this master's thesis challenges the cognitivist view of language as amodal symbols in the brain (Barsalou, 2008) by showing how language impairments, specifically in non-literal language comprehension, indicate the necessity of taking the person's individual environment into account. The findings could then be taken as arguments in favor of embodied cognition (Barsalou, 2008), as language impairments, especially of pragmatic language, appear to be more than the sum of its parts (Martin & McDonald, 2003). Pointing out how the tumor's location is not necessarily decisive for the occurrence of a language impairment (Gempt et al., 2017) can also underline connectionist approaches (Bechtel & Abrahamsen, 1991) to cognition in contrast to modular paradigms (Fodor, 1983). Other cognitive science paradigms such as neurophenomenology (Varela, 1996) will only shortly be addressed in the discussion.

3.2 Research Question & Hypotheses

Based on the theoretical background, current state of research and the relevance of the topic for the scientific community and the study of cognitive science, the following all-encompassing research question (RQ) was formulated:

- **RQ:** How are language impairments in individuals with primary or secondary brain tumor of the left or right hemisphere of mainly frontal or temporal lobes characterized and diagnosed?

More specifically, the master's thesis' objective is to find out whether communicative abilities differ between individuals with right or left mostly frontal or temporal brain tumors and the healthy population (represented by reference values from standardized language tests). Furthermore, it should be analyzed if a difference can be found between pre- and postoperative language tests immediately after surgery in individuals with mostly frontal or temporal brain tumors of the left or right hemisphere. In addition, the aim of this work is to research if language is dissimilar in individuals with a frontal or temporal brain tumor of the left hemisphere in comparison to those with a frontal or temporal brain tumor of the right hemisphere, and if tumor size and grade are determinative of the severity of the language disorder.

To explore these questions, the succeeding hypotheses (H1-H4) were phrased. The underlying evidence for assuming these hypotheses comes from the theoretical background described up to this point and will be shortly summarized below them:

- **H1:** Pre-surgical language abilities are selectively impaired in verbal fluency, spontaneous speech and both text and metaphor comprehension measured by the standardized language tests RWT, ACL and MEC in individuals with mostly frontal or temporal brain tumors of the left or right hemisphere in comparison to healthy individuals, represented by the normative data of the language tests.

Prior evidence suggests reduced semantic and lexical verbal fluency (Bartha et al., 2000; Faulkner et al., 2017; Papagno et al., 2012; Satoer et al., 2012), especially in semantic and lexical task-switching (Bette et al., 2020), as well as disturbed spontaneous speech characterized by an increase in incomplete sentences and self-corrections (McCarron et al., 2017; Satoer et al., 2018) and impaired pragmatics (Arcara et al., 2018). Even though no study was found which explored text comprehension in brain tumor patients before, an impairment was assumed in the hypothesis, because reduced word comprehension has been observed before in a study by (Brownsett et al., 2019) and because executive and other non-linguistic functions are believed to be involved in text comprehension (Ferstl et al., 2005).

- **H2:** Individuals with mostly frontal or temporal brain tumors of the left hemisphere show a different pattern of language impairment than those with a frontal or temporal brain tumor of the right hemisphere, pre- or postsurgically.

Delayed verbal recall and impaired picture-naming seem to be more common in left- than in right-hemisphere tumors (Davie et al., 2009; Papagno et al., 2012). Verbal fluency is frequently affected by both left- or right-hemisphere tumors (Bartha et al., 2000; Faulkner et al., 2017; Papagno et al., 2012). No difference with regard to pragmatic disabilities could be found between left- and right-hemisphere gliomas (Arcara et al., 2018).

- H3: A larger brain tumor volume in cubic centimeters of frontal or temporal brain tumors in the MRI and high-grade tumors (WHO grade III and IV) are expected to be correlated with more severe language disabilities in standardized language tests, especially of verbal fluency, pre- and postoperatively.

Larger and higher-grade tumors lead to more severe effects in cognition and language before and after surgery, especially in the field of verbal fluency (Bette et al., 2020; Talacchi et al., 2011; Tucha et al., 2000; Yuan et al., 2020).

- H4: More severe language impairments in the standardized language tests ACL, RWT and MEC can be identified immediately post- in comparison to pre-operatively in individuals with mostly frontal or temporal brain tumors.

Possibly due to (transitory) damage to intrahemispheric compensatory structures close to the brain tumor, a decline in language abilities in comparison to prior to the operation can be observed immediately after surgical brain tumor removal before further intra- and interhemispheric compensation takes place (Duffau et al., 2003; Heiss et al., 2003; Satoer et al., 2012; Thiel et al., 2001).

3.3 Participants

15 German native speakers of the Department of Neurosurgery of the state clinic *Landesklinik Wiener Neustadt* participated in the research project *EFRONESonko - Einfluss frontaler Netzwerke auf die Sprachverarbeitung bei Hirntumorpatienten [Influence of Frontal Networks on Language Processing in Brain Tumor Patients]* between 2017 and 2018. The study was designed and conducted by Simon Sollereder, MSc as the principal investigator and Prim. Univ.-Doz. Dr. Johannes Burtscher, and was conducted in cooperation with the *Fachhochschule Wiener Neustadt* (Sollereder & Burtscher, 2021). Inclusion criteria were malign or benign tumors of the central nervous system, inpatient treatment and the necessity of brain surgery. Another inclusion criterium was an age of at least 18 years at the time of the first assessment. A maximum age was not defined. The highest degree of education of participants was documented on a threefold scale as *secondary education I* (compulsory school), *secondary education II* (high school certificate or professional training) or *postsecondary or tertiary education* (university degree). The tumor type was classified according to the WHO grading scheme (Reifenberg et al., 2006) and the site of lesion was described as either left- or right hemispherical. The drug administration before and after surgery followed a standardized procedure and was documented. The medication involved some but not

necessarily all of the following: thrombosis prophylaxis, pain medication, antibiotics, cortisone, anticonvulsive drugs. Untreated hydrocephalus, stroke, other cranial surgery, prior radiotherapy or chemotherapy were defined as exclusion criteria. Participants with an administration of drug doses which pass the blood-brain barrier were excluded.

Persons who participated in the study were recruited by neuro-oncologists of the clinic and had to give informed consent. When they first agreed to participate as a subject, a more extensive dialogue was held for clarification. The subjects were allowed to withdraw their participation at any point in time without giving reasons. An ethic approval was obtained by the *Ethikkommission Niederösterreich (Ethics Commission of Lower Austria*).

Handedness was checked via the *Edinburgh Handedness Inventory (EHI)* in which participants must indicate their preferred handedness for ten activities such as writing, using the scissors or toothbrushing. A laterality quotient between -100 and 0 for left-handedness, 0 and 100 for right-handedness is then calculated (Oldfield, 1971). In the experiment, the short version of the EHI containing 10 items was conducted. Neither left- nor right-handedness was defined as an exclusion criterion. In recent years, many researchers have started grouping the laterality quotient individually, introducing ambidexterity the closer the participant is to zero. However, this classification is not consistently applied and different to the originally described laterality quotient (Edlin et al., 2015). Thus, and because any type of handedness was not defined as exclusion criterion, an analysis according to the original version was conducted.

The orientation of participants was measured by means of the *Fragebogen zur Orientierungsprüfung (FOP) [Questionnaire about Orientation]*, which estimates personal, situational, geographical and calendrical orientation, the sum of which display global orientation (von Cramon & Säring, 1982). The questionnaire holds a total of 20 open questions with one point each and a score of less than 16 is considered to be an indication of an impaired orientation (Hupfeld, 2009). It was employed to ensure that orientation was given at the time of the language assessment and that patients with reduced vigilance, orientation or attention were excluded.

Parts of the standardized *Neglect-Test (NET)* (& Geissner, 1997) were performed to exclude patients with a diagnosis of neglect. The test involves the following subtests: copying figures, cutting lines into halves, copying an address, picture-naming, reading from a newspaper and a menu, reading the time from a digital and non-digital clock, setting a clock, free drawing of a clock, crossing out lines, stars and letters. The maximum score amounts to 170 points. A score lower than 130 indicates a neglect with a high probability, a score below 112 with a very high probability. In addition, the scoring allows to grade the severity of the diagnosed neglect (Fels & Geissner, 1997). For the experiment, only the subtest where stars and letters have to be crossed out was performed. In the star- and letter crossing task, a maximum of 54 points can be reached (Fels & Geissner, 1997).

3.4 Materials

In the experiment, all patients underwent a standardized language assessment. Parts of the *Aphasie-Check-Liste (ACL)* (Kalbe et al., 2002), namely the assessment of language comprehension via the subtests reading comprehension, auditory comprehension and the color-figure test were administered. For language production, the subtests picture-naming, lexical and semantic verbal fluency, reading, repetition and writing of real words were performed. Additionally conducted tests were the semantic and lexical category switching task of the *Regensburger Wortflüssigkeits-Test (RWT) (Aschenbrenner et al., 2000)*, the *N-Back Verbal (NBV)* (Schellig & Schuri, 2009) and the subtests metaphor comprehension, text comprehension, spontaneous speech analysis of the *MEC Testverfahren*, in the original called *Protocole Montréal d' Evaluation de la Communication (MEC)* (Scherrer et al., 2016).

The *Aphasie-Check-Liste (ACL)* is a standardized screening procedure for the diagnosis of a cerebral language disorder and the assessment of cognitive capacity in the fields memory, attention and logical thinking. It comprises seven language-specific subtests covering all modalities of language. Each subtest results in a score which indicates either no, a mild, moderate or severe impairment. The maximum score of all subtests amounts to 148 points, and a score of 135 is defined as the cut-off for aphasia. The ACL was normed with 106 healthy and 168 aphasic subjects and has a sensitivity of 94.2% and specificity of 95.2% for diagnosing aphasia (Kalbe et al., 2002).

The *Regensburger Wortflüssigkeits-Test (RWT)* is a standardized diagnostic tool which aims at the evaluation of verbal fluency in patients with acquired brain damage. It entails four subtests, two with a focus on formal lexical verbal fluency, and two with a focus on semantic verbal fluency (Aschenbrenner et al., 2000). In the experiment, only the category switching tasks were conducted. In the semantic category switching subtest, subjects must alternatingly name as many sports and fruits or garment and flowers as possible within two minutes. In the lexical category switching subtest, participants are asked to name as many words as possible in two minutes starting with the letter "G" and "R" or "H" and "T" in alternation. The result is a percentile rank. Normed results are based on a study with 634 healthy persons and the diagnostic tool has been checked for objectivity, interrater- and retest-reliability. Apart from diagnosing a language impairment, the RWT can also be administered to persons with neurological disorders other than of language, as it requires cognitive processes such as executive functioning and has been used with a broader patient population before (Aschenbrenner et al., 2000). Verbal fluency tasks are one of the most used tests for executive functions and have been proven to be sensitive to detect lesions of the frontal lobe, especially of the left hemisphere and specifically when looking at lexical in comparison to semantic verbal fluency tasks. However, the specificity is still debated, as persons with non-frontal left hemisphere lesion expose comparable problems (Alvarez & Emory, 2006). In addition, it is not fully clear which executive functions are measured by the verbal fluency tasks which possibly involve working memory for maintaining instructions, inhibition to avoid incorrect responses and repetition, and cognitive flexibility for switching (Shao et al., 2014). The *MEC Testverfahren* or *Protocole Montréal d' Evaluation de la Communication (MEC)* is a standardized language test which was developed with the aim to not only capture more classic linguistic (dis-)abilities in areas such as semantic or syntax, but also discourse, prosody and pragmatic aspects of communication which are more frequently impaired in language impairments following a brain damage of the right hemisphere. It is comprised of 14 subtests (Scherrer et al., 2016). In the experiment underlying this master's thesis, only the subtests metaphor and text comprehension as well as spontaneous speech analysis were performed. In the metaphor comprehension task, participants have to verbally explain the meaning of a metaphor and subsequently choose the correct explanation. In the text comprehension task, they hear a text and have to answer questions, retell parts of the text, retell the complete text and give the text a title. In the spontaneous speech analysis, a dialogue is analyzed, and points are subtracted for criteria such as word-finding difficulty, problems of understanding questions or extensive talking. Only the scores in metaphor explanation, whole text retelling, questions about the text and spontaneous speech can be transformed to scores of impairments. The remaining parts of the subtests can be described without such transformation. The MEC was standardized with 180 healthy participants (Scherrer et al., 2016).

The *N-Back Verbal (NBV)* is a non-standardized test for verbal working memory. The tested person is presented with consonants appearing one after another and has to react when a consonant corresponds to another consonant displayed "n" times before. For instance, in the 2-back paradigm, the tested person has to react when the shown consonant is identical to the one two places before. The control task is to react whenever a certain predetermined stimulus appears on the screen (see *Figure 2*). Regardless of the type of n-back paradigm, activation in simultaneous fMRI has shown an activation of the inferior parietal lobule bilaterally, the rostral and caudal middle frontal gyrus, the medial, caudal and anterior superior frontal gyrus as well as the inferior frontal gyrus involving Broca's area and the anterior insula (Schellig & Schuri, 2009; Sweet, 2011). The results of the NBV can be taken as an indication of executive functioning, because, it measures working memory (Schellig & Schuri, 2009), working memory is considered to be a part of executive functioning (Diamond, 2013), and prior research has shown the involvement of executive functions in the task (Gajewski et al., 2018). In the experiment, the 2-back paradigm was performed by the subjects.

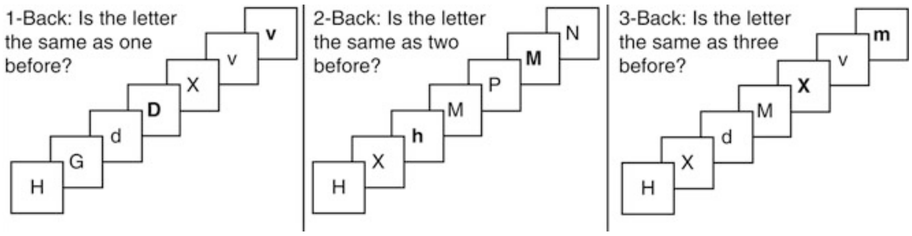


Figure 2: Example of the NBV (Sweet, 2011)

The tests were conducted by a speech therapist and recorded as video- and audio files according to a protocol regulating the order of testing in the following order: EHI (Oldfield, 1971) on paper, FOP (Hupfeld, 2009) recorded as an audio file, NET (Fels & Geissner, 1997) documented as a video-recording, spontaneous speech in the MEC (Scherrer et al., 2016) recorded via audio, parts of the ACL (Kalbe et al., 2002), MEC (Scherrer et al., 2016) and parts of the RWT (Aschenbrenner et al., 2000) as video- or audio-recording. In the end, the NBV (Schellig & Schuri, 2009) was conducted on a computer.

3.5 Data Processing

The author of this master's thesis received the audio- and video files of the standardized language tests for pre-processing. All materials were priorly blinded with regard to personal information, as well as assessment time (before or after surgery), exact diagnosis (type, grade and location of the brain tumor). As video files could potentially enable an identification of the tumor site or time of assessment, audio files were assessed first. Also, spontaneous speech analysis was transcribed and analyzed at the end of the pre-processing, as listening to the participant's spontaneous speech could also lead to the identification of assessment time and provide information about the tumor.

All language test batteries were scored according to their manual. In a few cases, the participants received a raw value in the RWT which was either that low or that high so that the chart for the conversion of raw values to percentile ranks did not offer an according percentile rank. In this case, it was defined that a percentile rank smaller than three was written down as two, a percentile rank lower than two was changed to one, a percentile rank lower than one was put down as zero, a percentile rank greater than 97 was put down as 98, greater than 98 was written down as 99 and a percentile rank greater than 99 was written down as 100.

All scores were entered into an excel file and then further statistically analyzed in the program *R* (R Core Team, 2017).

The pre-surgical MR data was analyzed in the freely available software *MRIcron* (Rorden & Brett, 2000). The T1-weighed MR images of all individuals in the study were re-aligned, co-registered and normalized in *SPM5* (Ashburner et al., 2009) according to the standard *Talairach space* (Talairach & Tournoux, 1988).

Then, manual lesion masking, which is the process of manually outlining the tumor on every slice, was performed in *MRIcron*. Further, the volumetric size was obtained by calculating the volume of each slice and summarizing the results to receive an overall tumor size in cubic centimeters. To identify brain areas affected by the tumor, marked lesions were projected onto the CJH average brain, a template based on 27 T1-weighed images by an individual named Colin (Holmes et al., 1998) and were then compared to the *Harvard Oxford Atlas* (Desikan et al., 2006) in *MRIcron*. A detailed overview of affected areas can be found in the *Appendix Part 5* next to individual MR images of the participants.

As many language subtests coming from three different language test batteries were conducted in the underlying experiment, there are no final three scores of these tests, but a high number of scores coming from subtests which makes a comparison of the individual's language abilities at the different points in time difficult. Therefore, it was decided to calculate an overall language score for each participant at each point in time. In other studies, the scores of different test batteries were normalized to obtain an overall score of language from zero to one (Saur et al., 2006).

Based on the score by Saur et al. (2006), the following formula for an overall language score was developed to compute a single score indicating the language abilities of one person at one point in time and to be able to further compare the linguistic abilities before and after surgery: overall language score (OLS) = $[(ACL_{RC} + ACL_{AC} + ACL_{PN} + ACL_{R} + ACL_{W} + ACL_{REP}) / 6 + ACL_{CFT} + (MEC_{TC1} + MEC_{TC2} + MEC_{TC3})/3 + MEC_{MC} + MEC_{SPS} + (ACL_{VFS} + ACL_{VFL} + RWT_{SCS} + RWT_{LCS}) / 4] / 6$.[5]

The formula was filled in with a normalized score based on the raw values in the tests. The use of the raw value was preferred over the converted value into grade of impairment because subtle changes in language can be better captured with the raw values.

To obtain this normalized overall language score, the subtests in the formula were each divided by their maximum score in the corresponding subtest. In the case of the MEC text comprehension task, where participants have to repeat parts of the text and receive points for the number of main ideas and number of ideas in total, only the number of main ideas was included, because including both aspects would be redundant, and because the presence of main ideas was considered to be more important for communication. In the subtest MEC metaphor comprehension, only the score for the definition of a metaphor was included in the formula, because the subtest where patients have to decide for one explanation between three written options was not performed with all patients. As the verbal fluency tasks of the ACL and RWT do not have a general maximum score and verbal fluency is highly age-

[5] RC = reading comprehension, AC = auditory comprehension, PN = picture-naming, R = reading, W = writing, REP = repetition, CFT = color-figure test, TC1 = text comprehension text parts, TC2 = text comprehension complete text, TC3 = text comprehension questions, MC= metaphor comprehension, SPS = spontaneous speech, VFL = verbal fluency lexical, VFS = verbal fluency semantic, SCS = semantic category switching, LCS = lexical category switching

dependent (Zimmermann et al., 2014), the age-dependent percentile rank in the RWT subtest was divided by 100 and then included in the formula, and the ACL maximum number of words was converted to the age-dependent score and then divided by ten, which is the maximum value.

The ACL color-figure test is placed outside the general ACL parenthesis, because it does not only measure auditory comprehension, but also mnestic abilities such as verbal working memory (Kalbe et al., 2002). The ACL verbal fluency tasks are separated from the ACL picture-naming subtest and joined with the RWT category switching tasks, because verbal fluency relies on executive functions (Aschenbrenner et al., 2000). Even though it is sometimes argued that category switching as a form of task-switching is closely related to cognitive flexibility as one of the key executive functions (Diamond, 2013) and may be even more sensitive to detect executive dysfunction (Narme et al., 2019), the tasks are very similar and therefore kept in the same parenthesis. The MEC subtest spontaneous speech was kept separate from other MEC subtests, as prior research has shown that the assessment of spontaneous speech is a valuable diagnostic tool to detect language impairments in individuals with brain tumors (Satoer et al., 2018). The MEC text comprehension and metaphor comprehension subtests require both receptive and productive abilities by asking the patient to listen to a story and repeat it or listen to a metaphor and explain it (Scherrer et al., 2016). As a result, it is argued that it is not a simple auditory comprehension task and should therefore not be treated equally with other auditory comprehension tasks in the ACL parenthesis. It rather fits pragmatic language, where executive processes are also assumed (Martin & McDonald, 2003). Another reason for keeping the MEC metaphor comprehension task separate is that one of the hypotheses of this thesis is that differences in language between left and right hemisphere tumor exist and such potential difference can then be better measured. As the right hemisphere is believed to be specifically involved in figurative language and text comprehension (Stemmer, 2015), the tasks were kept separate to sufficiently capture such potential difference.

4. Results

4.1 Demographic Results & Missing Data

In this chapter, the results from descriptive statistics are presented. In the succeeding chapters, the results in view of the other three hypotheses will be presented. All results are rounded to the nearest hundredth.

Out of 15 participants in total, seven underwent testing at three points in time, namely before (T1), shortly after surgery (T2) and a few weeks after surgery (T3). All 15 subjects were tested at T1. Nine of 15 subjects completed the testing at T1 and T2. Seven participated in the first and the third testing session. Reasons for dropping out of the study before completion of three test points were either that the subjects did not find the time for the testing or that they quit without giving further reasons.

At T1, the test results in auditory comprehension in the ACL is missing for one participant. Also at T1, the results in the MEC text comprehension task where questions have to be answered is not available for one subject. The results of these subtests in the following paragraphs are therefore reported for 14 instead of 15 persons. In the case of one participant who suffered from a severe language impairment, the ACL and RWT were performed, but the MEC was not feasible. Here, the subject received scores of zero in the MEC. At T2, the result of one participant in the ACL reading and reading comprehension task is excluded, because the test instructor read part of the sentences to the patient, thereby changing the task to an auditory comprehension task. In one other case at T2, the lexical category switching task of the RWT as well as parts of the text comprehension task of the MEC are missing. As a result, the test scores are reported for eight instead of nine persons. To simplify the identification of the participant number for the reader, the number will always be provided in the affected subtest. It is not documented why some subtests are missing. Upon inquiry, one of the principal investigators reported that the lack of audio- or video files of these subtests are probably a consequence of having either not recorded them in the first place or having lost the data.

The test date before surgery (n=15) ranged between one to up to six days before surgery (mean M=1.87, standard deviation SD= 1.46). Immediately after surgery at T2 (n=9), the language test batteries were conducted four to nine days after surgery (M=6, SD=1.5). The third test point (n=7) lay between 33 and 189 days after surgery (M=67.14, SD=54.87).

Participants had an age between 38 and 77 years (median MED=68, M=62.73, SD=11.69). Gender was distributed unequally among the 15 subjects with eleven men and four women (see *Figure 3).* The most frequent educational degree was secondary education II with a high school diploma or professional training in eight people, followed by six persons having completed secondary education I, which is only compulsory school, and one person holding a university degree as postsecondary or tertiary education.

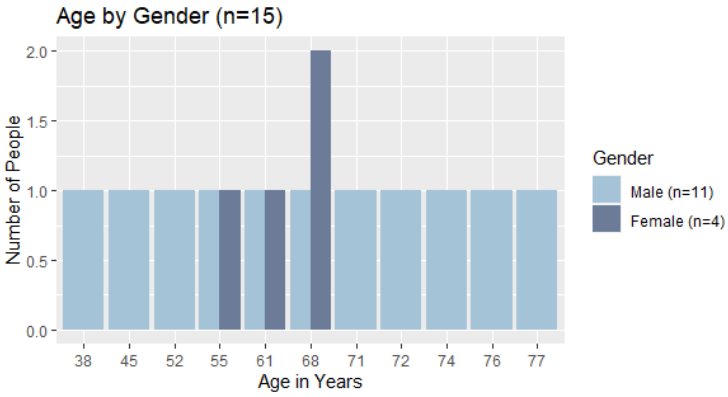


Figure 3: Age and Gender of the Study Group

Eleven of the 15 participants suffered from a primary brain tumor, while four had the diagnosis of a secondary or metastatic brain tumor. The primary brain tumors were meningiomas in four cases, five glioblastomas and one astrocytomas. One subject was diagnosed with a cavernoma. The participant with cavernoma was not excluded, as other studies concerning language in brain tumor patients such as Ilmberger et al. (2008) or Thiel et al. (2001) also included subjects with cavernoma into their subject groups, even though it is a benign cluster of small blood vessels (Mattle & Mumenthaler, 2017). Most subjects had a tumor of the left hemisphere (eleven out of 15), the remaining four tumors were localized in the right hemisphere. The majority of tumors in this study's subjects was localized in the frontal lobe with eight in 15 subjects, followed by three temporal, two fronto-parietal, and two parieto-occipital lobe tumors. The WHO grade ranged between I and IV, a grade for secondary tumors is not available. Among the primary brain tumors, the most common WHO grade was IV in five of 10 persons, followed by grade I in two cases and grade II three cases. The exact distribution of tumor type, hemisphere, WHO grade and lobe can be found in *Figure 4* and *Figure 5.*

participant	tumor type	lobe	hemisphere	WHO grade
1	meningeoma	frontal	right	II
2	glioblastoma	parieto-occipital	right	IV
3	meningeoma	frontal	left	I
4	metastasis	frontal	left	-
5	meningeoma	frontal	left	I
6	cavernoma	temporal	left	-
7	metastasis	frontal	left	-
8	meningeoma	frontal	left	II
9	glioblastoma	temporal	right	IV
10	glioblastoma	temporal	right	IV
11	glioblastoma	frontoparietal	left	IV
12	metastasis	frontoparietal	left	-
13	glioblastoma	frontal	left	IV
14	metastasis	parieto-occipital	left	-
15	astrocytoma	frontal	left	II

Figure 4: Participant Overview

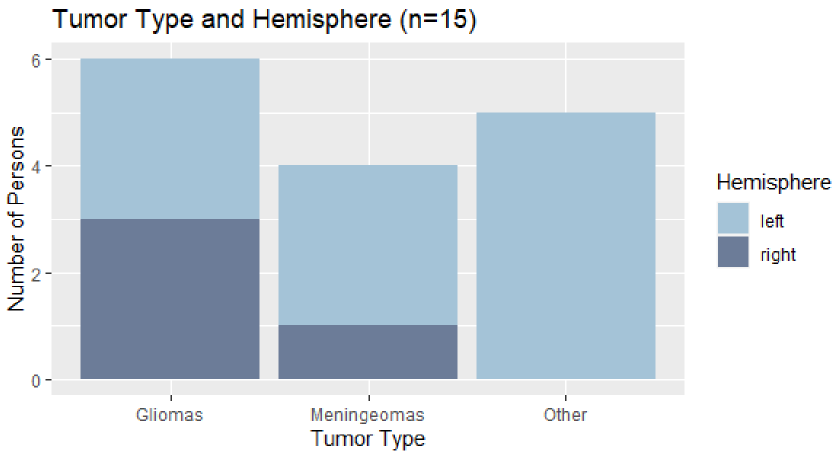


Figure 5: Participants' Tumor Type and Hemisphere

The tumors in the study group (n=14) before surgery had volumetric sizes between 0.96 and 82.44 cubic centimeters (cm^3), with a mean size of M=30.98 cm^3 and a median of MED=24.05 cm^3. An overview of WHO grade I to IV and tumor size in cm^3 can be found in *Figure 6*. Note that some tumors have the grade zero in the figure, because metastatic brain tumors are not assigned a WHO grade. In addition, the numbers are reported and displayed for 14 subjects only, because of one individual, only a post-surgical MR image was available. The MR image was identified as post-surgical, because it shows evidence of an osteoplastic trepanation with metal as osteosynthesis material, and because a dural contrast medium image typical of post-surgical MR, was taken.

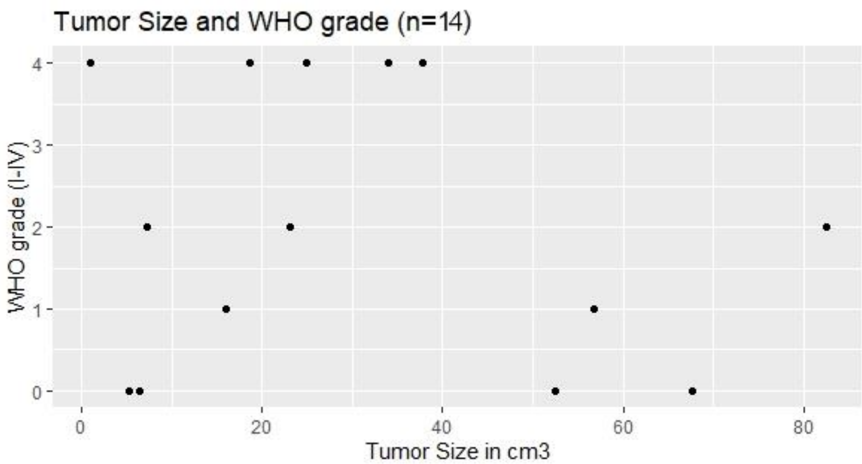


Figure 6: WHO Grade and Tumor Size

Detailed multislice MRI images of all participants can be found in the *Appendix Part 5*. In addition, lesion overlay images according to the affected hemisphere, projected onto the CHJ standard brain (Holmes et al., 1998), are located in the *Appendix Part 6*.

All subjects were right-handed in the EHI (Oldfield, 1971) with a laterality quotient between +40 and +100 (MED=90, M=81.99, SD=20.65). According to the FOP (Hupfeld, 2009), all 15 patients were oriented at T1 with scores ranging from 16 to 20 points (MED=20, M=18.8, SD=1.52, cut-off < 16). At T2, all nine subjects were oriented with 18 to 20 points (MED=19, M=19, SD=0.71). At the third point in time, the seven subjects scored between 17 and 20 points for orientation (MED=20, M=19.43, SD=1.13). In the NET (Fels & Geissner, 1997), the transformed results ranged between 0.94 and 1 (MED=1, M=1, SD=0.2) at T1 (n=15), which means that none of the participants were diagnosed with a neglect. At T2 (n=9), the subjects had results between 0.88 and 1 (MED=1, M=0.98, SD=0.4). At T3 information from one participant was missing(n=6), and the scores lay between 0.89 and 1 (MED=1, M=0.99, SD=0.01).

Before surgery, the 2-back paradigm of the NBV (Schellig & Schuri, 2009) was conducted in the test form S1 (n=10) or S2 (n=4), and the test is missing for one participant (in total n=14). A raw value, the percentile rank and t-value are available for the number of correct, wrong, and missing answers. Additionally, mean reaction times for correctness and errors as well as an overall processing time are calculated. In reference to Meule (2017) discussing the various results of n-back tasks and their interpretation, only the correctness and reaction times scores are reported and further used.

The number of correct answers ranged between zero and 14 (M=8.5, MED=9, SD=3.89), which translates to a percentile rank of correct answers of M=23.86 (MED=17, SD=24,45, range from two to 100) and correctness t-values of M=42.29 (MED=40, SD=11.78, range from two to 87). The mean reaction times are reported for n=13 because the data is missing for an additional person, where due to a software fault, no reaction times were assessed. Mean reaction times for correct answers were between 0.524 and 1.287 milliseconds (M=0.864, MED=0.852, SD=0.193), which indicates a mean reaction time percentile rank for reaction times of correct answers of M=34.23 (MED=23, SD=24.22, range from four to 81) and t-values of M=44.92 (MED=43, SD=7.67, range from 32 to 59).

Immediately after surgery, the NBV S1 test form was conducted in 8 of 9 cases and one subject's results are missing (n=8). The scores lay between five and elven correct answers (M=9.67, MED=10, SD=1.89), which is a percentile rank of correctness of M=21.78 (MED=23, SD=8.05, range from six to 29) and t-values between 39 and 43 with M=41.67 (MED=43, SD=3.23). Mean reaction times for correct answers were M=0.896 (MED=0.956, SD=0.197, range from 0.588 to 1.228), indicating percentile ranks of M=33.56 (MED=19, SD=27.77, range from five to 87) and t-values of M=44.56 (MED=41, SD=9.25).

Since the just reported numbers are based on different sample sizes, the correct results for the nine individuals who completed the test at both times are summarized in the following *Figure 7*, resulting in a mean percentile rank of 31.11 (MED=23, SD=27.18) before and 21.78 (MED=23, SD=8.05) after surgery, a mean t-values of 45.78 (MED= 42, SD= 12.94) pre- and 41.67 (MED=43, SD=3.23) post- operatively, as well as mean reaction times of 0.9242 milliseconds (ms) (MED=0.9320, SD=0.1820) before and 0.8764 ms (MED=0,9560, SD= 0.1973) after tumor resection.

subject	T1			T2		
	percentile rank	t-value	reaction times (ms)	percentile rank	t-value	reaction times (ms)
1	29	44	1.287	23	43	0.588
2	17	40	1.085	6	34	0.989
3	4	32	1.026	15	40	1.055
4	27	44	0.852	13	39	1.228
5	23	43	0.768	29	44	0.956
6	13	39	0.962	29	44	0.911
7	100	80	0.727	23	43	0.713
8	17	40	0.932	29	44	0.988
9	50	50	0.679	29	44	0.640

Figure 7: NBV Results at T1 and T2

4.2 Pre- and Post-Surgical Language Impairments

Now, the results from the standardized language tests before (T1, n=15) and shortly after surgery (T2, n=9) are presented. T3 will not be further be described, because it is not related to any hypotheses from the thesis and provides little information given the small number of participants who performed the tests at all three points in time. Whenever data is missing, it will be described. First, the general occurrence of impairment in the different language tests will be depicted, then a description of the results in the subtests will be given.

Some of the subjects could be considered as outliers, because their scores were much lower or higher than the mean of their group. Nevertheless, they were not removed from the subsequent statistical analysis, because the study is concerned with persons with language impairments which can range from mild to severe impairments. Excluding these subjects would mean that the presented results would present a picture of only more severe or only more mild language impairments, even though both can be true. Moreover, it was ensured through strict inclusion- and exclusion criteria such as checking for disorientation and the presence of neglect that the results would be comparable. The median (MED) will be reported for the results, as it is more robust to outliers.

In general, most subjects (nine in 15 participants) were impaired in two modalities of language in the ACL at T1 (n=15), the modalities being comprehension, naming and verbal fluency as one, reading and writing joined, and repetition. Three participants were impaired in three, one person in four and one subject in only one modality of language. The number of impaired modalities in the ACL is missing for one participant, where a subtest of the ACL is missing, but the available data of this person shows an impairment in at least two modalities. None of the participants were unimpaired in all modalities of language. At T2 (n=9), most subjects (four persons) had an impairment of two modalities of language in the ACL, followed by an impairment in three modalities (two persons) or only one modality (two per-

sons). Similar to before, a subtest is missing for one participant whose available data suggests an impairment in at least two language modalities. None of the nine participants had zero impaired language modalities.
In the three subtests of the MEC at T1 (n=15), namely text comprehension, metaphor comprehension and spontaneous speech analysis, most participants (nine persons) were impaired in two of the three subtests. Further five were even impaired in all three subtests. No one had an impairment of only one subtest, but one subject was unimpaired in all three subtests. At T2 (n=9), the majority of persons (five participants) was impaired in two MEC subtests and less persons (three subjects) in three subtests. For one subject, text comprehension is missing, but the subject is unimpaired in the other two subtests.
The RWT does not offer a grading into impairment, but a percentile rank less or equal to 40 was found in 12 in 15 participants in semantic, and in 11 in 15 in lexical category switching before surgery. After surgery, a percentile rank less or equal to 40 was found in eight of nine participants in semantic, and in 6 of 9 in lexical category switching.
In the ACL color-figure test at T1 (n=15) (see *Figure 8),* participants reached a mean score of 16.27 out of 20 points in total (SD=3.67, MED=18), which translates to no impairment in two cases, a mild impairment in eleven subjects, and a moderate and severe impairment each in one participant. Thus, the majority of 87% was impaired in the color-figure test at T1. At T2 (n=9), subjects reached a mean score of 17.33 of 20 points in total (SD= 1.22 , MED=18), thereby one subject showed no impairment while seven persons were mildly and one person moderately impaired. No severe impairments were found. This result means that the majority of 89% had an impairment in the color-figure test at T2.

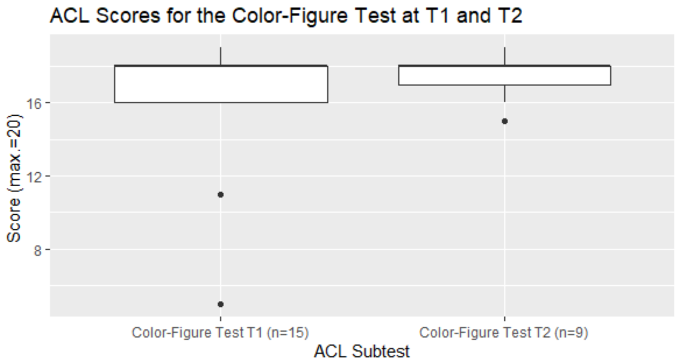


Figure 8: ACL Color-Figure Test at T1 and T2

In the semantic verbal fluency task in the ACL at T1 (n=15) *(see Figure 9),* between zero and 30 words with a mean of 14 words were generated by the participants (SD= 8.25, MED=15). The number of words indicates no impairment in four cases, five subjects with a mild, four with a moderate and two with a severe impairment. Consequently, 73% had at least a mild impairment. At T2, the participants (n=9) named between five and 23 words

(mean M= 16, SD=6.10, MED=16). The semantic verbal fluency of three persons was unimpaired, two were mildly and four moderately impaired. No severe impairments were detected at T2. To summarize, 66% of subjects had an impaired semantic fluency at T2.
In the lexical verbal fluency task of the ACL *(see Figure 9),* between zero and 16 words (M= 6.93, SD= 4.85, MED=7) were generated at T1 (n=15). with two unimpaired, one mildly, nine moderately and three severely impaired persons. This results in a total of 87% impairment in lexical verbal fluency at T1. At T2 (n=9), a range of naming three to sixteen words was found (M=6.89, SD=4.31, MED=5), with two unimpaired and seven moderately, but no mildly or severely impaired persons. Thus, the majority of 78% exposed an impairment in the lexical verbal fluency task at T2.

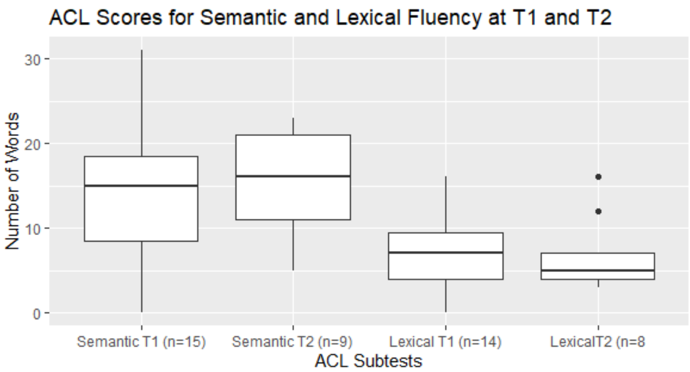


Figure 9: ACL Verbal Fluency

Between four and the total of 18 pictures (M= 15, SD=3.48, MED=16) were correctly named in the picture-naming test of the ACL at T1 (n=15) (see *Figure 10).* Eight persons had no impairment, followed by five with a mild, one with a moderate and 1 with a severe impairment. The minority of 47% was impaired in picture-naming at T1. At T2 (n=9), the number of correctly named pictures ranged between 15 and 18 (M=16.56, SD=0.88, MED=17). Thus, eight in nine persons (89%) were unimpaired in picture-naming at T2.
In the repetition subtest of the ACL (see *Figure 10),* subjects (n=15) reached a score between 13 and the maximum of 18 (M= 17.33, SD=1.29, MED=18). Only one participant (7%) had a severe impairment, all other participants were unimpaired (93%). No mild or moderate impairment was found. The repetition at T2 reached a mean score of M=17.89 (SD=0.33, MED=18), with a minimum of 17 and a maximum of 18 points reached by the participants (n=9). This means that all nine participants were unimpaired.

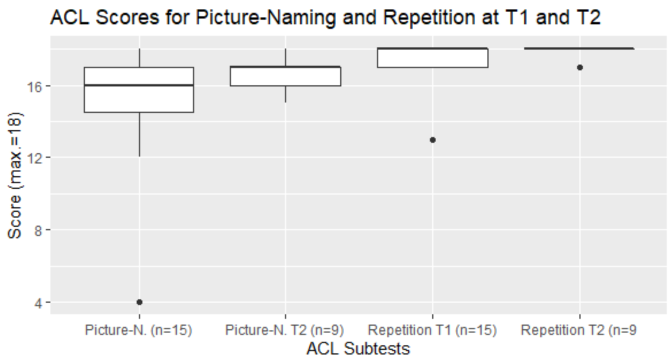


Figure 10: ACL Picture-Naming and Repetition

Of 18 words to be read aloud in the ACL (see *Figure 11),* between six and 18 words (M=17.13, SD=3.09, MED=18) were correctly read at T1 (n=15). 14 out of 15 showed no impairment of reading and one person was severely impaired. Hence, 93% were unimpaired in reading aloud at T1. At T2, in the case of one participant, the instruction was read to the patient by the conductor instead of letting them read by themselves and choose the picture accordingly. As a result, both reading aloud and reading comprehension of this subject was excluded from the analysis. Therefore, of eight instead of nine participants at T2, all participants were unimpaired with a maximum of 18 points.

In the writing task of the ACL (see *Figure 11),* subjects (n=15) scored a mean of M= 14.13 points (SD=5.93, MED=17) within a range of zero to the maximum of 18 points. Ten participants were unimpaired, a mild and moderate were each found once. A severe impairment was identified in three cases. Thus, the minority of 67% was unimpaired. At T2, one participant cancelled the writing subtest due to motoric struggle when writing. Only half of the subtest was therefore conducted. As the complexity of items rises with the later part of the subtests and the data is not available, the complete subtest of this participant was excluded. Therefore, the reported results of writing are based on n=8 instead of n=9 at T2. Between 13 and 18 points were reached with a mean of M =16.88 points (SD =1.73, MED=17.5). Six participants showed no impairment, while one had a mild and one a moderate impairment. No severe impairments were diagnosed. The majority of 75% were unimpaired.

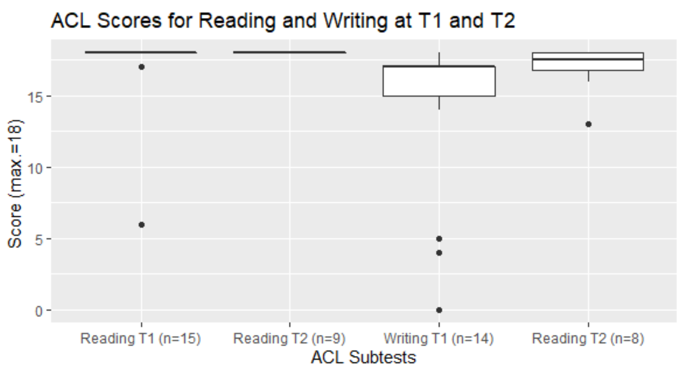


Figure 11: ACL Reading and Writing

In auditory comprehension of the ACL at T1 (see *Figure 12),* the data of one participant is missing. Thus, the results are reported for n=14 instead of n=15. The number of correct answers ranged from ten to 18 with a mean of 16.50 points (SD=2.34, MED=17.5). Ten participants where unimpaired, two had a mild, one a moderate and one a severe impairment, thereby resulting in a minority of 28% being impaired. At T2, all scores are available for auditory comprehension (n=9). The maximum points ranged between 17 and the total score of 18 with a mean of M=17.67 points (SD=0.5, MED=18). All nine participants exposed no impairment.

The mean score in reading comprehension in the ACL at T1 (n=15) (see *Figure 12)* amounted to M= 14.6 (SD=3.81, MED=15) with a range from two to 18 correct answers. Four persons were unimpaired, each five had a mild or moderate and one a severe impairment. Consequently, 73% of subjects had at least a mild impairment. Again at T2, reading comprehension was calculated based on the eight subjects where the test was performed correctly. Between 14 and 18 points were reached with a mean of M=15.88 points (SD= 1.73, MED=16). Three persons had no impairment, two were mildly and three moderately impaired. No severe impairments were found. To summarize, 63% showed an impaired reading comprehension at T2.

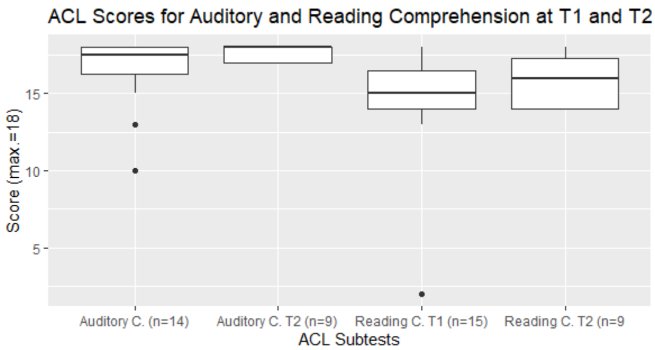


Figure 12: ACL Auditory and Reading Comprehension

In the RWT semantic category switching at T1 (n=15) (see *Figure 13*), a mean of M=12.27 words (SD=7.50, MED=15) were named, with a minimum of zero and a maximum of 21 words. These scores translate to a percentile rank ranging between zero and 85 with a mean percentile rank of M=24.80 (SD=28.60, MED=17). In the lexical category switching task at T1 (n=15) (see *Figure 13*), between zero and 29 words were named with a mean of M=12.93 words (SD=7.68, MED=12). This means that the percentile rank ranges from one to 99 with a mean of M=27.33 (SD=30.86, MED=13). At T2 (n=9), the mean value for semantic category switching was M=14.89 words (SD=3.10, MED=14) within a range from 12 to 20 words. These results indicate percentile ranks from zero to 51 with a mean of M=24.89 (SD=16.60, MED=25). In the lexical category switching task at T2, data was missing from one participant (n=8), and the means score was M=16.50 (SD=10.27, MED=15) within two to 34 words. The percentile rank was between zero and 100 with a mean of M=34.88 (SD=41.34, MED=20.5).

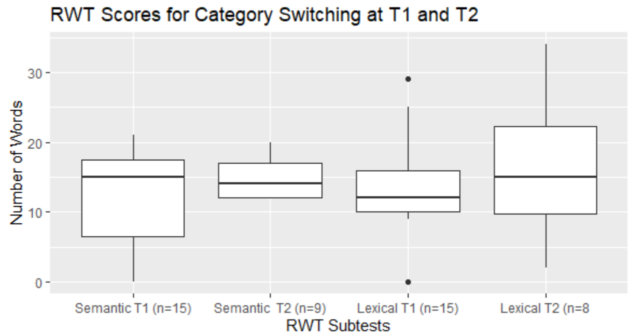


Figure 13: RWT Semantic and Lexical Category Switching

In the RWT semantic switching task at T1 (n=15), zero to three repetitions (M=1.33SD=1.35, MED=1) and zero to six breaches of rules (M=0, SD=1.85, MED=0) occurred. Zero to one category error (M=0.13, SD=0.26, MED=0) and zero to one perseveration of category (M= 0.13, SD=0.35, MED=0) were found. At T2 (n=9), zero to five repetitions (M=1.56, SD=1.94, MED=1), zero to four breaches of rules (M=1.33, SD= 1.66, MED=1), zero to four category errors (M=0.44, SD=1.33, MED=0) and zero to four category perseverations (M=0.67, SD=1.32, MED=0) were found.

In the RWT lexical switching task at T1 (n=15), repetitions ranged between zero and seven (M=1.20, SD=1.90, MED=1), zero to seven breaches of rules (M=1.53, SD= 1.88, MED=1), zero category errors and zero to 2 category perseverations (M=1.33, SD=0.52, MED=0) occurred. At T2, the data of one participant in the lexical switching task is missing. As such, zero to eight repetitions (M=1.5, SD=2.67, MED=1), zero to four breaches of rules (M=1.63, SD=1.41, MED=1.5) as well as zero category errors and zero category perseverations were observed at T2 (n=8).

In the first part of the MEC text comprehension subtest at T1 (n=15) (see *Figure 14*), where parts of a text are retold, out of a total of 17 points indicating the presence of central ideas when retelling the story, the number of central ideas ranged between zero and 16 points (M= 8.87, SD=5.08, MED=9). The mean number of not only central, but total information was M=12.27 points (SD= 6.88, MED=13) with a range from zero to 23 of totally 30 points. A conversion of these points to levels of impairment do not exist. The results of the first MEC text comprehension task at T2 (n=9) show a range of 8 to 15 of a total of 17 points with a mean of M=11.89 points (SD=2.20, MED=12) for the presence of central ideas, as well as a mean of M=17.22 points (SD= 3.42, MED=18) ranging between 12 and 23 of in total 30 points for number of total information.

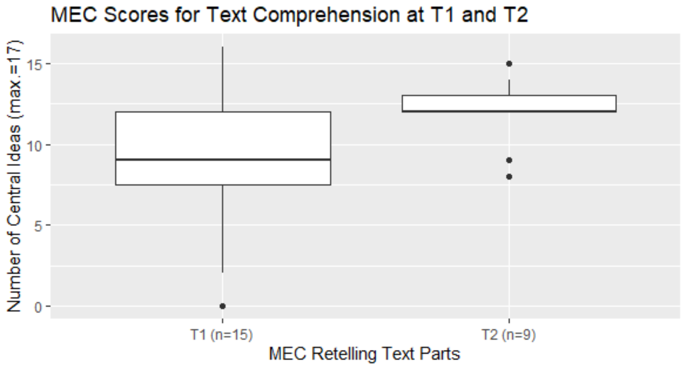


Figure 14: MEC Retelling Parts of a Text

In the second part of the MEC text comprehension at T1 (n=15) *(see Figure 15),* where the whole text is retold, participants retold between zero to the test's maximum of 17 main ideas (M=7.93, SD=4.10, MED=7). This translates to unimpaired text comprehension in eight (53%) out of 15 participants. A grading into the severity of impairment does not exist for this test. At T2, the data of one participant was missing, and the remaining subjects (n=8) had scores between seven and 13 of in total 30 points (M=9.88, SD=2.03, MED=9.5) for retelling the complete text. This converts to four of eight persons being unimpaired and four being impaired.

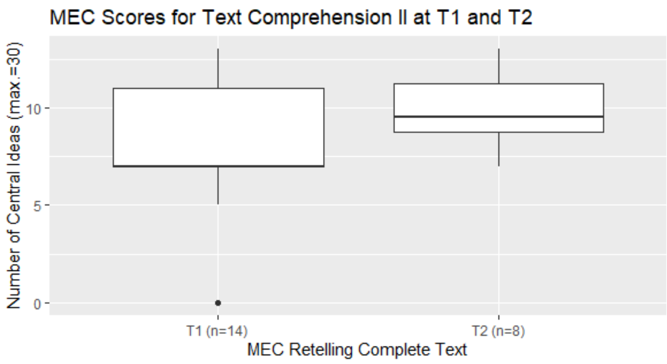


Figure 15: MEC Retelling the Whole Text

The third part of the MEC text comprehension task at T1 includes giving a title and answering questions to a text. The data of this subtest was missing for one person (n=14). The mean score for coming up with a title was M=1.50 points (SD=0.76, MED=10) within a range from zero to the maximum score of two. Most participants earned the total score of two (65%), only 21% received one point and 14% no points. The score is not transferable to a grading indicating the impairment or severity of impairment. At T2, the data is based on n=8, because the data is missing for one participant. The remaining subjects (n=8) received between zero and two of in total two points for naming a title with a mean of M= 1.38 points (SD=0.92, MED=9.5). Most participants, namely five in eight, earned the total of two points. Meanwhile one received only one point and the remaining two subjects received zero points. When answering the questions about the text at T1, zero to twelve answers were correct

(M=9, MED=10, SD=4.10), meaning that only 36% were impaired. At T2, 62% were impaired in giving correct answers with a score between eight and 12 (M=9.63, MED=9.50, SD=1.60).

The MEC metaphor comprehension test (see *Figure 16*) results is based on 15 participants at T1. The mean score for understanding new metaphors was M=12.27 points (SD=5.44, MED=13), with results ranging from one to 19 of in total 20 points, and for old metaphors M=12.53 points (SD=5.97, MED=13) with a range from zero to the maximum of 20. In the combined score for understanding old and new metaphors with a maximum of 40 points, the participants received a mean result of M=24.08 points (SD=10.96, MED=27), ranging from one to 37 points. When converted, these results indicate no impairment in three persons (27%) and an impairment in eleven persons (73%). At T2, the participants (n=9) reached between ten and 19 of in total 20 points (M=13.67, SD= 2.5, MED=14) for their comprehension of new metaphors and between seven and 19 of 20 points (M=14, SD=3.84, MED=15) for old metaphors. For the complete metaphor comprehension task, the mean was M=23.67 points (SD=5.94, MED=30) with results between 17 and the total of 34 points. Seven out of nine subjects where therefore impaired, and only two unimpaired.

The second metaphor comprehension score, where participants must choose between three alternatives of meaning for a metaphor, will not be reported or further used for analysis. The reason for this is that the instructor can either present it to the tested person regardless of their explanation or only when the explanation is insufficient. Thus, if the instructor perceives the explanation to be sufficient and does not ask for choosing among the alternatives, the participant automatically receives the highest point. However, the employment was differing between the two instructors.

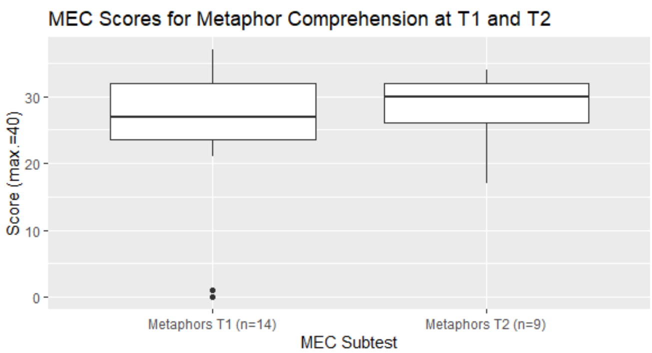


Figure 16: MEC Metaphor Comprehension

In the MEC spontaneous speech analysis at T1 (see *Figure 17),* the mean score was M=30.87 points (SD=3.85, MED=32) of in total 34 points, with participants (n=15) scoring between 21 and 34 points. After conversion, these results indicate an impairment in eleven persons (73%) and no impairment in the other four persons (27%). The subjects at T2 (n=9) showed scores between 26 and 34 points with a mean of M=31.11 points (SD=2.85, MED=32) in spontaneous speech. Thus, seven in nine persons (78%) had an impairment, leaving two persons (22%) without an impairment.

Types of errors in the spontaneous speech analysis at T1 were in descending occurrence: repetitions of what was already said (six persons), imprecise expression of thoughts (five persons), missing self-corrections (five persons), looking for words (four persons), extensive talking (three persons), decelerated speech (three persons), the use of incorrect words (three persons), interrupting the communicative partner (three persons), deviations from the topic or sudden topic changes (two persons), accelerated speech (two persons), talking without a common theme (two persons), reduced verbal drive (one person), not understanding a question (one person), and talking with a monotone voice (one person).

At T2, the most common errors were repetitions of what was already said (four persons), extensive talking (four persons), the use of incorrect words (three persons), imprecise expression of thoughts (three persons), looking for words (two persons), missing self-corrections (two persons), deviations from the topic or sudden topic changes (one person), talking without a common theme (one person), accelerated speech (one person), not understanding a question (one person), and reduced verbal drive (one person).

Unexpected or inadequate comments, indifference towards humor, and reduced understanding of indirect speech did either not occur or were not present in the conversation at T1 and T2. Judging the facial expression and eye contact for their accuracy is not possible at both points in time, as the spontaneous speech was recorded as an audio file.

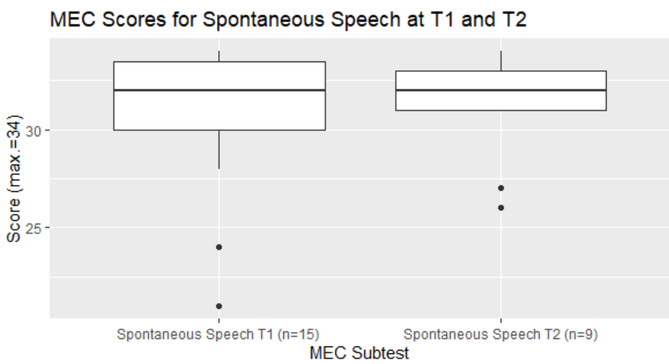


Figure 17: MEC Spontaneous Speech Analysis

To give a comprehensive overview of the distribution of impairments across the different modalities and to display the severity within these modalities before surgery, the results were also plotted as a heatmap *(see Figure 18)* with the color dark blue indicating normalized low scores in the tests, very light blue standing for scoring high in the tests, and white for missing data (the latter in the case of participant 10 for MEC MC and participant 1 for ACL AC).

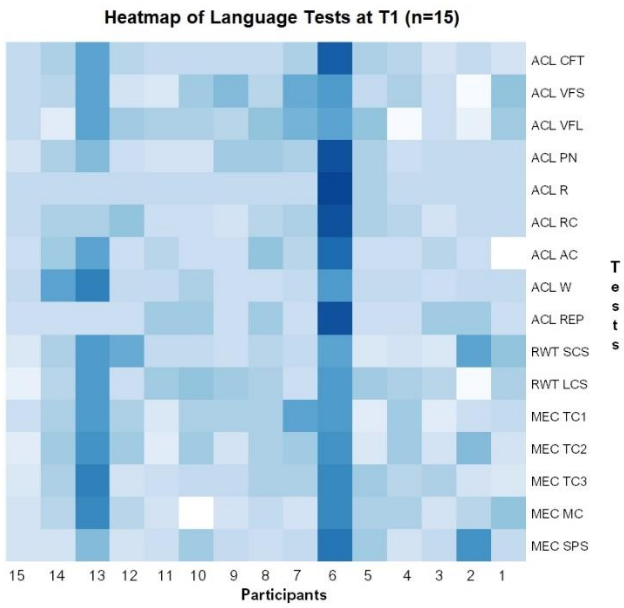


Figure 18: Heatmap of Impairment at T1[6]

To summarize, the subtests in the ACL at T1 (n=15) with least impairments were repetition and reading (in both subtests all subjects were unimpaired except for one with a severe impairment), followed by writing, auditory comprehension, picture-naming, reading comprehension, semantic and lexical verbal fluency as well as color-figure test in descending order (see *Figure 19*). The percentile rank of the RWT (n=15) was below 25 in the majority in the semantic (10 persons) and lexical category (nine persons) switching task. The MEC subtests (n=15 except answering questions n=14) with least impairments was answering questions in text comprehension (nine unimpaired), followed by retelling the whole text (seven unimpaired), metaphor comprehension (four unimpaired) and spontaneous speech (four unimpaired).

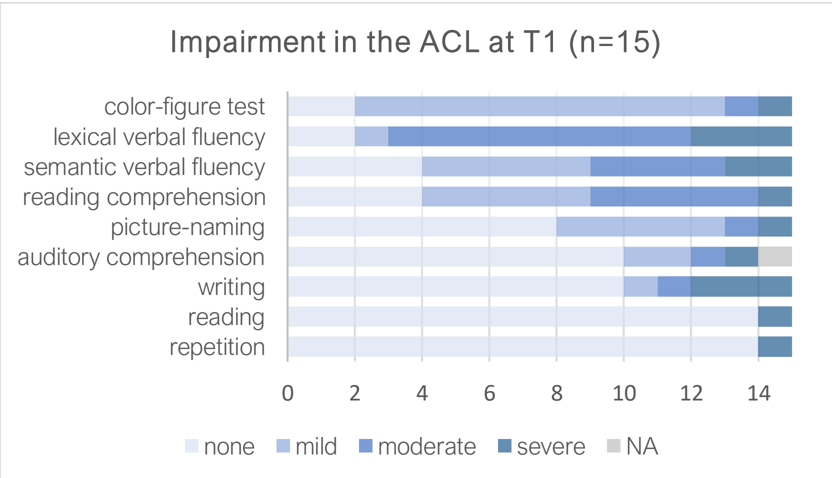


Figure 19: Overview of ACL at T1

[6] RC = reading comprehension, AC = auditory comprehension, PN = picture-naming, R = reading, W = writing, REP = repetition, CFT = color-figure test, TC1 = text comprehension text parts, TC2 = text comprehension complete text, TC3 = text comprehension questions, MC= metaphor comprehension, SPS = spontaneous speech, VFL = verbal fluency lexical, VFS = verbal fluency semantic, SCS = semantic category switching, LCS = lexical category switching

At T2 in the ACL (n=9) (see *Figure 20),* all subjects were unimpaired repetition, reading and auditory comprehension, followed by the subtests indicating least impairments in descending order in picture-naming, writing, reading comprehension, semantic and lexical verbal fluency and the color-figure test. In the RWT (n=9 except n=8 for the lexical subtest), the percentile rank was 25 or below in four persons each in the semantic and lexical category switching task. Least impairments in the MEC (n=9 except n=9 for answering questions) were found in retelling the whole text (four unimpaired), answering questions about the text (three unimpaired), metaphor comprehension (two unimpaired) and spontaneous speech (two unimpaired).

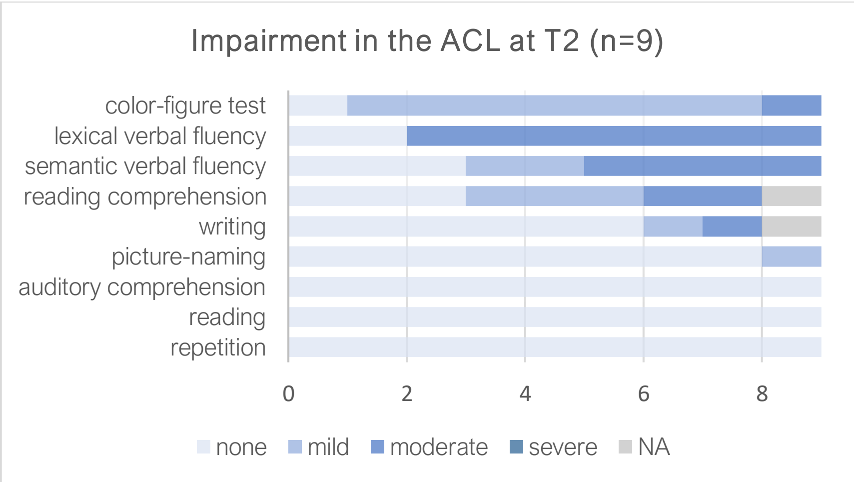


Figure 20: Overview of ACL at T2

The results described up to this points and *Figure 19* and *20* should not already be mistakenly interpreted as an improvement of language from T1 to T2, because the results are based on a different number of subjects and it cannot be ensured that the participants not present at T2 really do show an improvement. Consequently, the available language tests of six persons will be further compared, which were present at both points in time and where all subtests are available.

To test whether the subject group improved or deteriorated in their language immediately after surgery, the overall language score composed of several subtests was compared for T1 and T2. Accordingly, a Wilcoxon signed rank test was performed. It is a non-parametric test which allows the comparison of the mean of two related conditions (Field et al., 2012). Results with $p<0.05$ are significant and $p<0.01$ highly significant. Due to the fact that 15 participants completed the testing at T1, but only nine of these 15 appeared for the testing at T2, and values from two subjects were missing at each point in time, the Wilcoxon signed-rank test was performed on the overall language score of six participants at T1 and T2. The overall language score at T1 was M=0.77 (SD=0.07) and at T2 M=0.75 (SD=0.07) (see *Figure 21*). To get a better overview over the performance of these 6 subjects whose results were up to now only reported within the bigger group, consult the *Appendix Part 3* for detailed results. The assumption of symmetry as a precondition for the Wilcoxon signed rank test was checked and given. The result of the Wilcoxon signed rank test was non-significant with p=0.69. Consequently, even though the group's mean performance at T2 was slightly lower than at T1, the difference was non-significant. Thus, no significant deterioration in language abilities was observed shortly after surgery.

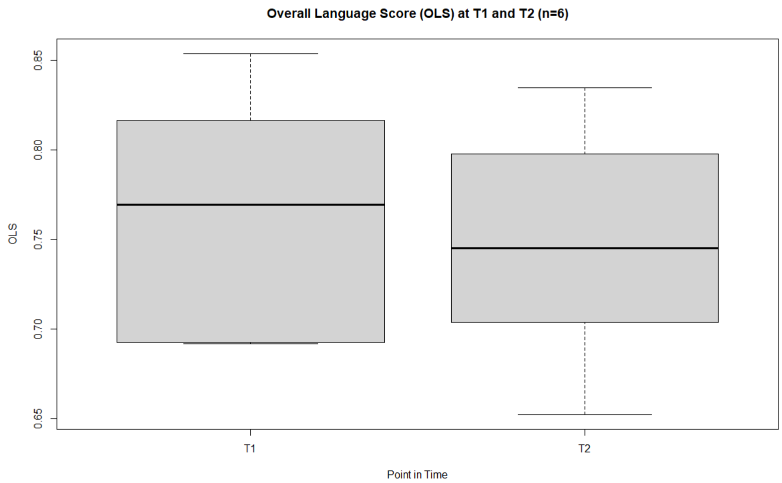


Figure 21: Comparison of OLS at T1 and T2

On a closer look at the individual level, however, a change of language to the worse can be described in the six participants, out of which all but one had more impaired subtests and the same or more moderate or severe impairments shortly after surgery in comparison to before surgical resection (consult *Appendix Part 3*).

Due to the high number of individuals with frontal lobe tumors in the study group, namely eight out of 15 persons, the results of the frontal group were separately analyzed too to identify the role of executive functioning for the overall result before surgery. As a detailed analysis and description of all subtests would go beyond the scope of this work, only the results in verbal fluency, spontaneous speech, metaphor and text comprehension and the color-figure test for T1 are reported, the reason being that those were the subtests with most impairments in the overall study group.

At T1 (n=8), 75% of individuals with frontal lobe tumors were impaired in the color-figure test and scored between 15 and 19 points (maximum score=20, mean M=17, median MED=17, SD=2.60). Semantic verbal fluency was impaired in 87% of subjects with three to 19 named words (M=12.88, MED=15, SD=6.20). In the lexical verbal fluency task, 87% of participants had an impairment with a generation of zero to 16 words (M=6.25, MED=4.50, SD=5.15). The score in the spontaneous speech analysis lay between 28 and the maximum of 34 points (M=31.88, MED=32.00, SD=2.03), which points to an impairment in 75% of cases. Metaphor comprehension scores ranged from zero to 37 out of the total of 40 points

(M=24.12, MED=24.50, SD=11.39), which indicates an impairment in 75% of subjects. In the text comprehension test where the complete text is retold, 38% were below the cut-off score with zero to 13 points (M=8.63, MED=9.50, SD=4.17). Finally, when answering questions about the text, half of the participants were disordered with a score between zero and 12 points (M=9.0, MED=10.0, SD=4.10).

Last but not least, a linear regression with the overall language score as dependent and the NBV correctness raw score as the predictor variables was performed to check whether a higher score in the NBV indicating working memory as an executive function would predict higher scores in language. The results are reported for n=12, because one participant's NBV results are missing and two other participants do not have an overall language score due to missing subtests. The result shows that the NBV correctness raw score is a significant predictor (p=0.04) of the overall language score at T1 (see *Figure 22*). For every 1% increase in the NBV raw score, there is a 0.02% increase in the overall language score. Then, the model fit was checked. The adjusted R-squared value of 0.2875 indicates that only 28.75% of variation in the overall language score before surgery can be explained by the model.

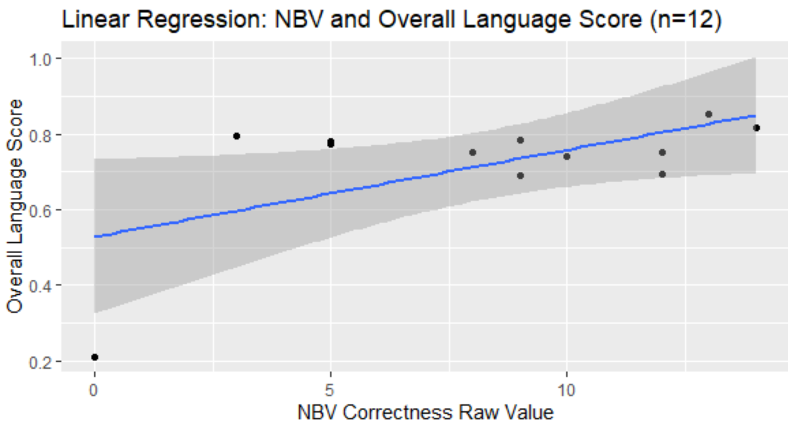


Figure 22: Linear Regression of NBV and OLS

The influence of correctness measures on the overall language score after surgery was not calculated, as the NBV values and the overall language score were only available for seven persons (see chapter 4.4 for further discussion about the role of subject size in regression).

4.3 Comparison of Left and Right Hemisphere Tumors

Due to the highly differing number of left- and right hemisphere tumor patients, their exact tumor diagnosis, WHO grade and differences in age, gender and education, it was not possible to divide the subjects into two comparable groups of similar size. Consequently, instead of statistically comparing a left- with a right hemisphere tumor group, it was decided to contrast three pairs of two persons each with tumors of either the left or the right hemisphere with similar demographics and selectively compare their language abilities. Three pairs were identified, none of the remaining subjects were similar enough for such comparison. The demographic information well as language abilities of these pairs are now reported.

The first participant (male, 52 years, secondary education I, right frontal meningioma grade II, 82.44cm^3), henceforth named participant F-RH (frontal, right hemisphere), was compared to the third participant (male, 45 years, secondary education I, left frontal meningioma grade I, 16.05cm^3) who is now called participant F-LH (frontal, left hemisphere) (see MR images in *Figure 23*). Here, only the tumor grade was different. The results of this comparison are reported in detail in the following paragraphs, as this pair exposed most demographic similarities.

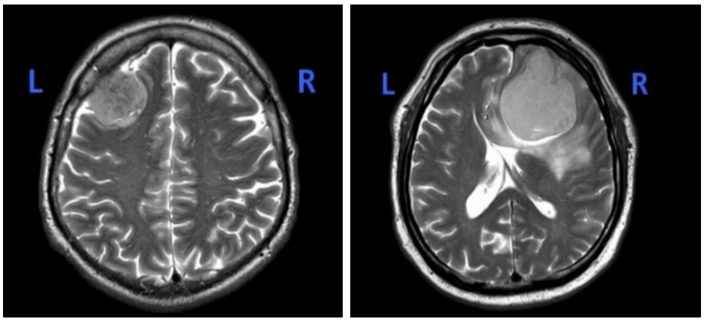


Figure 23: T2-weighted MR image of F-LH (left side) and F-RH (right side)

A comparison of F-LH and F-RH at T1 (see *Figure 24* and *Appendix Part 4)* shows that F-LH had a lower number of impaired subtests (F-LH 4 and F-RH 5) and less moderate or severe impairments (F-LH 1, F-RH 2). Both participants were unimpaired in the ACL color-figure test (both 19 out of 20 points), picture-naming (both 16 out of 18 points), reading (both 18 of 18 points) writing (participant F-RH 17 and participant F-LH 18 out of 18 points) and repetition (participant F-RH 18 and participant F-LH 17 out of 18 points). Participant F-RH was more impaired in the ACL semantic verbal fluency task (10 words, moderate impairment) than participant F-LH (19 words, mild impairment). More specifically, F-RH repeated the generic term “food” and exposed one semantic neologism “Auswärtsgeräte” (“devices for outside”), while F-LH’s performance was characterized by repetitions or unusual generic terms like “Kaffezubehör” (“coffee equipment”). In the lexical verbal fluency task F-RH named less words (five words, moderate impairment) than F-LH (10 words, moderate impairment), but both results reside within the same grade of impairment. Here, both named very few but correct words. Participant F-LH was unimpaired in auditory comprehension subtest (17 out of 18 points), and the subtest was missing for participant F-RH. In the reading comprehension task F-RH had a mild impairment (16 out of 18 points) because of the number of self-corrections after wrongly choosing the distractor image and F-LH was unimpaired (18 points).

At T1, participant F-LH exposed more errors (three repetitions) in the RWT semantic category switching task than participant F-RH with one repetition. Similarly, participant F-LH made more breaches of rules (seven) than participant F-RH with one breach of rules. In the lexical category switching task, the committed errors were one repetition by F-RH and three by F-LH. No other errors occurred. Participant F-RH named only nine words in the semantic and 12 in the lexical category switching task, while participant F-LH named 21 and 15.

In the MEC text comprehension test at T1, participant F-RH and F-LH were both unimpaired in retelling the whole story with 11 points each out of a total of 13 points. Both committed the same errors, namely the omission of central information. Other types of errors were not observed. When retelling parts of the story, which cannot be transferred to a severity grade, participant F-RH offered less central ideas with 11 points than participant F-LH with 16 out of a total of 17 points, and also a lower number of total information with 17 out of 30 for F-RH and 23 out of 30 for F-LH. F-RH's retelling of the text was characterized by omissions, while F-LH additionally change some of the information. Participant F-RH answered less questions about the text correctly with a score of 7 (impaired) than participant F-LH with 12 correct answers out of 12 (unimpaired). When looking at the errors in more detail, F-RH had difficulties in coming up with a short title ("Wie ich es schaffte einen Brunnen zu graben mit einer List, doch nicht zu graben", "How I managed to dig a well with a trick not to dig it at all") and judged a situation of the text incorrectly (question by the instructor: "Do you think that the neighbors will be happy?" [after being tricked into digging the well for the farmer], answer by F-RH: "Yes, I think the luck will be that Michael was not in there").

Participant F-RH was better in the MEC metaphor comprehension task with 37 out of 40 points, which is unimpaired, while participant F-LH reached only 25 points, which indicates a mild impairment. F-LH's explanations of the metaphors were characterized by imprecise definitions, referral to the literal meaning of the metaphor and the addition of unnecessary information. For instance, when having to explain the metaphor "Die Frauen sind fleißige Bienen" ("The women are busy bees"), F-LH referred to the literal meaning by saying "Speziell wenn die Frauen beim Apfel ernten, Ribisel ernten […] sagt man, das ist ein Bienenstock" ("Especially when women harvest apples, currant […] one says this is a beehive"). An example of his addition of unnecessary information when having to explain "Das Lexikon ist eine Goldgrube" (literal: "The lexicon is a gold mine", figurative: "The lexicon holds a lot of information") was "Ich würde sagen, dass irgendwo in einer Stellage ein Buch steht, das für einen bestimmten Menschen wichtig ist, dem er viel Information entziehen kann" ("I would

say that there is a book in some rack that is important for a specific person and where they can get a lot of information"). It appears that the information that the book is in a certain rack or that it is important to someone, is not relevant to the explanation of the metaphor.
In the MEC spontaneous speech analysis, both participants received 32 points which indicates an impairment. F-RH made repetitions and interrupted the communication partner, F-LH had mild difficulties finding words with conduit d'approche ("Wenn es mich nicht täuscht war es die Südsteiermark, ähm, mit Oliven... ah, nicht Olivenöl… Kernölpresserei" ("If I am not mistaken, it was South Styria, ehm, with olives.. eh, not olive oil.. pumpkin seed oil press").

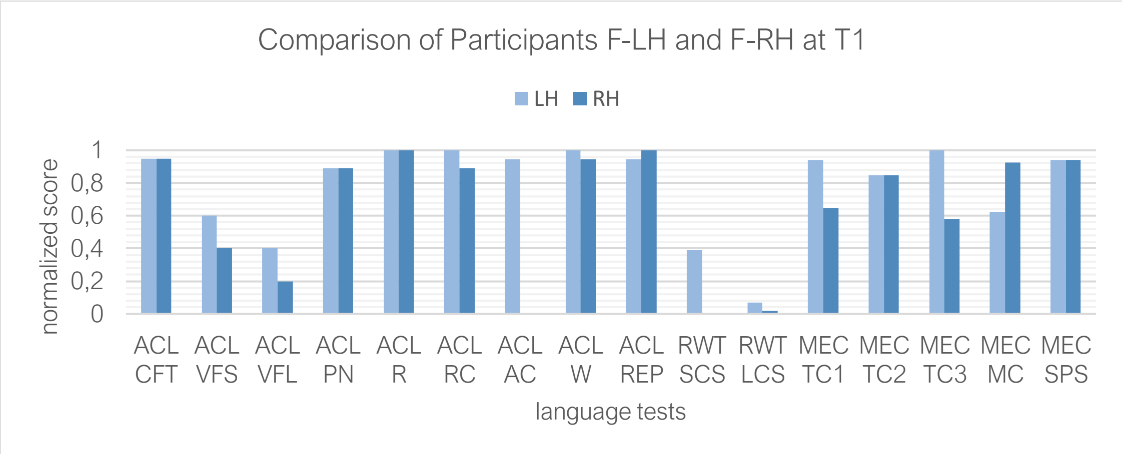


Figure 24: Participant Comparison T1[7]

The comparison of F-LH and F-RH at T2 (see *Figure 25* and *Appendix Part 4)* shows that F-LH had more impairments (F-LH 5 versus F-RH 5 impairments), but the same number of moderate or severe impairments (both 2). Both were mildly impaired in the ACL color-figure test (F-RH 16 and F-LH 17 out of 20 points). F-RH chose the wrong objects in the syntactically more complex part of the test. F-LH's reactions were delayed and one chosen object was wrong too in the syntactically complex part. F-LH also repeated the instructions for himself. A moderate impairment was identified in both subjects in the ACL semantic verbal fluency task, with F-RH naming eleven and F-LH coming up with 15 words. Lexical verbal fluency was also moderately impaired in both. F-RH had a final count of five and F-LH of six named words. F-RH's performance in the verbal fluency tasks was characterized by repetitions of already mentioned words and insecurity about having already used them before. F-LH also repeated some words, but also used many generic terms such as "Getränke" ("drinks") or "Gemüse" ("vegetables") instead of naming them separately.
Picture-naming was unimpaired in both subjects with a score of 17 out of a total of 18 points. F-RH's error was that he produced one incomplete sentence with missing information by naming "Das ist auf einer Insel... dort beim Lagerfeuer… Palmen… zwei Damen" ("That's

[7] Note that the ACL auditory comprehension task (ACL AC) does not hold the value zero but is missing for participant RH. MEC TC1 refers to retelling the whole text, TC2 to parts of the text and TC3 to answering questions about it.

on an island… there at the bonfire…palms.. two women”). F-LH’s sentence of the same picture was also missing some details but presented in a syntactically complete sentence.
Reading aloud and reading comprehension were unaffected in F-RH who reached the maximum score of 18, and the subtests by F-LH cannot be evaluated, as indicated in the chapters before. However, in the two examples in the reading and reading comprehension task that were conducted according to the manual, F-LH read the sentences correctly and immediately chose the correct picture. Similar performance was also seen in auditory comprehension (unimpaired in both with F-RH 18 and F-LH 17 out of 18 points) and repetition (both no impairment with the maximum score of 18). A difference could only be identified in writing, where F-RH was unimpaired with 17 out of 18 points, but F-LH only reached 16 points which translates to a mild impairment. The impairment in the subtest comes from a high number of delayed responses and self-corrections.

In the RWT semantic category switching task at T2, F-RH named only twelve words, which converts to a percentile rank of zero. F-LH named twenty words, which translates to a percentile rank of 30. F-LH repeated words more often (five times) than F-LH (only once), committed more breaches of rules (F-LH once, F-RH none). A category perseveration was only observed for F-LH once, and never for F-RH. Category errors were not committed by either participant. In the lexical category switching task, repetitions occurred to the same degree in F-RH and F-LH (both once). F-LH committed more breaches of rules (F-LH four, F-RH 1), mostly by using proper names. No category perseverations or errors were found. In this task, F-RH named 21 words (percentile rank of 31) and F-LH came up with nine words (percentile rank of zero). It should be mentioned that F-RH explicitly addresses his insecurities concerning the test by reassuring that he has to continue with the other letter in the lexical category switching task.

In the retelling of the whole text in the MEC at T2, both subjects were unimpaired (F-RH 10 and F-LH 12 out of 13 points). Both omitted some information. In the MEC text comprehension test were parts of a story have to be retold (maxmimum of 17), a similar number of central ideas was retold by F-RH (12 central ideas) and F-LH (13 central ideas). Also, the amount of total information (maximum of 30) was comparable in F-RH (18) and F-LH (23). F-RH only omitted information, F-LH additionally made changes to the story. For instance, he said that the farmer hid his clothing (even though he put it next to the well) and said that the friend then saw the clothing (even though in fact the friend saw the half-full well). Both gave the text a correct title. In the third part where questions about the text have to be answered, F-RH had an impairment (nine out of 12 points), but F-LH was unimpaired with the maximum score of 12. The type of errors that F-RH committed were answering with slight changes to the story. Even though F-LH was unimpaired, he once exposed a phonological paraphasia by saying “am Brunde des Bodens” (“on the fase of the floor”) instead of “am Grunde des Bodens” (“on the base of the floor”).

Subject F-RH was better in the metaphor comprehension task with 33 out of 40 points, which indicates no impairment. The explanations were sometimes characterized by imprecisions and F-RH often repeated the metaphor before explaining it. F-LH only reached 32 points, which is shortly below the cut-off value and therefore translates to an impairment. F-LH focused his explanations on less essential or not related aspects of the metaphor. For instance, "Die Frau schwebt in den Wolken" (literal: „The woman is floating in the clouds", figurative: "The woman has her head in the clouds") was explained as "Ich hab…äh..in den Wolken…äh… ich habe einer Frau ein Geschenk gemacht und sie fühlt sich wohl" („I have.. ehm...in the clouds…eh…I have given a woman a present and she feels fine").

In the spontaneous speech analysis, they performed similarly with F-RH reaching 31 and F-LH scoring 32 out of the total of 34 points, both of which indicates no impairment. F-RH's spontaneous speech analysis showed imprecise expression of thoughts, excessive talking and repetitions. In the conversation, F-LH clearly addressed his word-finding difficulties by saying "Wie sagt man das?" ("How does one express this?") and sometimes, the choice of words seemed odd, such as when saying "Ich fühle mich sehr gut hergestellt." ("I feel very well manufactured."), while the person was probably trying to say "Ich fühle mich sehr gut wiederhergestellt" ("I fell very well recovered").

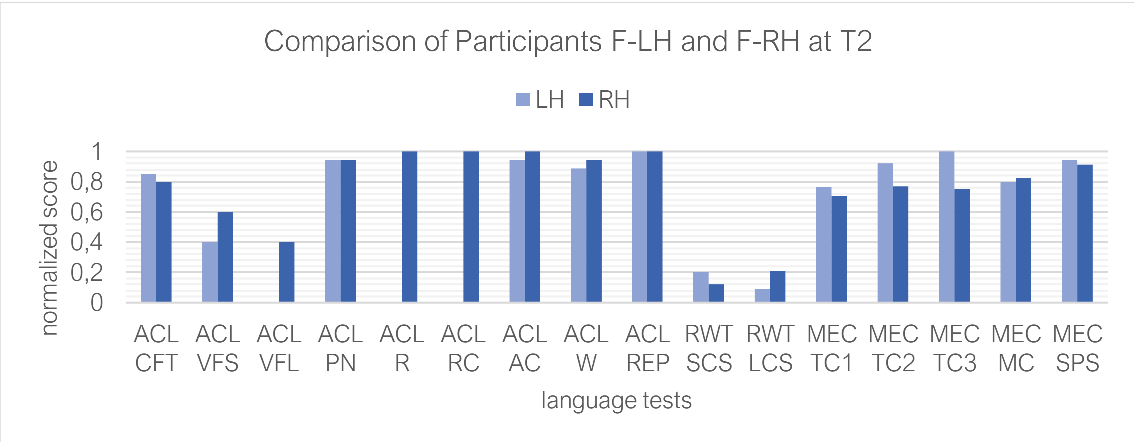


Figure 25: Participant Comparison T2[8]

Following this detailed comparison of the frontal brain tumor pair, the results of the second comparison with the parieto-occipital tumor pair will now be reported shortly.

The second participant (male, 77 years, secondary education I, right parieto-occipital glioblastoma grade IV, 18.61cm^3), henceforth named PO-RH (for parieto-occipital right hemisphere), was compared to the 14th participant (female, 61 years, secondary education II, left parieto-occipital metastasis, 0.96cm^3), now referred to as PO-LH standing for parieto-occipital left hemisphere (see MR images in *Figure 26*). Thus, gender, education, tumor type and grade were differing.

[8] Note that the ACL reading and reading comprehension task is not zero, but missing for participant LH.

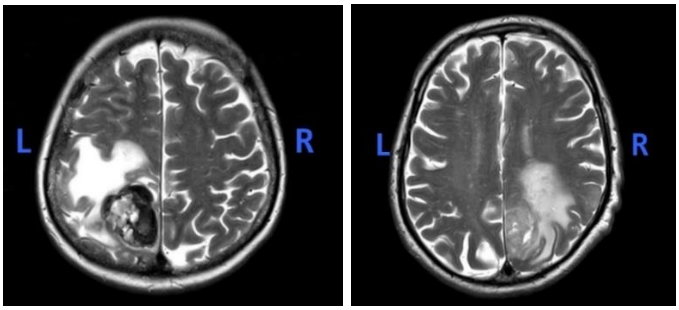


Figure 26: T2-weighted MR images of PO-LH (left side) and PO-RH (right side)

The comparison of the patient pair with parieto-occipital brain tumors at T1 (see detailed results in the *Appendix Part 4*) shows that PO-LH was impaired in a higher number of subtests (PO-LH 9, PO-RH 4) and had more moderate or severe impairments (PO-LH 2, PO-RH 0). Both their performance was unimpaired in reading, repetition and answering questions about the text. Similar scores with a mild impairment were seen in the color-figure test and retelling the whole text. The language abilities were different in the remaining subtests, PO-LH had a mildly disordered auditory comprehension, picture-naming, semantic and lexical verbal fluency and metaphor comprehension where PO-RH was unimpaired. PO-LH also exposed a moderate impairment of reading comprehension and severe impairment of writing, while PO-RH had only a mild impairment in the comprehension of read words and sentences, and unimpaired writing skills. A reduced number of named words as well as repetitions and breaches of rules were observed in the semantic and lexical category switching tasks in both patients, but PO-LH named less words. The only part where PO-RH performed worse than PO-LH was spontaneous speech, where PO-LH had no impairment, and PO-RH's speech was characterized by conduit d'approche, lexical and semantic paraphasia, wrong choice of words, imprecise speech, extensive and repetitive talking and accelerated speech.

At T2 of the same pair (consult details in the *Appendix Part 4*), PO-RH had slightly more impairments (PO-RH 5, PO-LH 3) and was the one to expose a moderate or severe impairment (PO-RH 1, PO-LH 0). The pair had similar abilities in auditory comprehension, semantic and lexical verbal fluency, lexical category switching task, reading, writing, repetition, and retelling a whole text, all of which were unimpaired. A mild impairment in the color-figure test was documented for both participants. A reduced number of generated words was described for both in the semantic category switching task. Diverging patterns were observable in reading comprehension, where PO-LH was only mildly and PO-RH moderately impaired. PO-RH was also the only one with an impaired retelling of parts of the text. PO-RH performed below the cut-off in picture-naming (mild impairment), answering text questions, and spontaneous speech, where PO-LH's performance was normal. PO-LH's abilities were below his partner only in metaphor comprehension, where PO-LH had an impairment and PO-RH did not.

Following this, the third pair with temporal brain tumors will now shortly be addressed. The sixth participant (male, 68 years, secondary education II, left temporal cavernoma, 67.60cm^3), called T-LH for temporal left hemisphere, was then compared to the ninth participant (male, 61 years, secondary education II, right temporal glioblastoma grade IV, 0.96cm^3), named T-RH referring to temporal right hemisphere (see MR images in *Figure 27*). Consequently, tumor type was dissimilar.

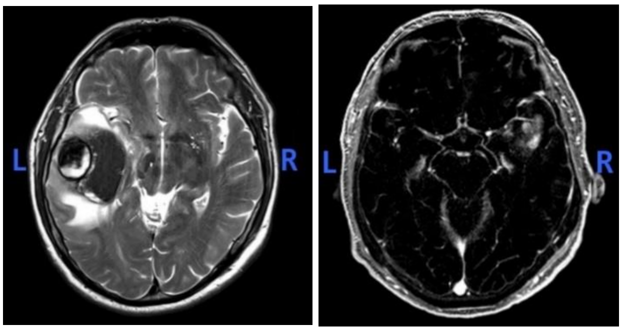


Figure 27: T2-weighted MRI of T-LH (left side) and T1-weighted MRI by T-RH (right side)

The comparison of the pair with temporal lobe tumors at T1 (consult a detailed overview in the *Appendix Part 4*) indicates that T-LH was more often as well as more severely impaired than T-RH (T-LH 13, T-RH 6 impairments in total, T-LH 9, T-RH 2 moderate or severe impairments). Both had an impaired metaphor comprehension and spontaneous speech, but with differing characteristics. T-LH often commented the metaphors without actually explaining them and T-RH was imprecise in explaining them and sometimes stuck to the literal meaning. The spontaneous speech by T-LH was amongst others characterized by a word-finding difficulty, missing corrections after choosing the wrong words, comprehension problems, while T-RH had a monotone and slow speech. Word generation in the lexical and semantic category switching tasked was reduced in both participants, especially in T-LH who named zero words. T-RH was insecure about having already named words and conducted breaches of rules. T-LH was more severely affected in the color-figure test, picture-naming (in both subtests T-LH severe, T-RH mild impairment), as well as semantic and lexical verbal fluency (T-LH severe versus T-RH moderate impairment). Again, T-LH named zero words, while T-RH named generic terms, repeated already named words and the overall count of words was reduced. T-RH performed better than T-LH in reading and auditory comprehension, reading, writing and repetition, all of which were unimpaired in T-RH and severely impaired in T-LH. Retelling parts as well as the whole text and answering questions about it were only impaired in T-LH but normal in T-RH.

Contrasting the language abilities at T2 of the same pair is not possible, as both dropped out of the study.

4.4 Role of Tumor Size and Grade

To identify the influence of tumor size on language, a linear regression with tumor size in cubic centimeters (cm^3) as the independent or predictor variable and overall language score as the dependent variable was conducted. Before surgery, the linear regression results in a score close to the significance level with p=0.571 (n=12 after having to remove two individuals without an overall language score due to the missingness of subtests necessary for the calculation of the overall score, and because of the removal of one participant where only a post-surgical MR image was available). The non-significant result suggests the tendency that for every 1% increase in tumor size, there is a 0.005 decrease in the overall language score. With a confidence interval of 95%, the true estimate lies between -0.001 and 0.0002 (see *Figure 28*). The adjusted R-squared value of 0.2477 indicates that only 24.77% of variation in the overall language score before surgery can be explained by the model.

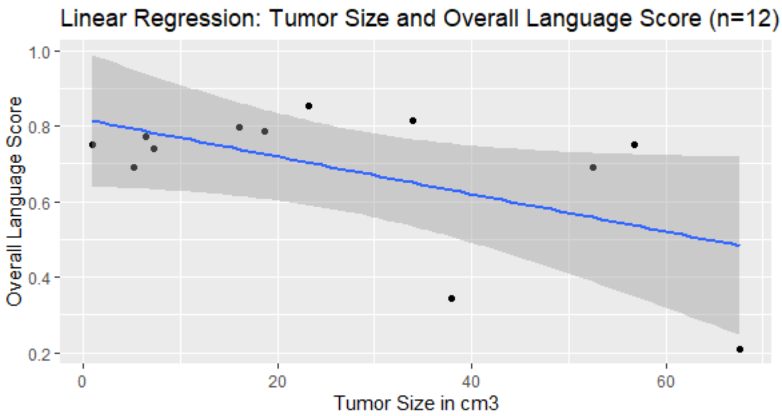


Figure 28: Result of the Linear Regression on Tumor Size and Language

The influence of tumor size on the overall language score after surgery was not calculated with a linear regression because of the low number of subjects at T2 (n=7, as only 9 subjects completed testing at T2 and for two persons, the overall language score could not be computed due to missing subtests). In the literature, differing numbers of minimal sample sizes are described for regression analysis to avoid type I and type II errors. The recommendations range from at least 10 to a minimum of 30 or even 50 participants (Van Voorhis & Morgan, 2007). Thus, the number of 10 participants was taken as the minimum to perform such analysis in this thesis.

Due to the described influence of tumor size on verbal fluency (Tucha et al., 2000b), a multiple regression with tumor size in cm^3 as the independent variable and the total number of generated word in verbal fluency tests at T1 (n=14) was performed. The results of 14 subjects could be included, because for one subject, the tumor volume was not available as the MR image was post-surgical. The verbal fluency tests used were the ACL semantic, ACL lexical, RWT semantic category switching and RWT lexical category switching was performed. Tumor size was not shown to be significantly predictive for the various verbal fluency scores. Tumor size and verbal fluency after surgery was not further analyzed due to the low number of participants at T2 (n=8, because 9 subjects were tested at T2 out of which one did not complete the RWT).

With the aim to find out whether WHO tumor grade was predictive of the language impairment at T1, a linear regression was initially planned with WHO grade as the independent variable and the overall language score as the dependent variable. Due to the missing values of two participants and the exclusion of five subjects with secondary brain tumors (which do not have a WHO grade), eight participants were available in total. Consequently, the planned linear regression was not performed with eight subjects. Similarly with less than 10 subjects, no linear regression for WHO tumor grade and overall language score at T2 or WHO tumor grade and semantic or lexical verbal fluency was calculated at T1 or T2.

In addition to these statistical analyses of tumor size and verbal fluency, the potential correlation was analyzed on an individual level by comparing two subjects with a glioblastoma WHO grade IV of the right temporal lobe with a smaller (0.96cm^3) and a larger (24,91cm^3) brain tumor as well as another subject pair with a meningeoma WHO grade II of the left frontal lobe with a smaller (16.05cm^3) and larger (56.70cm^3) tumor. The other subjects were, as in the matching process of left and right hemisphere patients, not similar enough for such comparison. The individual analysis was not conducted with the overall language score, because it was not available for all of these subjects with some subtests missing. Semantic and lexical verbal fluency in the ACL were moderately impaired in both subjects with a right temporal brain tumor, and the RWT percentile rank for semantic (PR 19 smaller tumor and PR 10 larger tumor) and lexical category switching (PR 4 smaller tumor and PR 1 larger tumor) was comparable. The other pair with left frontal brain tumors also exposed similar performance in ACL semantic (mild impairment in smaller tumor, no impairment in larger tumor) and lexical verbal fluency (both moderately impaired). In the RWT, the pattern was even suggesting an inverted pattern with a smaller percentile rank of 39 (smaller tumor) and PR of 85 (larger brain tumor) in the semantic, and a PR of 7 (smaller brain tumor) and 23 (larger brain tumor) in the lexical category switching task.

To summarize, none of the statistical analyses or individual analyes related to tumor size resulted in tumor size being a significant predictor of overall language or verbal fluency before surgery.

5. Discussion

5.1 Interpretation of Results

Now, the results of the previous chapter will be interpreted in view of the literature, hypotheses will be assumed or discarded, thereby answering the research question.

The first hypothesis was that pre-surgically, individuals with predominantly frontal or temporal brain tumors would expose a selective impairment in verbal fluency, spontaneous speech, text and metaphor comprehension in the tests RWT, ACL and MEC when compared to the normative data of the language tests.

Even though strictly speaking, it was not possible to identify such selective impairment with disordered verbal fluency, spontaneous speech, text and metaphor comprehension, and spared language abilities other than those just mentioned, more frequent and more severe impairments were indeed found for some of these parts of language. The results in the ACL (Kalbe et al., 2002), RWT (Aschenbrenner et al., 2000) and MEC (Scherrer et al., 2016) suggest that repetition and reading were almost exclusively unimpaired in the study group, followed by a small number of impairments in writing, auditory comprehension and picture-naming, but a higher number of disordered reading comprehension, semantic and lexical verbal fluency and category switching, performance in the color-figure test, text and metaphor comprehension as well as spontaneous speech. Apart from the incidence, more severe impairments were also found in these more frequently affected subtests.

Consequently, the hypothesis in its original version must be discarded, but it can be followed instead that verbal fluency, spontaneous speech, auditory comprehension in the color-figure test, reading comprehension of words and sentences, and text- and metaphor comprehension are more frequently and partly more severely impaired in brain tumor patients in this study. Repetition, reading, writing, auditory comprehension, and picture-naming, on the other hand, are less frequently and less severely impaired in the study. Given the small number of subjects and disparate distribution of tumor type, grade and hemisphere, it is problematic to generalize to all brain tumor patients. Especially in view of the high percentage of frontal brain tumors in the study group, the results might not be representative of temporal and parieto-occipital brain tumor patients.

The results are in accordance with another study, where repetition, reading and writing were also found to be unaffected in a group of persons with primary brain tumors of mostly the frontal lobes in majorly language-relevant areas (Satoer et al., 2012). Reading, repetition, writing and comprehension (including auditory and reading comprehension) were only unfrequently and mildly affected in a study with subjects with brain tumors of the left perisylvian cortex (Bartha et al., 2000). Thus, the relatively high proportion of persons (over 70%) with impaired reading comprehension in this master's thesis is in contrast to the study by Bartha et al. (2000) which reports that reading comprehension was not or only mildly disordered.

The difference in result may be explained by differences in tumor type, grade or the use of differing language tests. The finding that metaphor comprehension was impaired in the study group is consistent with Arcara et al. (2018) who found a disordered comprehension of figurative language in a test which amongst others entails metaphors in subjects with primary brain tumors of the left or right hemisphere of different locations. These results are connected to the discussion about a lateralization of figurative language processing in the brain (Bohrn et al., 2012; Stemmer, 2015) (see *chapter 2.2*).

The outcome in the color-figure test cannot be compared to the literature, as the ACL has not been used with brain tumor patients before. However, under the assumption that it is comparable to the Token Test (Huber et al., 1982), the percentage of impairments found in this master's thesis is higher than in a larger study with left or right temporal lobes tumor patients, where only around 22% subjects with a tumor of the left and 5% of the right hemisphere were impaired in the Token Test (Noll et al., 2016). The difference may be explained by the higher amount of persons with a frontal brain tumor in the underlying study of this master's thesis under the assumption that the color-figure test requires executive functions such as working memory (Kalbe et al., 2002). Ilmberger et al. (2008) used the Token Test as well but did not report the specific results before surgery.

The high number of impaired spontaneous speech coincides with other experiments which have shown the importance of spontaneous speech in language testing within this clinical population (McCarron et al., 2017; Rofes et al., 2018; Satoer et al., 2018). Before surgery, spontaneous speech was characterized by incomplete sentences in patients with primary brain tumors in language eloquent areas of the frontal or temporal lobes (Satoer et al., 2018). Rofes et al. (2018) detected that most participants with primary brain tumors of the temporal, frontal or parietal lobes also exposed incomplete sentences, followed by errors such as phonological paraphasia, perseveration and conduit d'approche. This symptom pattern does not fully reflect the spontaneous speech analysis in this master's thesis, where repetitions of what had already been said was the most common error before and after surgery. An imprecise expression of thoughts was common before, and extensive talking after surgery. This difference may be explained by the fact that the MEC (Scherrer et al., 2016) does not offer an analysis of incomplete sentences.

Although picture-naming was only impaired in less than half of the subjects, it must be conceded that the results do not match the picture described by other studies. Chakraborty et al. (2012) give accounts of preserved naming accuracy, but unusual long times to name the picture correctly in a study with left frontal brain tumor subjects. The difference might be explained by the fact that Chakraborty et al. (2012) used a test where pictures have to be named on a word level only, while the test in this thesis requires naming on a sentence level too. Papagno et al. (2012) report specific results for tumors of the left frontal versus the left temporal lobes. Such detailed comparison and description are not feasible in this thesis, because the number of persons with temporal brain tumors in comparison to frontal brain tumors is too low. However, the finding that 47% were impaired in picture-naming in this master thesis' mixed group of temporal, frontal and parietal lobe tumors of mainly the left hemisphere is similar to Papagno et al. (2012) who observed 41% impaired object picture-naming in persons with left frontal brain tumors. Again, the results are only partially comparable, because different test batteries were used. Word-finding difficulty may be a cardinal symptom in the study group of this master's thesis and in other studies on language impairments in persons with brain tumors (Davie et al., 2009), because being able to access and retrieve word appears is described to be based on a wide cortical network, thereby possibly being more frequently affected by brain tumors than other language functions (Davie et al., 2009). In the literature, it is suggested that the frontal and temporal gyrus of the left hemisphere are highly relevant for both memory and naming by means of a complex, multimodal process (Zambrano-Cruz & Méndez-Ramírez, 2018). This is in line with the results of this master's thesis, as the majority of subjects suffered from a brain tumor of the left frontal or left temporal lobes and also exposed difficulties in the working memory task.

Last but not least, the high incidence of impairment and severity degree found for semantic and verbal fluency are in agreement with the literature, where such impairment is described for persons with brain tumors of either hemisphere (Faulkner et al., 2017; Morrison et al., 2016). The finding by Bartha et al. (2000) that semantic fluency was more impaired than lexical fluency in left hemisphere tumors could not be replicated, as lexical fluency was shown to be more frequently and severely impaired in the study of this thesis. Data for comparing the results in the category switching tasks are not available, as only Bette et al. (2020) used such task with brain tumor patients but did not report the findings before surgery. Yet, the result that a large number of subjects in this master's thesis had a very low percentile rank in the RWT category switching task (Aschenbrenner et al., 2000) could hint at the cognitive flexibility of participants. At least in healthy subjects, the category switching task appears to be more strongly linked to cognitive flexibility as an executive function than other verbal fluency tasks (de Paula et al., 2015). Thus, the low performance in the subtest may be explained by the high proportion of frontal brain tumors in the study group.

The observation that most impairments were mild or moderate confirm the already well-reported occurrence of rather mild in comparison to severe language impairments in individuals with brain tumors, like Ilmberger et al. (2008) who found mostly mild and no severe impairments or Davie et al. (2009) who also describe mostly mild or moderate and almost no severe language disorders in a comparably heterogenous study group with primary tumors of the mostly frontal, but also temporal, parietal and insular lobes. In the literature, this low frequency of severe impairments are explained by the brain's compensatory mechanisms (Duffau et al., 2003).

On a more general note, it could be argued that the results confirm a higher involvement of executive functions in certain language abilities and language subtests. For instance, the ACL color-figure test, which was impaired in a high number of participants of this study, requires mnestic abilities (Kalbe et al., 2002). Another example would be the necessity of executive functions for the verbal fluency (Aschenbrenner et al., 2000) and category switching tasks (de Paula et al., 2015) which were also among the abilities majorly impaired in the study group. This comes as no surprise given that verbal fluency tasks were found to be sensitive for detecting frontal lobe lesions (Alvarez & Emory, 2006) and a high percentage of frontal lobe tumors can be found in the study group. The theory that the results can be traced back to executive dysfunctioning in a study group with many individuals with frontal brain tumors is further endorsed by separately analyzed results of the frontal brain tumor group. In the separate analysis of the frontal brain tumor participants, impairments were more frequently found in semantic and lexical verbal fluency (both 87% of cases) than in the overall brain tumor group (73% respectively 78% impaired), spontaneous speech (75% in the frontal and 73% in the overall tumor group), metaphor comprehension (75% in the frontal and 73% in the overall tumor group). This can be taken as evidence in favor of an involvement of executive functions in these subtests. Nevertheless, it must be acknowledged that the separate analysis also shows that the frontal brain tumor group showed less impairments in the color-figure test (75% of frontal brain tumor patients impaired versus 78% in the overall tumor group) and similar results in the text comprehension tasks (38% of frontal and 36% overall tumor group impaired in retelling the whole text, 50% of frontal group and 62% of overall tumor group impaired in answering questions about the text).

With regard to usefulness and reliability of available language test batteries (Brownsett et al., 2019; Miceli et al., 2012; Wacker et al., 2002), it can be followed that even though all of the language tests were not initially developed for and evaluated with brain tumor patients, the tests or some of the subtests can be used for the diagnosis of language impairments in individuals with brain tumors to some extent. However, with regard to the already mentioned high amount of frontal brain tumors in the group and other limitations such as the heterogeneity of subjects, the use of the ACL (Kalbe et al., 2002), RWT (Aschenbrenner et al., 2000) and MEC (Scherrer et al., 2016) must be precautious, as no generalization to the general clinical population is possible. By having diagnosed some impairments in the study group, it can be followed that the language tests are capable of identifying some impairments. Nevertheless, the results do not allow to draw conclusions about how many language impairments were not identified at all or wrongly diagnosed. For such a conclusion, it would be necessary to validate the tests by help of an acknowledged test battery for this clinical population or additional clinical assessment of language by speech therapists.

Another point is that the results show the importance of testing specific aspects of language to ensure that individuals with brain tumors are not wrongly diagnosed with unimpaired language even though they experience problems. Judging by the result that especially verbal fluency and category switching, reading comprehension of words, sentences and texts, metaphor comprehension, as well as spontaneous speech were impaired in the subject group, it should be ensured that these modalities of language are routinely checked in brain tumor patients before and after surgery. On a more general note this would imply that not only the ACL (Kalbe et al., 2002) should be used for language testing, as it does not entail the testing of more pragmatic aspects of language, but the MEC (Scherrer et al., 2016) as well as the RWT (Aschenbrenner et al., 2000) for a more extensive diagnosis of verbal fluency.

A comparison of the language tests used in this study with the first and up to now only existent language test for (English speaking) brain tumor patients, the *Brief Language Assessment for Surgical Brain Tumor Patients (BLAST)* by Faulkner et al. (2017) suggests that brain tumor patients should be tested in additional modalities. The subtests partly overlap, namely repetition, auditory comprehension, picture-naming, letter and category fluency. However, the BLAST (Faulkner et al., 2017) additionally looks at non-word repetition and includes a verb generation task where the tested person has to associate a verb with a picture. At the moment, it is not possible to add the association test to the diagnostic procedure with German speaking brain tumor patients in a standardized manner. Non-word repetition could be checked in a standardized manner by use of the ACL (Kalbe et al., 2002). Unfortunately, this subtest was not included in the experiment.

The detection of majorly mild language disorders, characterized by impaired verbal fluency, spontaneous speech, metaphor comprehension, reading comprehension of words, sentences and texts, point towards a cognitive-communication disorder rather than classical aphasia. First of all, because the term aphasia is usually associated with the standard syndroms such as Broca's aphasia (Heidler, 2005) which do not fit the described impairment pattern in the study group. Secondly, some of the observed symptoms are known from other cognitive-communication disorders. For instance, relatively preserved picture-naming but impaired word-finding in spontaneous speech, unaffected comprehension of words but difficulties with text comprehension (Büttner & Glindemann, 2019; Jaecks et al., 2012). Thirdly, it has been argued in the paragraphs before that the findings in language may be explained by mnestic and other executive dysfunctioning. Thus, cognitive-communication disorders as language impairments caused by primarily impaired non-linguistic cognitive processes (American Speech-Language-Hearing Association, 2005) would fit the assumed mechanism behind the language impairment. However, it has been pointed out before (see *chapter 2.3*) that language impairments usually have more than one underlying cause (Regenbrecht & Guthke, 2017) and even more importantly that language impairments should be understood as a neural network disorder (Stockert & Saur, 2017) given the complex and broadly distributed language processing network (Tremblay & Dick, 2016). The assumption of such a network disorder should be particularly considered in view of the knowledge that brain tumors gradually infiltrate the brain and do not cause as direct lesions as stroke (Anderson et al., 1990) and that very localized changes can still lead to disturbances of the whole cerebral network (Heimans & Reijneveld, 2012).

The second hypothesis predicted that individuals with mostly a frontal or temporal brain tumor of the left hemisphere show a different language impairment pattern than those of the right hemisphere, before and after tumor resection.

Following the detailed description of the pair's language impairments, the pre-surgical language abilities will be compared to the literature, then it will be discussed whether a detectable difference between the two patients in view of the affected hemisphere exists.

Pair with Frontal Brain Tumors

The reduced lexical verbal fluency in both patients matches the results by Morrison et al. (2016) with a mixed tumor type group of the left and right hemisphere, where three to 13 words were named in 60 seconds. However, the main reason for the low number of words was delayed reaction time at least for higher grade tumor patients in their study. F-LH's result (person with a frontal left hemisphere brain tumor) is not attributable to slow reaction times but is characterized by a relatively high number of breaches of rules. F-RH (person with a frontal right hemisphere brain tumor) paused a lot, but also received a low score partly due to the number of repetitions. The insight that semantic verbal fluency was affected in both subjects reflects the findings that no significant difference in impairment between left and right frontal and temporal hemisphere tumor patients was found before tumor resection in a study by Faulkner et al. (2017). That both subjects named few words is not surprising, given that at least lexical verbal fluency tasks are assumed to be sensitive but not necessarily specific for detecting frontal lobe lesions of diverse etiology (Alvarez & Emory, 2006). The results in semantic and lexical category switching cannot be compared to the literature in detail, because only Bette et al. (2020) included such a task in their study with brain tumor patients, but do only report a deterioration after surgery instead of specific results for the assessment before tumor resection. Interestingly, it seems that even though both participants had difficulties in the lexical and semantic category switching tasks, F-RH was more impaired, and F-LH had more problems with the lexical than the semantic task.

That both subjects were below the cut-off for a normal spontaneous speech is partly in conformity with other studies. The characteristics of F-LH's impaired spontaneous speech with word-finding difficulties and conduit d'approche as a symptom thereof go together with McCarron et al. (2017) who report of lexical access difficulties before surgical resection of left hemisphere tumors. Satoer et al. (2018) additionally mention incomplete sentences, frequent self-corrections, and a decreased mean length of utterance before surgery in left hemisphere tumor patients. These symptoms were not detected in patient F-LH.

Spontaneous speech in individuals with right hemisphere tumor has not specifically or extensively been studied yet. However, the pattern by F-RH's spontaneous speech with repetitions of already expressed ideas as well as interruptions of the communicative partner, is not surprising given the accounts of impaired pragmatic language in other clinical populations such as in traumatic brain injury (Büttner & Glindemann, 2019) and the ongoing discussion about the special involvement of the right hemisphere in pragmatics (Stemmer, 2015). Still, this interpretation faces the difficulty that the only available study on pragmatic language in brain tumor patients of either hemisphere negates a difference between these groups (Arcara et al., 2018).

The lower performance of F-RH in comparison to F-LH in one part of the MEC text comprehension test (Scherrer et al., 2016) and the reading comprehension part of the ACL (Kalbe et al., 2002) could be seen as an indication in favor of right hemisphere activation for texts. However, the findings regarding text comprehension are vastly contradictory, with some authors reporting mainly left, other mainly right and other bilateral activations, which may be explained by the different tasks and demands used for the assessment of text comprehension (Stemmer, 2015). Problems with (implicit) main ideas in a text comprehension task have been described for persons with traumatic brain injury before (Ferstl et al., 2005), but were not detected in this master's thesis for either F-LH or F-RH, who were both unimpaired.

That F-RH was better in metaphor comprehension than F-LH reflects the assumption that a bilateral fronto-temporal network for metaphor comprehension is assumed, most importantly of the anterior temporal regions without a special role of the right hemisphere (Ferstl et al., 2008). The higher scores of F-RH than F-LH in metaphor comprehension may therefore be explained by the exact location of the tumor.

For picture-naming, accounts of similar picture-naming abilities for left and right hemisphere tumor patients (Amoruso et al., 2021) as well as delayed picture-naming in left frontal brain tumors (without comparison to right hemisphere tumors) (Chakraborty et al., 2012) and reduced correctness in object, action and people naming only for left frontal brain tumors exist (Papagno et al., 2012). Consequently, the finding that F-LH and F-RH were both unimpaired in picture-naming underlines the finding of the first study.

Hemisphere-specific changes to repetition, reading, auditory comprehension and writing were not detected and also not expected based on the literature (Bartha et al., 2000; Satoer et al., 2012; Tucha et al., 2000). The color-figure test has not been used with brain tumor patients before. Therefore, no comparison to the literature is possible. However, both performed similar anyway with no impairment and similar errors.

The fact that F-RH was overall more frequently and more severely impaired than F-LH seems contradictory, as left frontal tumors are described to more severely affect expressive and receptive language (Noll et al., 2016). The reason for this might be that F-RH had a higher tumor grade (II) than F-LH (I). Yet, it has to be conceded and it has already been mentioned before that the relation between tumor grade and impairment severity is not fully understood and that studies who have reported more severe impairments in persons with higher tumor grades usually contrast low grade (I-II) to high grade (III-IV) gliomas (Yuan et al., 2020). The finding may be additionally explained by not so much focusing on the general prevalence of impairment, but the modalities which were impaired as well as the type of errors which were committed.
Semantics and different aspects of pragmatics were impaired in both, phonology was unaffected in both, and morphology and syntax were impaired only in the left hemisphere tumor patient. To recapitulate, some errors were typical of a frontal lesion, but no clear left- from right hemisphere differentiating picture of pragmatic language before surgery emerges.

Pair with Parieto-Occipital Brain Tumors

Following this interpretation of the first pair, the presurgical language of the pair with parieto-occipital lobe tumors will now be discussed. As the literature does not hold specific information on language impairments in individuals with parieto-occipital brain tumors, usually being either excluded or a small minority among participants in other studies, frequency and type of language impairment cannot be directly related to other studies.
The observation that the patient with the left parieto-occipital brain tumor (PO-LH) was more frequently and severely impaired than the right (PO-RH) before surgery might stem from the edema around PO-LH's tumor which can be seen in *Figure 26* and appears to affect far more than the parieto-occipital lobe. The edema reaches to the temporal lobe, potentially being the reason for some of the other characteristics of language of PO-LH. Additionally, an edema can increase the intracranial pressure, which in turn can also negatively affect the functioning of the brain (Sorribes et al., 2019). Noll et al., 2016 suggests more frequent impairments in left hemisphere tumors of the temporal lobes, but occipital lobe tumors are not included.
Auditory comprehension, writing and picture-naming may be impaired in PO-LH but not PO-RH because of the temporal lobe's relevance in underlying processes such as phonology and semantics (Gierhan, 2013).
The finding that only PO-LH had deficits in metaphor comprehension and PO-RH did not, underlines the finding that a left hemispheric fMRI and PET activation is reported for metaphor processing (Bohrn et al., 2012) in the long-term discussion about the right hemi-

sphere's role in figurative language (Stemmer, 2015). However, as the MEC metaphor comprehension task (Scherrer et al., 2016) requires productive language too, the differences between the pair may be attributable to deficits in other areas of language.
Both were unaffected in repetition, which involves the SLF-III tract (supramarginal gyrus to posterior inferior frontal cortex) for articulation and the SLF-tp (posterior temporal cortex to angular gyrus) for phonological processing (see *Figure 1* in chapter 2.2) (Gierhan, 2013). Thus, repetition may be preserved because the tumor might not affect the white matter in these cases or because at least the SLF-III is spared by the tumor's location.
PO-RH performed worse than PO-LH only in the spontaneous speech analysis. However, the errors vary from paraphasia and conduit d'approche, which could be seen as processes relying on semantic and phonology.
The color-figure test was similar in impairment severity and error type in both patients. Reading comprehension of words and sentences were impaired in both, but more severely in PO-RH, a finding that cannot be explained by prior studies with similar subjects (Bartha et al., 2000; Faulkner et al., 2017). Text comprehension was impaired in retelling the whole text in both patients with similar error types.
Verbal fluency was only affected in the left tumor patient. The literature reports verbal fluency difficulties in tumors of both hemispheres (Morrison et al., 2016), but does not look at tumors of the parieto-occipital lobes.
Pragmatics, semantics and phonology appeared to be impaired in both, while morphology and syntax appeared to be unaffected in both. To summarize, both participant's language abilities before surgery do not paint a clear picture which would allow a distinction between the left and the right hemisphere tumor. The findings are in favor of the left hemisphere being the eloquent area of language, other than that no impairment pattern can be found. The overall difference seems to be on a quantitative level with more impairments in PO-LH, but not so much on the qualitative level with different symptoms, as both share characteristics of language.

Pair with Temporal Brain Tumors

Following this, the pre-surgical results of the participants with temporal lobe tumors will now be discussed.
It is in line with the literature (Noll et al., 2016) that T-LH (person with the temporal left hemisphere tumor) had considerably more impairments in the language tests as well as a very high number of severe impairments in comparison to T-RH (individual with the temporal right hemisphere tumor).
It is also in accordance with prior research (Papagno et al., 2012) and the described involvement of the left temporal lobes in naming (Zambrano-Cruz & Méndez-Ramírez, 2018) that T-LH had a word-finding difficulty in the picture-naming task, where T-RH did not have

such problem. Interestingly, T-RH also exposed semantic paraphasia in the picture-naming task, even though the inferior fronto-occipital fascicle (IFOF) in the left hemisphere is described to be involved in semantic processing (Gierhan, 2013). However, it could be argued that the error comes from impaired executive functioning and must not necessarily be a linguistic impairment per se. It was described in the theoretical part that executive functioning is involved in language processes, for instance by inhibiting competing alternatives or selecting words (Ye & Zhou, 2009). Consequently, T-RH may expose semantic paraphasia due to an executive involvement. More likely, as T-RH's tumor is not very close to the frontal lobe, the location of the tumor in the right insular cortex and superior temporal gyrus (see *Appendix Part 5, patient 6*) is the reason for semantic paraphasia, as cortical and subcortical language mapping in the right insular cortex and superior temporal sulcus of the right hemisphere have been shown to be sites involved in semantic processes in persons with temporal lobe tumors (Duffau et al., 2005).

Paragraphia in writing was only observed in T-LH, which matches the finding by (Bartha et al., 2000) who reports such problem only for an individual with a tumor of the left perisylvian cortex. Impaired repetition was present in T-LH, which comes as no surprise given that it has been reported for a tumor patient of the left temporal lobe before (Bartha et al., 2000) and that the fiber tracts SLF-III and SLF-tp both reside in or reach to the left temporal lobe (Gierhan, 2013) (see *Figure 1* in chapter 2.2).

The result that T-LH and T-RH had a reduced verbal fluency matches the literature (Morrison et al., 2016). A clear difference in the performance in verbal fluency can be detected. Even though both participants had impaired verbal fluency, T-LH seemed to have problems with accessing words by naming zero words, while T-RH was able to name some words but committed errors of repetition, named generic terms or committed breaches of rules. T-RH's errors could be interpreted as a mainly mnestic problem or missing strategies (Troyer et al., 1998). Referencing the number of named words of T-LH and T-RH in the lexical or semantic category switching tasks to the literature is not possible, as such results were not reported for subjects before surgical resection in other studies.

The observation of reference to literal meaning in the metaphor explanation task only for T-RH points towards the ever-more discussed role of the right hemisphere in figurative language (Stemmer, 2015). Furthermore, only T-RH added additional information in the text comprehension task. Moreover, the spontaneous speech analysis exposes a contrary picture to the literature, as T-RH was mainly slowed in his speech, but T-LH committed pragmatic errors in addition to word-finding difficulties. For instance, T-LH interrupted his communicative partner.

As expectable based and prior findings (Bartha et al., 2000; Faulkner et al., 2017) only T-LH had difficulties in reading aloud, reading comprehension and auditory comprehension of

words and sentences. Errors in the color-figure test were similar for both subjects and to not permit assumptions based on the affected hemisphere.
Semantics, pragmatics, morphology and syntax were impaired in both subjects, phonology only in T-LH. To conclude, impairment severity, frequency as well as characteristics are in favor of the left hemisphere, especially of the temporal lobes, being highly relevant for language processes. Also, the pattern exposed by the left hemisphere tumor patient clearly matches the neuronal correlates. As for the right hemisphere tumor, no clear and diverging pattern could be identified, as the left hemisphere patient also exposed pragmatic errors.

Overall Language Pattern: Left versus Right Hemisphere
Abstracting from the individual to all three pairs, it was not possible to clearly identify a differing language impairment pattern between left and right hemisphere tumor patients except for impairment frequency and severity. Rather, differences between the affected lobes were found.
In two of three cases, the person with the left hemisphere tumor was impaired in more subtests and exposed more moderate or severe language impairments. The most severe and the most frequent impairments were found in the pair with the temporal brain tumors.
In general, pragmatic problems were detected in all individuals of this comparison, regardless of the affected hemisphere. No clear difference in the understanding and use of figurative language was found, as references to literal meaning were present in both left and right hemisphere tumor patients. In addition, other pragmatic errors like interrupting the partner in a dialogue, were also noted in both hemisphere groups. The most frequent errors in pragmatic language were identified in the frontal tumor pair. The only hint at a difference between left and right hemisphere tumor patients was that two out of three individuals with a tumor of the right hemisphere outperformed the one with a left hemisphere tumor in metaphor comprehension, suggesting that figurative language is indeed more related to the left hemisphere (Bohrn et al., 2012).
In many cases, the tests which could be considered to test pragmatic language exposed diverging results within subjects. Here, it seems essential to follow that pragmatic language summarizes a high number of different abilities under one (Martin & McDonald, 2003). It could further be argued that the problems with pragmatic tests are not attributable to one hemisphere, but rather correlated with complexity. It could therefore be said that these individuals exposed pragmatic impairments due to the complex nature of pragmatic tests, while less complex tasks were more easily solved.
A very small tendency towards more frequent and severe impairments in verbal fluency in left hemisphere tumor patients was found, especially for semantic fluency tasks. Nevertheless, semantic problems in other tasks were not specific to left hemisphere patients, but present in all. These findings match the literature where verbal fluency was shown to be

impaired in persons with a brain tumor of either hemisphere (Faulkner et al., 2017), but equally that semantics are related to the left temporal lobe (Gierhan, 2013).
Importantly, it was seen that problems sometimes only occurred in the dialogue in spontaneous speech when other prior subtests were normal. For instance, semantic paraphasia was not identified in the picture-naming or verbal fluency task, but in spontaneous speech analysis. This reflects the findings by Satoer et al. (2018).
It is essential to mention that the right hemisphere tumor group is in itself highly heterogeneous as far as the affected location and tumor size are concerned. *Figure 29* depicts the tumors of the four individuals with right hemisphere brain tumors in pink, red, orange and yellow on the CJH average brain (Holmes et al., 1998).

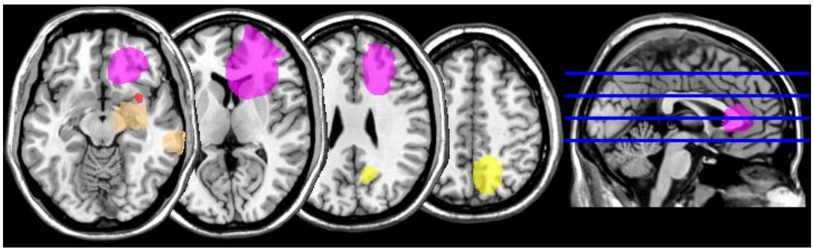


Figure 29: Lesion Overlay of Right Hemisphere Tumors

The same holds true for the left hemisphere group, where the lesion location and size are highly differing (see *Figure 30*), depicted on the CJH average brain (Holmes et al., 1998).

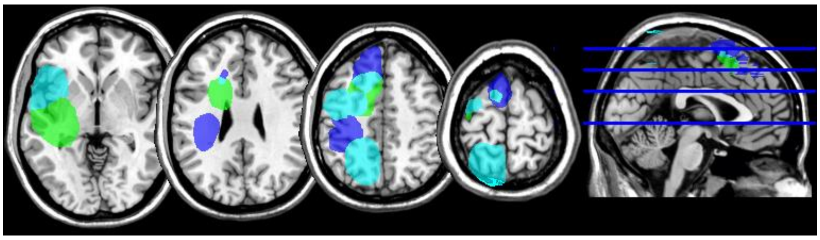


Figure 30: Lesion Overlay of Left Hemisphere Tumors

The contrasting comparisons of these tumor pairs are not representative and not generalizable to other individuals with brain tumors. As a double-case comparison is drawing only on the data of two participants, it should also be mentioned that individual differences in brain anatomy associated with cognitive performance exist (Kanai & Rees, 2011).
Even though the role of the right hemisphere in (pragmatic) language has long been discussed (Stemmer, 2015), more critical accounts of this theory exist. Grande and Huber, (2005) report that a protolanguage, defined as a universal, innate language system for the basic use of linguistic symbols, exists for both hemispheres. However, through brain maturation, a more specialized left hemisphere dominance evolves and in case of a left-hemisphere lesion, the existent protolanguage of the right hemisphere leads to the incorrect use of syntax and grammar. The findings by Saur et al. (2006) support the theory that the right in addition to the left hemisphere plays an essential role in language recovery after stroke. However, they point out that the (re-)activation of the left hemisphere is critical for positive

recovery, while right hemisphere activation is rather associated with severe lesions of the left hemisphere, where such left (re-)activation is not possible (Saur et al., 2006) (see *chapter 2.3*). A similar finding is reported by Heiss et al. (1999) who describe an

> "inferior role of the right hemisphere language-related network for recovery from poststroke aphasia; […] restoration of language function […] can only be achieved if the temporal eloquent areas of the dominant hemisphere are morphologically preserved and can be reintegrated within the functional network" (Heiss et al., 1999, p. 437).

The third hypothesis forecast that larger brain tumor volumes in cubic centimeters of mostly frontal or temporal brain tumors in the MRI and high-grade tumors (WHO grade III and IV) would be correlated with more severe language impairments in standardized language tests, especially of verbal fluency, pre- and postoperatively.

No significant predictive value of volumetric tumor size in cubic centimeters on the overall language score or verbal fluency scores in the ACL or RWT before surgery was found. A non-significant tendency, suggesting that larger brain tumors in cubic centimeters lead to a decrease in the overall language score, was identified. Given the result is below the significance level and that is based on a very small subject group, it should not be stated that such finding holds generally true.

Both evidence in favor or against such negative influence on tumor size on language or cognition in general can be found in the literature. On the one hand, larger tumor volumes before surgery were found to result in a higher number (Tucha et al., 2000) and more severe cognitive difficulties (Talacchi et al., 2011). Verbal fluency seemed to be specifically affected by tumor size (Tucha et al., 2000). On the other hand, other studies do not come to such conclusion. On the contrary, the severity and subtype of language impairment did not depend on tumor grade (Davie et al., 2009). The different findings in these studies may be explained by the different types of tumors, the fact that one study explored tumor size and the other tumor grade, the use of differing tests of cognition and language, or differences in measuring tumor size. It must be further pointed out that the volumetric tumor sizes of the study group lay between 1.6cm^3 and 399.2cm^3 (Tucha et al., 2000) while the variability of tumor size in this master's thesis was considerably lower and the maximum value was around 80cm^3.

The measurement strategy seems to be of special interest, given that brain tumors can be measured in various ways. Overall, manual segmentation is considered to be an accurate but time-consuming technique. Traditionally, tumor size measurements are uni- or bidimensional. These linear measurements have the disadvantage of being less sensitive to the actual size of tumors with a very irregular shape in three-dimensional space. Volumetric measurements can overcome the problem of accurately measuring tumor size in tumors of irregular shape. Still, the challenge of differentiating actual tumor tissue from normal tissue remains difficult when the conspicuity of the tumor against the underlying tissue is low. It is important to address conspicuity in volumetric measurements of tumor size, as a correct detection of tumor margins is a requirement for detecting the correct tumor size, more so than in linear measurements where only one slice requires accurate edge detection. It is not only more difficult to measure irregular, but also smaller tumors (Goldmacher & Conklin, 2012).

Apart from these differences in measurement technique, the precision of tumor size measurements generally depend on the individual's anatomy, tumor shape and margin, the rater, slice thickness and contrast administration (Goldmacher & Conklin, 2012).

Further analyses of either tumor size or WHO grade and the overall language score or verbal fluency after surgery were not performed due to the very low number of subjects at that point in time. Here, it would have been interesting to see whether even after the surgical removal of tumors, such correlation could be found. The reason for this assumption would have been that larger brain tumors require a larger resection, thereby leading to a bigger lesion area after surgery which would in turn affect language more seriously.

In addition, it would have been of interest to gain new insight regarding the influence of WHO tumor grade on language, as fast growing tumors lead to significantly more severe impairments in the performance subtests of the *Wechsler-Bellevue Intelligence Scale* (Wechsler, 1941) in a study by Hom & Reitan (1984) and in lower language scores of spontaneous speech, comprehension, repetition and naming (Yuan et al., 2020). Such a negative influence of fast-growing tumors with a higher WHO grade would also go hand in hand with the assumption that the brain has less time to adapt to the fast-growing tumor (Heiss et al., 2003a; Hom & Reitan, 1984).

It must be pointed out again, that especially in the analysis of tumor size and grade, the results are based on an even smaller number of participants, because secondary brain tumors do not have a WHO tumor grade, and because some data was missing, thereby resulting in the exclusion of some participants.

> The fourth hypothesis was the prediction that more severe language impairments in the standardized language tests ACL, RWT and MEC would be diagnosed immediately post- in comparison to pre-operatively in individuals with mostly frontal or temporal brain tumors.

The comparison of six participants before and immediately after surgery suggested a slight deterioration of language when considering the mean overall language score and looking at the results in detail, but the difference was not significant. The reason for the insignificant result might be the small number of participants or that the deterioration was too light.

The fact that five out of six participants had more impairments and the same number or more moderate or severe impairments in the language tests immediately after surgery can be taken as a tendence towards a post-surgical deterioration. This is in line with the literature where at least shortly after surgery, language abilities can become worse because of the surgical resection of compensatory structures (Duffau et al., 2003) or due to other processes such as edema (van Kessel et al., 2020) or inflammation (Vaidya et al., 2019).

The resection of intrahemispherically compensating structures (Heiss et al., 2003) has to be considered especially in the case of high-grade gliomas which are often more extensively resected to ensure a longer life expectancy (Sanai & Berger, 2008). However, when looking at the individuals' performance before and after surgery and their tumor type and grade, no clear picture emerges. There was one subject with a glioblastoma grade IV who performed a lot worse after in comparison to before surgery, which would be in line with the theory that a more extensive resection and potential removal of compensatory structures took place. Nevertheless, other subjects in the study group had a glioblastoma too and only showed a less pronounced deterioration or suffer from a low-grade astrocytoma and still experienced a more severe language impairment after surgery. This may be explained by the practice to also resect low grade glioma more extensively when they are considered to be at risk for changing to malignant tumor types (Sanai & Berger, 2008).

The finding that the study group's performance non-significantly diminished immediately after surgery is a novel and interesting finding in the subgroup consisting of persons only with frontal or parietooccipial tumors given that such functional recovery has so far only been described for patients with tumors in primary language areas (Duffau et al., 2003). Even though the group is very small and the difference was insignificant in the statistical analysis, it should be considered that a slight deterioration in language abilities shortly after tumor resection might be witness not only in primary language areas but also in persons who suffer from language impairments caused by frontal or parieto-occipital brain tumors.

As only six of the initially 15 participants conducted the complete language testing procedure at two points in time, it is essential to indicate that the presented results were based on an even smaller subject group and that some relevant information is missing due to the dropping-out of some participants. For instance, one of the subjects that showed a quite severe impairment in most language tests, did not further participate in the study. Therefore, it is not known whether the described pattern of language before and after surgery is equally true for those individuals who experienced more severe language impairments. A reason for dropping-out was not always given, but it can be assumed that probably those with more severe impairments were in need of neurorehabilitative measures and may therefore have ceased their participation in the study.

5.2 Exploratory Observations

In addition to the findings revolving around the hypotheses in the last chapters, other observations concerning language impairments caused by brain tumors were made and are now described here.

In the MEC text comprehension task (Scherrer et al., 2016), retelling the story was often characterized by missing information, but not so much by addition or changes of information. This may be interpreted as an indication of impaired mnestic and other non-linguistic cognitive abilities necessary for this task. Ferstl et al. (2005) highlight the complexity of reading comprehension by pointing out that it is a skill which, apart from the necessity to linguistically decode the message, involves cognitive processes such as attention, memory and executive functioning. Attention is required to be able to listen to longer texts, and verbal working memory enables storing information. Executive functions are involved insofar that they organize and integrate information with other knowledge and monitor comprehension.

Interestingly, most subjects were better at retelling the whole story, while retelling parts of the story resulted in the elision of more information. At first sight, this may come as a surprise, because the retold parts were sometimes shorter than whole story. On the other hand, it could be argued that, as the whole story holds only the most important and thereby maybe more salient information, that it is easier to remember these key points than to retell even shorter points of less importance. This goes hand in hand with Ferstl et al. (2005) who confirm that it is easier to answer questions about main ideas than about details, and that questions about implicit are more difficult to answer than about explicit information.

In one of the MEC text comprehension tasks (Scherrer et al., 2016), the tested person is asked to give the text a title. The text deals with a lazy farmer who outwits his neighbors so that they unknowingly dig a well for him in the belief that the farmer is burried in the well (Scherrer et al., 2016). The title is then judged by whether it is related to the story and infers to the deceit, only refers to the story in general without the inference or is not related to the story at all. Examples for these three steps in the study group were "Michael, der schelmische Brunnengräber" ("Michael, the prankful well-digger") for relation to the story and reference to the implications, "Der Brunneneinsturz" ("The collapse of the well") for a reference to the story without the inference, and the very generic title "Ein aufregender Tag" ("An exciting day") without a specific relation to the story at all. Even though the majority of patients managed to express the inference, it is interesting to mention that many had difficulties with understanding the concept of giving a title. One subject, for instance, came up with "Schlau, intelligent" ("clever, intelligent") which are basically adjectives for describing what is happening, but not a complete title. Büttner and Glindemann (2019) already pointed towards the difficulties with giving a title, which they interpret as a deficit in abstracting and generalizing information from the text level to a title.

In the MEC metaphor task (Scherrer et al., 2016), it was observed that many subjects who had described metaphors adequately before tumor resection, used personal anecdotes when explaining the metaphors after surgery. With regard to the error types, some subjects explained the metaphors literally, but far more often, explanations were imprecise or, on the contrary, characterized by additions of unnecessary to the definition. The pattern of adding personal information might be considered a problem of abstracting. It could be argued that the personal explanation is the more salient meaning, while a more abstract and general explanation is more difficult to retrieve. This idea is backed by a study on metaphor interpretation in Alzheimer's patients by Roncero & de Almeida (2014). The study suggests that the ability to abstract as an executive function is a prerequisite for comprehending and further explaining metaphors. By possessing appropriate abstraction abilities, it is supposed to be easier to understand the relation between two concepts and that metaphors are usually based on such relation. The authors argue that abstraction is a skill which is related to inference, and inference is necessary for figurative language, where the figurative is inferred from the literal meaning (Roncero & de Almeida, 2014).

Additionally, it was noted that many participants would repeat the metaphor before explaining it only after surgery. For instance, the instructor would read "Dieser Lehrer ist eine Schlaftablette" (literal: "This teacher is a sleeping pill", figurative: "This teacher puts me to sleep") and the patient would first repeat this exact sentence and only then continue to explain "Er hat zu wenig zu tun […]" ("He does not have a lot to do"). One possible explanation would be that the patient is repeating the instructed metaphor to keep it present in their working memory. Interestingly, some patients repeated the metaphor, but did not further explain it. This could again be a sign of a mnestic disorder, where the instruction to explain the metaphor is forgotten by the time the person repeats the metaphor. At least in healthy adults, verbal short-term memory as the capacity of holding information, was shown to be a positive predictor of performance in a metaphor explanation task, meaning that the better the verbal short-term memory, the better the explanations of metaphors. By contrast, working memory as the manipulation of held memory, and divided attention were less influential on correct explanations (Iskandar & Baird, 2014).

Also, some subjects were unimpaired in the ACL (Kalbe et al., 2002) in reading and auditory comprehension tests but showed uncertainty when choosing the appropriate picture with regard to the distractor. Sometimes, the participants would choose the distractor and then correct themselves. As self-corrections are allowed to some degree and only result in little changes to the final score, looking at the frequency of self-corrections in healthy versus the brain damaged population would be of interest. Executive functions which are associated with the frontal lobes, are described to be involved in the inhibition of competing alternatives in language comprehension (Ye & Zhou, 2009). Accordingly, the high number of choosing the distractors could be a result of executive dysfunction.

A similar consideration concerns the RWT category switching task (Aschenbrenner et al., 2000) where errors such as category perseverations are written down, but the number and types of errors cannot be compared to a normed sample. It is mentioned that errors are unusual in the healthy population (Aschenbrenner et al., 2000). Crowe (1992) showed that errors in verbal fluency tasks are more common in individuals with brain damage in comparison to healthy persons. Seeing how some participants generated a considerable number of words and committed a large number of errors, such analysis would be of interest.

Some subjects repeated named words and where unsure whether they had used a word before in the verbal fluency and the category switching task. During the scoring of the RWT (Aschenbrenner et al., 2000), it was noted that some patients appeared to have difficulties with inhibiting the explanation about not being allowed to use proper names. Especially at the beginning, they would use proper names, then realize it was not allowed, continue with other words, and then sometimes even go back to using proper names again. Again, it could be argued that this is caused by impaired inhibition of competing alternatives or as deficient selection mechanisms of verbal answers (Ye & Zhou, 2009). Perseveration has been described as a sign of a frontal lobe lesion before, but it remains unclear whether it should be understood as a deficit in verifying that a given answer is incorrect and should therefore be discarded or a problem with coming up with only one solution and no other alternatives (Crowe, 1992).

Most patients did not seem to follow a certain strategy when being asked to name as many words as possible in the verbal fluency tests of the ACL (Kalbe et al., 2002). Some started out by naming very broad terms, only to end up not finding any more broad terms. Other participants named untypical words in the semantic fluency task, such as notebooks when being asked for what products can be bought at the supermarket. The lack of strategy in the group could be interpreted as reduced problem-solving abilities, which in turn seems to rely on a large brain network that encompasses the executive function network too (Bartley et al., 2018). In the literature, the two strategies clustering (searching words withing a certain subcategory) and switching (alternatingly searching for words between subcategories) are described for verbal fluency tasks. Clustering is associated with the functioning of the temporal lobes and switching with the frontal lobes (Troyer et al., 1998). In their study, Troyer et al. (1998) reported that persons with frontal lobe lesions used less switching but the same amount of clustering as healthy persons. The results for temporal lobe lesions were less clear-cut in either direction. The authors follow that the most reliable differentiation is to expect impaired lexical switching in patients with frontal lobe lesions and impaired semantic clustering in individuals with temporal lesions. Such comparison is not possible here, because the group of temporal lobe brain tumor patients is far smaller. However, in this master's thesis, it was noted that a few subjects used the strategy of clustering.

5.3 Results in View of Cognitive Science

In cognitive science, grounded cognition is a theory of cognition which rejects traditional, cognitivist or representationalist views which understand cognition as a computation with amodal symbols which represent knowledge in a modular system that is kept separate from perception, action and introspection. Instead, grounded cognition assumes that "cognition is typically grounded in multiple ways, including simulations, situated action, and on occasion, bodily states" (Barsalou, 2008, p. 619). These simulations refer to reenacting of perceptual, motor or introspective states from earlier experiences in the world. As such, when one sits in a chair, a multimodal experience of the chair's look, associated feelings such as comfort and the action of sitting in the chair, are reactivated (Barsalou, 2008). With reference to language, embodied cognition would argue that perception and action are recruited in language processing, for instance to grasp the meaning of a linguistic symbol (Knoeferle et al., 2010). Examples of the role of the motor system for language processes are that the motor system has been shown to be activated when someone hears a word such as "kick" or that somatosensory areas in charge of imagination were shown to be recruited when reading a text about someone interacting with something (Fischer & Zwaan, 2008).

The embodied understanding of language has consequences for this thesis as well as for the diagnostics and therapy of language impairments. Ahlsen (2008) points out that similar to the mentioned cognitivist ideas of general cognition, cognitivist linguistic models should be rejected or adapted to incorporate findings from grounded cognition. For instance, updated models should take a serial language perception and production process and the close link of gesture and language into account. A further aspect which should be addressed by the newer models would be to not only look at one communicating individual, but at the interaction with someone else in a context. Last but not least, certain cognitive processes such as concept formation in language should be considered with its association to movement and action. Specific suggestions for speech therapy are the analysis of video-recorded communicative interaction, the study of activity-based communication as well as the consideration of multimodal communicative patterns (Ahlsen, 2008).

With respect to this master's thesis, it should therefore be followed and criticized that the diagnostic tools used with the brain tumor patients did not incorporate non-verbal language. Even though the MEC's spontaneous speech analysis (Scherrer et al., 2016) provides criteria relating to gesture and mimics, it was not possible to evaluate these aspects because no video-recordings were taken of this task. On the other hand, it must be pointed out that not only the individual's communicative abilities in tests were evaluated, but the spontaneous speech analysis is a method where dialogue is taken into account. Some of the rating criteria in the test also incorporate aspects such as interrupting the communicative partner.

Nevertheless, it must be conceded that the majority of tasks used in this study were traditional diagnostic methods which require the tested person to give answers, write or read or solve another problem without being embedded in a communicative situation.
On a more general level, it must be said that some knowledge from embodied cognition has been integrated to or already present in speech therapy. For example, the observation of action performed by the speech therapist, the observation and execution of action of the speech therapist and the patient, and the observation of action in a videoclip in verb retrieval training in persons with aphasia have been shown to be beneficial for verb production in comparison to the control condition without such movement (Bonifazi et al., 2013). A further example of taking grounded cognition in speech therapy into account is the employment of aphasia group therapy, where the communicative situation is more natural, involves interaction between members and offers a greater variety of communicative partners (Elman, 2007). It is also not new that gesture as nonverbal communication is used in aphasia therapy for compensatory and facilitatory reasons to improve communication. Gesture training according to a standardized protocol and combined with verbal training has been proven to have a positive effect on language in aphasics (Rose, Raymer, et al., 2013). Considering the importance of multimodal experience in grounded cognition (Barsalou, 2008), it should be mentioned that multi-modal treatment of aphasia involving not only verbal tasks but also drawing, writing or gesturing are quite common (Rose, Attard, et al., 2013). An attempt to not only treat but also measure multimodal communication in persons with language impairments is the *Scenario Test* (van der Meulen et al., 2010).
It has already been mentioned that cognitivist paradigms are criticized in modern cognitive science. An example of such modular views regarding neuroscience would be modularity, a symbolic and localist paradigm which designates the idea that cognition is organized as psychological faculties in the human mind. It is based on the idea that cognitive abilities are neurologically hardwired, meaning that they have a specific and localized neural basis (Fodor, 1983). Even though this approach is not supported in this master's thesis, it must be conceded that lesion studies such as this one have representationalist features.
Lesion studies look back at a long history of researching the neuronal basis of human behavior in fields such as language or memory. The idea behind it is the mapping of certain cognitive dysfunctions to a lesioned area. However, even combination of neuroimaging methods with a clinical population does not allow to directly infer from a symptom to the region, because it is not possible to distinguish the involvement of such region from its necessity in that cognitive process. The most effective and reliable way to proof the necessity is by a high number of subjects, controlling for the premorbid function, using control groups and patients with diseases of similar etiology, and the use of neuropsychological tests which do not involve a high number of cognitive functions (Vaidya et al., 2019). Accordingly, even

though the participants in this master thesis' study were similar in demography and standardized tests were used, it must be acknowledged that some of the language tests such as the metaphor comprehension task require various cognitive functions. Here, assumptions about the cause and consequence should be made cautiously. Nevertheless, lesion studies can provide vital insight into the functioning of the brain and possibly improve the treatment of patients with a neurological disease (Vaidya et al., 2019).

After having mentioned lesion studies and their relevance for neurological diseases, the topic of clinical work in neurology and its similarities and differences to neuroscientific research should be addressed. It appears that the insight from clinical diagnostics and treatment support neuroscientific research and, equally, that neuroscientific research is essential for clinical work. However, it seems that it is not always feasible to combine both, and that the exchange of information is too little. For instance, the evidence that cognition is grounded (Barsalou, 2008), the insight that language is based on a complex distributed network (Gierhan, 2013) and that standard aphasia syndromes are based on an outdated, simplified brain anatomy (Tremblay & Dick, 2016) as well as the knowledge that lesion studies should be treated with precaution (Vaidya et al., 2019) should be considered in clinical work. Nonetheless, some differences appear to stem from the objectives persons have in their clinical or scientific work, as clear terminology such as for aphasia types is handy in clinical work. Another example of such seemingly superficial but convenient differentiation is the separation of cognition from language in clinical neurology. It has been addressed in the theoretical part of this thesis that cognitive scientists disagree over whether language and cognition should be viewed as separate or whether language is based on cognition (Harris, 2006). In view of the distributed language processing network (Gierhan, 2013), the involvement of executive functions in language (Ye & Zhou, 2009), and the findings in this thesis about impaired language in individuals with brain tumors in areas described to be less or non-relevant to language, it seems difficult to completely separate cognition from language.

Although this master's thesis did not involve any computational linguistics or modelling, it should be addressed that research in these fields seems to be promising, as seen in a study by Keidel et al. (2010). The divergent patterns of symptoms and rehabilitation in stroke in contrast to slow growing brain tumors (Anderson et al., 1990; Duffau et al., 2003) have been a subject of study in neurocomputational modelling. Neuronal network models were developed and either stroke was simulated by suddenly and completely deleting one hidden layer of the network, or brain tumor was simulated by slow and stepwise weight decay of one hidden layer. The stroke simulation resulted in a large performance decline with a dissociation between a task where the layer was necessary and another unaffected task. The brain tumor simulation, on the other hand, exposed a smaller decline in performance (Keidel et al., 2010).

5.4 Limitations

The findings of this master's thesis are limited by factors concerning the study group, methods and restrictions from the underlying theory, all of which will be addressed now.

First and foremost, a major limitation of the study is that the subject group is rather small, but also very heterogenous with regard to tumor type and location. A larger study group consisting of persons with only frontal brain tumors or tumors of one hemisphere only would have made it easier to generalize to the clinical population.

Even though the participants of the experiment only received medication according to a standard procedure and orientation was checked before every language testing, it cannot be completely ensured that the medication did not affect cognition at any point in time. The reason for this being that it is not documented which medication was given on the day of the testing and some medication is known to possibly cause changes in cognitive abilities. Among the described medication, two drugs were found to be possibly influential, Keppra (250mg, non-proprietary name Levetiracetan) and Convulex (500mg capsules, non-proprietary name Valproate). Common side effects of Keppra which may be relevant for a language testing are irritability, aggression, and fatigue (EMA, 2009). A common cognitively relevant side effects of Convulex is fatigue (Diagnosia, n.d.).

Since the *Fragebogen zur Orientierungsprüfung (FOP)* is based on a very small sample and information about aspects such as retest reliability are missing (Hupfeld, 2009), it should be considered to use orientation tests in future studies which meet these quality criteria. As the *Aphasie-Check-Liste (ACL)* entails subtests to assess non-linguistic cognitive functions relevant to language (Kalbe et al., 2002), future studies interested in the role of non-linguistic cognitive processes in language should include these subtests. In a review of the *Neglect Test (NET)* (Fels & Geissner, 1997), it has been criticized that ceiling effects could arise in patients with a very mild neglect (Schmitt & König, 1999). Even though the *Regensburger Wortflüssigkeitstest (RWT)* was standardized with 634 subjects, the standardization relies on healthy subjects only (Aschenbrenner et al., 2000). As such, percentile ranks for persons with a neuropsychological disorder following acquired brain injury are not available. A similar problem comes with the use of the *MEC Testverfahren* (Scherrer et al., 2016) which was also standardized with healthy subjects only. With regard to the actual conduction of the language tests in the experiment, it should be mentioned that the validity of the results of single subtests is inferior to the conduction of a complete test batteries.

Moreover, in order to come to a valid conclusion about the usefulness of the ACL for brain tumor patients, it would be necessary to conduct a study were the results are compared to other language tests or to a clinical evaluation, as it was done in the study by (Wacker et al., 2002).

In addition to these considerations about the tests, it should be mentioned that it is a challenge to judge certain pathological aspects of spontaneous speech, such as the completeness of sentences or the number of repetitions of already mentioned aspects. The spontaneous speech of healthy adults is also characterized by pauses, repetitions of what was already said or false starting of sentences which form fluent and hesitant periods of speaking (Pakhomov et al., 2011), which complicates a differentiation from morpho-syntactic abnormalities in a clinical population.

Regarding socio-demographic aspects, it has been addressed before that verbal fluency tasks are age-dependent and that an age-dependent score exists for ACL verbal fluency tasks. However, it should also be mentioned that those tasks are also dependent on education. Zimmermann et al. (2014) have shown that education has a significant effect on accuracy and total scores of phonemic but not semantic fluency, meaning that persons with a higher education performed better in phonemic verbal fluency than those with a lower education. This insight is highly relevant, because the ACL verbal fluency tasks do not take education into account.

Concerning the *NBV* (Schellig & Schuri, 2009) it should be said that even though it is a task of widespread use in neuropsychological experiments, few studies have actually explored which cognitive ability it actually measures (Jacola et al., 2014). Recently, it was found that the task is related to different cognitive processes depending on age. Whilst the performance is related to executive functions in individuals until the age of 40 years, older individuals of up to 60 years of age tend to expose additional attentional processes and at an even older age of up to 80 years no involvement of executive processes (Gajewski et al., 2018). Apart from these limitations concerning the healthy population, it has been debated how verbal abilities are an essential prerequisite in the NBV. In a pilot study with individuals with aphasia of vascular etiology comparing the performance to healthy subjects in three n-back paradigms with differing linguistic load, people with aphasia performed worse and were less able to make use of linguistic knowledge in some of the tasks. Thus, it should be considered that aphasia has an effect on the results in such working memory tasks (Christensen & Wright, 2010).

A problem in the discussion of terminology of cognitive-communication disorders is that even those resources which define brain tumor as causal continue to describe symptoms and treatment based on literature that mainly studies individuals with traumatic brain injury such as the book on cognitive-communication disorders by (Büttner & Glindemann, 2019) or clinical guidelines (College of Audiologists and Speech-Language Pathologists of Ontario, 2012; College of Audiologists and Speech-language Pathologists of Ontario, 2018). Consequently, it is very difficult to draw conclusions about language impairments in brain tumor patients and to relate the findings to the literature.

A similar problem arises when discussing the involvement of executive functions in language. Executive functions are a very big concept with varying definitions (Stuss, 2011).
Another closely related limitation of this work is that it has been pointed out several times, how in the literature information regarding brain tumor patients in general, and not only in view of cognitive-communication disorders, is lacking. In the discussion the results are consequently compared to language impairments caused by other neurological disorders.
In view of the role that the brain tumor's location is conceded within this master's thesis for explaining language impairments, the topic of dissociation logic should be addressed. In lesion studies, showing the specificity of a certain region for a specific function A, but not for function B (dissociation) has been proven to be more reliable than displaying the involvement of a certain region in one function (association). Nevertheless, this type of single dissociation provides weaker evidence than a crossover double association, where an area is relevant for function A but not B, and another region is involved in function B but not A (Vaidya et al., 2019).
It is significant to mention that studies about language representation may also come to different findings due to the experiments' language, such as it was shown in a study about the neural basis of pragmatic language processing showing fronto-temporal activation in Germanic languages, recruitment of left frontal in Romance languages and right medial prefrontal cortex activations in Japanese (Reyes-Aguilar et al., 2018).
Last but not least, it must be pointed out again that tumor size can be highly dependent on the measurement technique, the rater and other factors such as image quality (Goldmacher & Conklin, 2012).
Despite these limitations, it should not be forgotten that the strengths of this study are its use of standardized language tests, strict exclusion and inclusion criteria and the reliance on not only behavioral but also neuroimaging data. In addition, the results of this rather small study group can contribute to an area of comparably small number of studies.

5.5 Future Directions

In addition to the up to this point described findings, the results also suggest aspects which should be considered in future studies of similar topic. The following suggestions are made. Due to the fact that subjective cognitive functioning is not always clearly associated with objective cognitive functioning in brain tumor patients (Nicol et al., 2019), it may be insightful to include subjective accounts of cognitive functioning of brain tumor patients in future studies. This could be done in the form of a neurophenomenological study (Varela, 1996), which enables the combination and integration of first-person data through phenomenological interviews with third-person data obtained by neuroscientific methods (Lutz & Thompson, 2003). However, the application of a neurophenomenological paradigm seems only feasible with very mild aphasia, as the methods presuppose intact or at least adequate communicative abilities as well as the ability to reflect. Another possibility would be to routinely include aphasia self-assessments or assessments which are filled out by close relatives such as the *Communicative Effectiveness Index (CETI)* (Lomas et al., 1989).

As the *Aachener Aphasie Test* (Huber et al., 1982) was already used with brain tumor patients and compared to clinical assessments of language (Wacker et al., 2002), and the underlying experiment of this master's thesis was the first one to use the *Aphasie-Check-Liste* (Kalbe et al., 2002), future studies could further combine these test batteries and compare their performance within this clinical population. Based on the discussion in chapter 5.3 about grounded cognition, the *Scenario Test* (van der Meulen et al., 2010) or a similar test could be used to evaluate nonverbal communication.

In view of the current state of research, it should also be considered whether other available aphasia tests from stroke research could be even more appropriate. Due to the fact that language impairments in individuals with brain tumors are usually depicted as being rather mild (Davie et al., 2009), knowledge from stroke patients with residual or mild aphasia could be employed to find appropriate diagnostic tools for brain tumor patients. It has already been described how mild aphasia after stroke is difficult to detect with certain test batteries and that speech therapists need to combine different methods to ensure an appropriate diagnosis. For instance, it is necessary to choose picture-naming tasks with words with a lower frequency or to include not only the reading comprehension of words but also texts (Jaecks, 2015). These insights should be transferred to the diagnosis of language impairments caused by brain tumors. Accordingly, it could be argued that the strongly "controlled" language subtests enable the subjects to give the right answer, while during the much more complex linguistic process of engaging in spontaneous speech, more errors come to light and thereby enable the diagnosis of a subtle language impairment. Apart from the level of control, the test should entail a spontaneous speech analysis, as some were relatively unimpaired in the ACL subtests (Kalbe et al., 2002), especially in picture-naming, but then exposed word-finding difficulties or semantic or phonematic paraphasia in the spontaneous speech analysis. This matches the findings by (Satoer et al., 2018) that an analysis of spontaneous speech might be more reliable in detecting language impairments than standardized language tests. This phenomenon can be compared to the area of residual aphasia following stroke, where standardized language tests sometimes fail to diagnose a subtle language disorder even though deficits occur in spontaneous speech (Jaecks et al., 2012). Similar to the first available English language test developed for brain tumor patients (Faulkner et al., 2017), the development of such a German test or the adaptation of the English version should be considered.

Owing to the essential role of executive functions in language (Fedorenko, 2014), the necessity of interdisciplinary research and interdisciplinarity in clinical practice should be addressed as well. Neuropsychologists and speech therapists should cooperate to ensure that the knowledge from both disciplines enables proper diagnosis and treatment.

6. Conclusion

The aim of this thesis was to research the characteristics and diagnostic methods of language impairments in individuals with mostly frontal or temporal brain tumors of primary or secondary nature of the left or right hemisphere before and after surgical tumor resection. Additional objectives were the exploration of potential differences between those with a tumor of the left or right hemisphere as well as the role of tumor size and WHO grade for language impairment severity.

The data of 15 individuals was collected at the Department of Neurosurgery of the state clinic *Landesklinik Wiener Neustadt* as part of the research project *EFRONESonko - Einfluss frontaler Netzwerke auf die Sprachverarbeitung bei Hirntumorpatienten* [Influence of Frontal Networks on Language Processing in Brain Tumor Patients] between 2017 and 2018 (Sollereder & Burtscher, 2021). The participant group consisted of elven men and four women with a mean age of 62,75 years who mostly had a secondary education II. All subjects were oriented, right-handed and had no neglect. Other inclusion criteria were at least 18 years of age, inpatient treatment, necessity of brain surgery and the diagnosis of a benign or malign tumor of the central nervous system. The brain tumors were located in the frontal (eight subjects), fronto-parietal (two subjects), temporal (three subjects) or parieto-occipital lobes (two subjects) and had a size between 0.96 and 82.44 cm^3. Most tumors were located in the left hemisphere and were of primary nature (both 11 out of 15 persons). Ethics approval was reached, and informed consent was given. A standardized medication procedure was followed. Language was assessed by means of parts of the standardized language tests *Aphasie-Check-Liste (ACL)* (Kalbe et al., 2002), *Regensburger Wortflüssigkeits-Test (RWT)* (Aschenbrenner et al., 2000) and *MEC-Testverfahren (MEC)* (Scherrer et al., 2016) one to six days before and four to nine days after surgery. The language tests were scored according to their manuals, blinded regarding demographic information or the time of the testing. Acquired MR images were analyzed in *SPM5* (Ashburner et al., 2009) and *MRIcron* (Rorden & Brett, 2000). The statistical analysis was performed in the program *R* (R Core Team, 2017).

The findings of this study suggest that language impairments in this study's individuals occur frequently and are predominantly mild but can also be severe in single cases. Additionally, they mostly affect specific aspects of language. Lexical and semantic verbal fluency and category switching, performance in the color-figure test, reading comprehension of words and sentences, text- and metaphor comprehension as well as spontaneous speech were more frequently and more severely impaired than other aspects of language. Repetition and reading were mostly spared, while writing, auditory comprehension of words and sentences as well as picture-naming were sometimes disordered.

Furthermore, it was detected that subtests requiring executive functioning were more frequently and severely impaired in the study group and this finding was backed by the even higher number of impairments in these subtests when looking at the persons with frontal brain tumors only. Some exploratory observations about the language impairments found in most subjects were an omission but no change of information in text comprehension, the use of personal anecdotes in the metaphor explanation task, self-corrections after having chosen the distractor in comprehension tasks, a lack of strategy as well as category perseverations in verbal fluency tasks. These characteristics could be interpreted as signs of impaired mnestic (Ferstl et al., 2005), abstraction (Roncero & de Almeida, 2014), inhibitory (Ye & Zhou, 2009) and problem-solving (Bartley et al., 2018) abilities, thus corresponding to the definition of a cognitive-communication disorder (American Speech-Language-Hearing Association, 2005).

No processing advantage of the right in comparison to the left hemisphere in pragmatic language could be corroborated in the subject group. Instead, tumors of the left and of the temporal hemisphere resulted in more frequent and severe language disabilities. Individuals with frontal brain tumors exposed a higher number of pragmatic errors. Metaphor comprehension were mostly spared in individuals with right hemisphere tumors. Semantic verbal fluency was more frequently and severely affected in persons with left hemisphere tumors.

The diagnostic methods *ACL* (Kalbe et al., 2002), *RWT* (Aschenbrenner et al., 2000) and *MEC* (Scherrer et al., 2016) used in the study were all capable of detecting some impairments in the study group and therefore seem to be at least partially suitable for this clinical population, even though they were not compared to other language tests and tumor-specific language tests are not yet available in German. Most importantly, it was found that some difficulties were only identified in the spontaneous speech analysis even when a subtest of a standardized language task testing word-finding was unimpaired.

Another finding was a slight but statistically non-significant deterioration of the overall language score immediately after surgery in comparison to before surgical resection. At an individual level, more impairments as well as more moderate and severe disorders of language were detected after in contrast to before surgery.

No clear influence of tumor grade and size in connection with tumor resection emerged, meaning that individuals of this study group with larger or more aggressive brain tumors and therefore possibly more extensive tumor resections were not necessarily more severely disordered after the operation.

Future studies with similar objectives should consider larger, more homogenous subject groups. In line with grounded cognition (Ahlsen, 2008; Barsalou, 2008), the use of tests which evaluate nonverbal communication or language in dialogue should be considered. In agreement with prior work (Jaecks, 2015; Satoer et al., 2018) and the findings of this thesis, speech therapists who diagnose and treat language impairments of this clinical population should consider routinely assessing language on a complex level, analyzing spontaneous speech, and choosing language tests which require executive functions.

References

Abrey, L. E., & Mason, W. P. (2003). *Fast Facts: Brain Tumors*. Health Oress.

AERA, APA, & NCME. (2014). Standards for educational and psychological testing. In. Washington: American Educational Research Association.

Ahlsen, E. (2008). Embodiment in communication - aphasia, apraxia and the possible role of mirroring and imitation. *Clin Linguist Phon*, *22*, 315. https://doi.org/10.1080/02699200801918879

Alther, B., Mylius, V., Weller, M., & Gantenbein, A. (2020). From first symptoms to diagnosis: Initial clinical presentation of primary brain tumors. *Clinical & Translational Neuroscience*, 1-7. https://doi.org/10.1177/2514183X20968368

Alvarez, J. A., & Emory, E. (2006). Executive Function and the Frontal Lobes: A Meta-Analytic Review. *Neuropsychol Rev*, *16*, 42. https://doi.org/10.1007/s11065-006-9002-x

American Speech-Language-Hearing Association. (2005). *Roles of Speech-Language Pathologists in the Identification, Diagnosis, and Treatment of Individuals with Cognitive- Communication Disorders: Position Statement* (Rescinded document for historical purposes only, Issue. www.asha.org/policy (rescinded document - for historical purposes only)

Amoruso, L., Geng, S., Molinaro, N., Timofeeva, P., Gisbert-Muñoz, S., Gil-Robles, S., . . . Carreiras, M. (2021). Oscillatory and structural signatures of language plasticity in brain tumor patients: A longitudinal study. *Hum Brain Mapp*, *42*, 1793. https://doi.org/10.1002/hbm.25328

Anderson, S. W., Damasio, H., & Tranel, D. (1990). Neuropsychological Impairments Associated With Lesions Caused by Tumor or Stroke. *Arch Neurol*, *47*, 379-405. https://doi.org/10.1001/archneur.1990.00530040039017

Arcara, G., Bambini, V., Skrap, M., & Campanella, F. (2018). *Lesion Lateralization and Pragmatic Deficits: Evidence from Brain Tumor Patients. Front. Psychol. Conference Abstract* XPRAG.it 2018 - Second Experimental Pragmatics in Italy Conference, Pavia, Italy.

Armstrong, T. S., Vera-Bolanos, E., Acquaye, A. A., Gilbert, M. R., Ladha, H., & Mendoza, T. (2016). The symptom burden of primary brain tumors: evidence for a core set of tumor- and treatment-related symptoms. *Neuro Oncol*, *18*(2), 252-260. https://doi.org/10.1093/neuonc/nov166

Aschenbrenner, S., Tucha, O., & Lange, K. W. (2000). *Regensburger Wortflüssigkeits-Test (RWT) [Regensburger Word Fluency Test (RWT)]*. Hogrefe.

Ashburner, J., Flandin, G., Henson, R., Kiebel, S., Kilner, J., Mattout, J., . . . Hutton, C. (2009). SPM5 Manual. The FIL Methods Group. In. London.

Baddeley, A. (2003). Working memory and language: an overview. *J Commun Disord*, *36*, 208. https://doi.org/10.1016/S0021-9924(03)00019-4

Barsalou, L. W. (2008). Grounded Cognition. *Annu Rev Psychol*, *59*, 645. https://doi.org/10.1146/annurev.psych.59.103006.093639

Bartha, L., Knosp, E., Pfisterer, W., & Benke, T. (2000). Intra- and perioperative monitoring of language functions in patients with tumours in the left perisylvian area. *Aphasiology*, *14*, 793. https://doi.org/10.1080/026870300412205

Bartley, J. E., Boeving, E. R., Riedel, M. C., Bottenhorn, K. L., Salo, T., Eickhoff, S. B., . . . Laird, A. R. (2018). Meta-analytic evidence for a core problem solving network across multiple representational domains. *Neurosci Biobehav Rev*, *92*, 337. https://doi.org/10.1016/j.neubiorev.2018.06.009

Barzilai, O., Ben Moshe, S., Sitt, R., Sela, G., Shofty, B., & Ram, Z. (2018). Improvement in cognitive function after surgery for low-grade glioma. *J Neurosurg*, 1-9. https://doi.org/10.3171/2017.9.JNS17658

Bechtel, W., & Abrahamsen, A. A. (1991). *Connectionism and the mind : an introduction to parallel processing in networks* (1. publ.. ed.). Blackwell.

Berg, K., Isaksen, J., Wallace, S. J., Cruice, M., Simmons-Mackie, N., & Worrall, L. (2020). Establishing consensus on a definition of aphasia: an e-Delphi study of international aphasia researchers. *Aphasiology*. https://doi.org/10.1080/02687038.2020.1852003

Bette, S., Gradtke, C. V., Cammardella, J. H., Albertshauser, J., Wiestler, B., Barz, M., . . . Gempt, J. (2020). Perioperative neurocognitive functions in patients with neuroepithelial intracranial tumors. *J Neurooncol*, *147*(1), 77-89. https://doi.org/10.1007/s11060-020-03398-8

Biniek, R., Huber, W., Willmes, K., Glindemann, R., Brand, H., Fiedler, M., & Annen, C. (1991). Ein Test zur Erfassung von Sprach- und Sprechtstörungen in der Akutphase nach Schlaganfällen: Aufbau und Durchführung [A Test for the Assessment of Language- and Speech Impairments in the Acute Phase after Stroke]. *Nervenarzt*, *62*(2), 108-115

Bohrn, I. C., Altmann, U., & Jacobs, A. M. (2012). Looking at the brains behind figurative language—A quantitative meta-analysis of neuroimaging studies on metaphor, idiom, and irony processing. *Neuropsychologia*, *50*, 2683. https://doi.org/10.1016/j.neuropsychologia.2012.07.021

Bonifazi, S., Tomaiuolo, F., Altoè, G., Ceravolo, M. G., Provinciali, L., & Marangolo, P. (2013). Action observation as a useful approach for enhancing recovery of verb production: new evidence from aphasia. *Eur J Phys Rehabil Med*, *49*(4), 473-481.

Brownsett, S. L. E., Ramajoo, K., Copland, D., McMahon, K. L., Robinson, G., Drummond, K., . . . De Zubicaray, G. (2019). Language deficits following dominant hemisphere tumour resection are significantly underestimated by syndrome-based aphasia assessments. *Aphasiology*, *33*, 1181. https://doi.org/10.1080/02687038.2019.1614760

Büttner, J., & Glindemann, R. (2019). *Kognitive Kommunikationsstörungen* (1. Auflage. ed.) [Cognitive Communication Disorders]. Hogrefe.

Caplan, D. (1996). *Language: structure, processing, and disorders* (First MIT Press paperback edition.. ed.). MIT Press.

Catani, M., Jones, D. K., & ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Ann Neurol*, *57*, 16. https://doi.org/10.1002/ana.20319

Cha, S. (2009). Neuroimaging in neuro-oncology. *Neurotherapeutics*, *6*(3), 465-477. https://doi.org/10.1016/j.nurt.2009.05.002

Chakraborty, A., Sumathi, T. A., Mehta, V. S., & Singh, N. C. (2012). Picture-naming in patients with left frontal lobe tumor - a functional neuroimaging study. *Brain Imaging Behav*, *6*(3), 462-471. https://doi.org/10.1007/s11682-012-9165-4

Chan, R. C. K., Shum, D., Toulopoulou, T., & Chen, E. Y. H. (2008). Assessment of executive functions: Review of instruments and identification of critical issues. *Arch Clin Neuropsychol*, *23*, 216. https://doi.org/10.1016/j.acn.2007.08.010

Christensen, S. C., & Wright, H. H. (2010). Verbal and non-verbal working memory in aphasia: What three n-back tasks reveal. *Aphasiology*, *24*, 762. https://doi.org/10.1080/02687030903437690

College of Audiologists and Speech-Language Pathologists of Ontario. (2012). *Preferred Practice Guideline for Cognitive-Communication Disorders*. https://caslpo.com/members/resources/standards-and-resources/slp-practice

College of Audiologists and Speech-language Pathologists of Ontario. (2018). Practice standards and guidelines for acquired cognitive communication disorders. In. Toronto.

Crowe, S. F. (1992). Dissociation of two frontal lobe syndromes by a test of verbal fluency. *J Clin Exp Neuropsychol*, *14*(2), 327-339. https://doi.org/10.1080/01688639208402832

Davie, G. L., Hutcheson, K. A., Barringer, D. A., Weinberg, J. S., & Lewin, J. S. (2009). Aphasia in patients after brain tumour resection. *Aphasiology*, *23*, 1206. https://doi.org/10.1080/02687030802436900

de Paula, J. J., Paiva, G. C. d. C., & Costa, D. d. S. (2015). Use of a modified version of the switching verbal fluency test for the assessment of cognitive flexibility. *Dement Neuropsychol*, *9*, 264. https://doi.org/10.1590/1980-57642015DN93000008

de Schotten, M. T., & Shallice, T. (2016). Identical, similar or different? is a single brain model sufficient? *Cortex*. https://doi.org/10.1016/j.cortex.2016.12.002

de Witte, E., & Mariën, P. (2012). The neurolinguistic approach to awake surgery reviewed. *Clin Neurol Neurosurg*, *115*, 145. https://doi.org/10.1016/j.clineuro.2012.09.015

Desikan, R. S., Ségonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., . . . Killiany, R. J. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *Neuroimage*, *31*, 980. https://doi.org/10.1016/j.neuroimage.2006.01.021

Diagnosia. (n.d.). *Convulex 500 Fachinformation*. https://info.diagnosia.com/de-de/p/1113366/convulex-300-mg

Diamond, A. (2013). Executive functions. *Annu Rev Psychol*, *64*, 135-168. https://doi.org/10.1146/annurev-psych-113011-143750

Dick, A. S., Bernal, B., & Tremblay, P. (2014). The Language Connectome: New Pathways, New Concepts. *Neuroscientist*, *20*, 467. https://doi.org/10.1177/1073858413513502

Duffau, H., Capelle, L., Denvil, D., Sichez, N., Gatignol, P., Lopes, M., . . . Van Effenterre, R. (2003). Functional recovery after surgical resection of low grade gliomas in eloquent brain: hypothesis of brain compensation. *J Neurol Neurosurg Psychiatry*, *74*, 907. https://doi.org/10.1136/jnnp.74.7.901

Duffau, H., Gatignol, P., Mandonnet, E., Peruzzi, P., Tzourio-Mazoyer, N., & Capelle, L. (2005). New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. *Brain*, *128*, 810. https://doi.org/10.1093/brain/awh423

Edlin, J. M., Leppanen, M. L., Fain, R. J., Hackländer, R. P., Hanaver-Torrez, S. D., & Lyle, K. B. (2015). On the use (and misuse?) of the Edinburgh Handedness Inventory. *Brain Cogn*, *94*, 51. https://doi.org/10.1016/j.bandc.2015.01.003

Elman, R. J. (2007). The Importance of Aphasia Group Treatment for Rebuilding Community and Health *Top Lang Disorders*, *27*(4), 300-308.

EMA. (2009). *Keppra: EPAR product information*. https://www.ema.europa.eu/en/documents/product-information/keppra-epar-product-information_en.pdf

Faithfull, S., Cook, K., & Lucas, C. (2005). Palliative care of patients with a primary malignant brain tumour: case review of service use and support provided. *Palliat Med*, *19*, 550. https://doi.org/10.1191/0269216305pm1068oa

Fang, S., Wang, Y., & Jiang, T. (2016). The Influence of Frontal Lobe Tumors and Surgical Treatment on Advanced Cognitive Functions. *World Neurosurg*, *91*, 340-346. https://doi.org/10.1016/j.wneu.2016.04.006

Faulkner, J. W., Wilshire, C. E., Parker, A. J., & Cunningham, K. (2017). An Evaluation of Language in Brain Tumor Patients Using a New Cognitively Motivated Testing Protocol. *Neuropsychology*, *31*, 665. https://doi.org/10.1037/neu0000374

Fedorenko, E. (2014). The role of domain-general cognitive control in language comprehension. *Frontiers in psychology*, *5*, 335. https://doi.org/10.3389/fpsyg.2014.00335

Fels, M., & Geissner, E. (1997). *Neglect-Test (NET). Ein Verfahren zur Erfassung visueller Neglectphänomene* (2 ed.) [Neglect Test. An Asessment for Visual Neglect Phenomena]. Hogrefe.

Ferstl, E. C., Neumann, J., Bogler, C., & von Cramon, D. Y. (2008). The extended language network: A meta-analysis of neuroimaging studies on text comprehension. *Hum Brain Mapp*, *29*, 593. https://doi.org/10.1002/hbm.20422

Ferstl, E. C., Walther, K., Guthke, T., & von Cramon, D. Y. (2005). Assessment of Story Comprehension Deficits After Brain Damage. *J Clin Exp Neuropsychol*, *27*, 384. https://doi.org/10.1080/13803390490515784

Field, A., Miles, J., & Field, Z. (2012). *Discovering statistics using R* (1. publ.. ed.). SAGE.

Finch, E., & Copland, D. A. (2014). Language outcomes following neurosurgery for brain tumours: a systematic review. *NeuroRehabilitation*, *34*(3), 499-514. https://doi.org/10.3233/NRE-141053

Fischer, M. H., & Zwaan, R. A. (2008). Embodied language: a review of the role of the motor system in language comprehension. *Q J Exp Psychol (Hove)*, *61*(6), 825-850. https://doi.org/10.1080/17470210701623605

Flinker, A., Korzeniewska, A., Shestyuk, A. Y., Franaszczuk, P. J., Dronkers, N. F., Knight, R. T., & Crone, N. E. (2015). Redefining the role of Broca's area in speech. *Proc Natl Acad Sci U S A*, *112*, 2875. https://doi.org/10.1073/pnas.1414491112

Fodor, J. A. (1983). *The modularity of mind : an essay on faculty psychology* MIT Press]. Cambridge, Mass. [u.a.]. https://ubdata.univie.ac.at/AC01789174

Gajewski, P. D., Hanisch, E., Falkenstein, M., Thönes, S., & Wascher, E. (2018). What Does the n -Back Task Measure as We Get Older? Relations Between Working-Memory Measures and Other Cognitive Functions Across the Lifespan. *Front Psychol*, *9*, 2208. https://doi.org/10.3389/fpsyg.2018.02208

Gao, S., Chu, Y., Shi, S., Peng, Y., Dai, S., Wang, Y., . . . Zeng, G. (1992). Standard Aphasia Battery of Chinese. *Chinese Mental Health Journal*, *6*, 125–128.

Gempt, J., Lange, N., Bette, S., Foreman, S. C., Cammardella, J. H., Albertshauser, J., . . . Ringel, F. (2017). Factors influencing neurocognitive function in patients with neuroepithelial tumors. *Sci Rep*, *7*, 10. https://doi.org/10.1038/s41598-017-17833-w

Gierhan, S. M. (2013). Connections for auditory language in the human brain. *Brain Lang*, *127*(2), 205-221. https://doi.org/10.1016/j.bandl.2012.11.002

Goldmacher, G. V., & Conklin, J. (2012). The use of tumour volumetrics to assess response to therapy in anticancer clinical trials. *Br J Clin Pharmacol*, *73*, 854. https://doi.org/10.1111/j.1365-2125.2012.04179.x

Goodglass, H., & Kaplan, E. (1972). *The assessment of aphasia and related disorders*. Lea & Febiger.

Grande, M., & Huber, W. (2005). Funktionelle Reorganisation bei Aphasie [Functional Reorganization of Aphasia]. *Sprache Stimme Gehör*, *29*, 149. https://doi.org/10.1055/s-2005-873122

Habets, E. J. J., Hendriks, E. J., Taphoorn, M. J. B., Douw, L., Zwinderman, A. H., Vandertop, W. P., . . . Klein, M. (2019). Association between tumor location and neurocognitive functioning using tumor localization maps. *J Neurooncol*, *144*(3), 573-582. https://doi.org/10.1007/s11060-019-03259-z

Harris, C. L. (2006). Language and Cognition. In N. Lynn (Ed.), *Encyclopedia of cognitive science* (pp. 1-7). Nature Publishing Group. https://doi.org/10.1002/0470018860.s00559

Heidler, M.-D. (2005). *Kognitive Dysphasien. Differenzialdiagnostik aphasischer und nichtaphasischer zentraler Sprachstörungen sowie therapeutische Konsequenzen* (Vol. 743) [Cognitive Dysphasia. Differential Diagnosis of aphasic and non-aphasic central language impairments and therpeutic consequences]. Peter Lang. Europäischer Verlag der Wissenschaften.

Heidler, M.-D. (2007). "Kognitive Dysphasien" - Klassifikation, Diagnostik und Therapie nichtaphasischer zentraler Sprachstörungen ["Cognitive Dysphasia" - Classification, Diagnostics and Therapy of non-aphasic central Language Impairments]. *Forum Logopädie*, *21*(1), 20-27.

Heimans, J. J., & Reijneveld, J. C. (2012). Factors affecting the cerebral network in brain tumor patients. *J Neurooncol*, *108*, 237. https://doi.org/10.1007/s11060-012-0814-7

Heiss, W. D., Kessler, J., Thiel, A., Ghaemi, M., & Karbe, H. (1999). Differential capacity of left and right hemispheric areas for compensation of poststroke aphasia. *Ann Neurol*, *45*, 438. https://doi.org/10.1002/1531-8249(199904)45:4<430::AID-ANA3>3.0.CO;2-P

Heiss, W. D., Thiel, A., Kessler, J., & Herholz, K. (2003). Disturbance and recovery of language function: correlates in PET activation studies. *Neuroimage*, *20*, 42-49. https://doi.org/10.1016/j.neuroimage.2003.09.005

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nat Rev Neurosci*, *8*, 402. https://doi.org/10.1038/nrn2113

Holmes, C. J., Hoge, R., Collins, L., Woods, R., Toga, A. W., & Evans, A. C. (1998). Enhancement of MR images using registration for signal averaging. *J Comput Assist Tomogr*, *22*(2), 324-333. https://doi.org/10.1097/00004728-199803000-00032

Hom, J., & Reitan, R. M. (1984). Neuropsychological correlates of rapidly vs. slowly growing intrinsic cerebral neoplasms. *J Clin Neuropsychol*, *6*(3), 309-324. https://doi.org/10.1080/01688638408401221

Huber, W., Poeck, K., Weninger, D., & Willmes, K. (1982). *Der Aachener-Aphasie Test (AAT)*. [The Aachen Aphasia Test (AAT)]. Hogrefe.

Hupfeld, J. (2009). Fragebogen zur Orientierungsprüfung (FOP) [Questionnaire about Orientation]. In D. Schelling, R. Drechsler, D. Heinemann, & W. Sturm (Eds.), *Handbuch neuropsychologischer Testverfahren. Band 1: Aufmerksamkeit Gedächtnis, exekutive Funktionen* (pp. 672-676). Hogrefe.

Ilmberger, J., Ruge, M., Kreth, F. W., Briegel, J., Reulen, H. J., & Tonn, J. C. (2008). Intraoperative mapping of language functions: a longitudinal neurolinguistic analysis. *J Neurosurg*, *109*(4), 583-592. https://doi.org/10.3171/JNS/2008/109/10/0583

Iskandar, S., & Baird, A. D. (2014). The Role of Working Memory and Divided Attention in Metaphor Interpretation. *J Psycholinguist Res*, *43*, 568. https://doi.org/10.1007/s10936-013-9267-1

Jacola, L. M., Willard, V. W., Ashford, J. M., Ogg, R. J., Scoggins, M. A., Jones, M. M., . . . Conklin, H. M. (2014). Clinical utility of the N-back task in functional neuroimaging studies of working memory. *J Clin Exp Neuropsychol*, *36*, 886. https://doi.org/10.1080/13803395.2014.953039

Jaecks, P. (2015). *Restaphasien [Residual Aphasia]*. Thieme. https://doi.org/10.1055/b-003-104194

Jaecks, P., Hielscher-Fastabend, M., & Stenneken, P. (2012). Diagnosing residual aphasia using spontaneous speech analysis. *Aphasiology*, *26*, 970. https://doi.org/10.1080/02687038.2012.663075

Kalbe, E., Reinhold, N., Ender, U., & Kessler, J. (2002). *Aphasie-Check-Liste (ACL) [Aphasia-Check-List (ACL)]*. Prolog.

Kanai, R., & Rees, G. (2011). The structural basis of inter-individual differences in human behaviour and cognition. *Nat Rev Neurosci*, *12*, 242. https://doi.org/10.1038/nrn3000

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston Naming Test* (Vol. 2). Lippincott, Williams & Wilkins.

Keidel, J. L., Welbourne, S. R., & Lambon Ralph, M. A. (2010). Solving the paradox of the equipotential and modular brain: A neurocomputational model of stroke vs. slow-growing glioma. *Neuropsychologia*, *48*, 1724. https://doi.org/10.1016/j.neuropsychologia.2010.02.019

Kertesz, A. (2006). *Western aphasia battery - revised*. Harcourt-Brace.

Khan, F., Amatya, B., Drummond, K., & Galea, M. (2014). Effectiveness of integrated multidisciplinary rehabilitation in primary brain cancer survivors in an Australian community cohort: a controlled clinical trial. *J Rehabil Med*, *46*, 760. https://doi.org/10.2340/16501977-1840

Kiely, K. (2004). Cognitive Function. In A. Michalos (Ed.), *Encyclopedia of the Quality of Life and Well-Being Research*. Springer. https://doi.org/https://doi.org/ 10.1007/978-94-007-0753-5_426

Knoeferle, P., Crocker, M. W., & Pulvermüller, F. (2010). Sentence processing and embodiment. *Brain Lang*, *112*, 142. https://doi.org/10.1016/j.bandl.2009.11.004

Liu, D. (2018). *Tumors and Cancers. Central and Peripheral Nervous Systems*. CRC Press/Taylor & Francis Group.

Lomas, J., Pickard, L., Bester, S., Elbard, H., Finlayson, A., & Zoghaib, C. (1989). The communicative effectiveness index: development and psychometric evaluation of a functional communication measure for adult aphasia. *J Speech Hear Disord*, *54*(1), 113-124. https://doi.org/10.1044/jshd.5401.113

Louis, D. N., Perry, A., Reifenberger, G., von Deimling, A., Figarella-Branger, D., Cavenee, W. K., . . . Ellison, D. W. (2016). The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*, *131*(6), 803-820. https://doi.org/10.1007/s00401-016-1545-1

Lutz, A., & Thompson, E. (2003). Neurophenomenology Integrating Subjective Experience and Brain Dynamics in the Neuroscience of Consciousness. *Journal of Consciousness Studies*, *10*(9–10), 31–52.
Martin, I., & McDonald, S. (2003). Weak coherence, no theory of mind, or executive dysfunction? Solving the puzzle of pragmatic language disorders. *Brain Lang*, *85*, 466. https://doi.org/10.1016/S0093-934X(03)00070-1
Mateos-Aparicio, P., & Rodríguez-Moreno, A. (2019). The Impact of Studying Brain Plasticity. *Front Cell Neurosci*, *13*, 66. https://doi.org/10.3389/fncel.2019.00066
Mattle, H., & Mumenthaler, M. (2017). Diseases of the Brain and Meninges. In *Fundamentals of Neurology. An Illustrated Guide.* (2 ed., pp. 132-140). Thieme.
McCarron, A., Chavez, A., Babiak, M. C., Berger, M. S., Chang, E. F., & Wilson, S. M. (2017). Connected speech in transient aphasias after left hemisphere resective surgery. *Aphasiology*, *31*, 1281. https://doi.org/10.1080/02687038.2017.1278740
McNeil, M. R., & Pratt, S. R. (2001). Defining aphasia: Some theoretical and clinical implications of operating from a formal definition. *Aphasiology*, *15*, 911. https://doi.org/10.1080/02687040143000276
Meule, A. (2017). Reporting and Interpreting Working Memory Performance in. *Front Psychol*, *8*, 352. https://doi.org/10.3389/fpsyg.2017.00352
Miceli, G., Capasso, R., Monti, A., Santini, B., & Talacchi, A. (2012). Language testing in brain tumor patients. *J Neurooncol*, *108*, 247-252. https://doi.org/10.1007/s11060-012-0810-y
Milman, L., Anderson, E., Thatcher, K., Amundson, D., Johnson, C., Jones, M., . . . Willis, D. (2020). Integrated Discourse Therapy After Glioblastoma: A Case Report of Face-To-Face and Tele-NeuroRehabilitation Treatment Delivery. *Front Neurol*, *11*. https://doi.org/10.3389/fneur.2020.583452
Morrison, M. A., Churchill, N. W., Cusimano, M. D., Schweizer, T. A., Das, S., & Graham, S. J. (2016). Reliability of Task-Based fMRI for Preoperative Planning: A Test-Retest Study in Brain Tumor Patients and Healthy Controls. *PLoS One*, *11*, e0149547. https://doi.org/10.1371/journal.pone.0149547
Myachykov, M., & Posner, M. (2005). Attention in Language. In L. Itti, G. Rees, & J. Tsotsos (Eds.), *Neurobiology of Attention* (pp. 324-329). Elsevier Academic Press.
Nabors, L. B., Portnow, J., Ahluwalia, M., Baehring, J., Brem, H., Brem, S., . . . Darlow, S. D. (2020). Central Nervous System Cancers, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*, *18*(11), 1537-1570. https://doi.org/10.6004/jnccn.2020.0052
Nandu, H., Wen, P. Y., & Huang, R. Y. (2018). Imaging in neuro-oncology. *Ther Adv Neurol Disord*, *11*, 1756286418759865. https://doi.org/10.1177/1756286418759865
Narayanan, N. S., Prabhakaran, V., Bunge, S. A., Christoff, K., Fine, E. M., & Gabrieli, J. D. E. (2005). The Role of the Prefrontal Cortex in the Maintenance of Verbal Working Memory: An Event-Related fMRI Analysis. *Neuropsychology*, *19*, 232. https://doi.org/10.1037/0894-4105.19.2.223
Narme, P., Maillet, D., Palisson, J., Le Clésiau, H., Moroni, C., & Belin, C. (2019). How to Assess Executive Functions in a Low-Educated and Multicultural Population Using a Switching Verbal Fluency Test (the TFA-93) in Neurodegenerative Diseases? *Am J Alzheimers Dis Other Demen*, *34*, 477. https://doi.org/10.1177/1533317519833844
Netwon, H. (2016). Overview of Pathology and Treatment of Metastatic Brain Tumors. In H. Newton (Ed.), *Handbook of Neuro-Oncology Neuroimaging* (2 ed.). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-12-800945-1.00003-3
Nicol, C., Ownsworth, T., Cubis, L., Nguyen, W., Foote, M., & Pinkham, M. B. (2019). Subjective cognitive functioning and associations with psychological distress in adult brain tumour survivors. *J Cancer Surviv*, *13*, 662. https://doi.org/10.1007/s11764-019-00784-8
Noll, K. R., Ziu, M., Weinberg, J. S., & Wefel, J. S. (2016). Neurocognitive functioning in patients with glioma of the left and right temporal lobes. *J Neurooncol*, *128*, 331. https://doi.org/10.1007/s11060-016-2114-0
Novick, J. M., Trueswell, J. C., & Thompson-Schill, S. L. (2005). Cognitive control and parsing: Reexamining the role of Broca's area in sentence comprehension. *Cogn Affect Behav Neurosci*, *5*, 281. https://doi.org/10.3758/CABN.5.3.263
Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*(1), 97-113. https://doi.org/10.1016/0028-3932(71)90067-4
Oliver, A. J., Lau, P. K. H., Unsworth, A. S., Loi, S., Darcy, P. K., Kershaw, M. H., & Slaney, C. Y. (2018). Tissue-Dependent Tumor Microenvironments and Their Impact on Immunotherapy Responses. *Front Immunol*, *9*, 70. https://doi.org/10.3389/fimmu.2018.00070
Pakhomov, S. V. S., Kaiser, E. A., Boley, D. L., Marino, S. E., Knopman, D. S., & Birnbaum, A. K. (2011). Effects of age and dementia on temporal cycles in spontaneous speech fluency. *J Neurolinguistics*, *24*, 635. https://doi.org/10.1016/j.jneuroling.2011.06.002

Papagno, C., Casarotti, A., Comi, A., Gallucci, M., Riva, M., & Bello, L. (2012). Measuring clinical outcomes in neuro-oncology. A battery to evaluate low-grade gliomas (LGG). *J Neurooncol*, *108*, 275. https://doi.org/10.1007/s11060-012-0824-5

Park, H.-J., & Friston, K. (2013). Structural and Functional Brain Networks: From Connections to Cognition. *Science*, *342*, 579-587. https://doi.org/10.1126/science.1238411

Piai, V., Witte, E. d., Sierpowska, J., Zheng, X., Hinkley, L. B., Mizuiri, D., . . . Nagarajan, S. (2020). Language neuroplasticity in brain tumor patients revealed by magnetoencephalography. *J Cogn Neurosci*, *32*, 1507. https://doi.org/10.1162/jocn_a_01561

Prigatano, G. P., Roueche, J. R., & Fordyce, D. J. (1985). Nonaphasic language disturbances after closed head injury. *Language Sciences*, *7*(1), 217-229. https://doi.org/10.1016/S0388-0001(85)80020-6

Pulvermüller, F. (2013). How neurons make meaning: brain mechanisms for embodied and abstract-symbolic semantics. *Trends Cogn Sci*, *17*, 470. https://doi.org/10.1016/j.tics.2013.06.004

R Core Team. (2017). *R: A language and environment for statistical computing*. In R Foundation for Statistical Computing.

Radanovic, M., & Scaff, M. (2003). Speech and language disturbances due to subcortical lesions. *Brain Lang*, *84*, 352. https://doi.org/10.1016/S0093-934X(02)00554-0

Regenbrecht, F., & Guthke, T. (2017). Kognitive Kommunuikationsstörungen in der Sprachtherapie und der Neuropsychologie [Cognitive Communication Disorders in Speech Therapy and Neuropsychology]. *Aphasie und verwandte Gebiete | Aphasie et domaines associés*, *1*, 16-29.

Reifenberg, G., Blümcke, I., Pietsch, T., & Paulus, W. (2006). Pathology and Classification of Tumors of the Central Nervous System. In J.-C. Tonn, M. Westphal, J. Rutka, & S. Grossman (Eds.), *Neuro-Oncology of CNS Tumors*. Springer.

Reyes-Aguilar, A., Valles-Capetillo, E., & Giordano, M. (2018). A Quantitative Meta-analysis of Neuroimaging Studies of Pragmatic Language Comprehension: In Search of a Universal Neural Substrate. *Neuroscience*, *395*, 88. https://doi.org/10.1016/j.neuroscience.2018.10.043

Rofes, A., Talacchi, A., Santini, B., Pinna, G., Nickels, L., Bastiaanse, R., & Miceli, G. (2018). Language in individuals with left hemisphere tumors: Is spontaneous speech analysis comparable to formal testing? *J Clin Exp Neuropsychol*, *40*, 732. https://doi.org/10.1080/13803395.2018.1426734

Rojkova, K., Volle, E., Urbanski, M., Humbert, F., Dell'Acqua, F., & Thiebaut de Schotten, M. (2016). Atlasing the frontal lobe connections and their variability due to age and education: a spherical deconvolution tractography study. *Brain Struct Funct*, *221*, 1766. https://doi.org/10.1007/s00429-015-1001-3

Roncero, C., & de Almeida, R. G. (2014). The importance of being apt: metaphor comprehension in Alzheimer's disease. *Front Hum Neurosci*, *8*, 973. https://doi.org/10.3389/fnhum.2014.00973

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behav Neurol*, *12*, 200. https://doi.org/10.1155/2000/421719

Rose, M. L., Attard, M. C., Mok, Z., Lanyon, L. E., & Foster, A. M. (2013). Multi-modality aphasia therapy is as efficacious as a constraint-induced aphasia therapy for chronic aphasia: A phase 1 study. *Aphasiology*, *27*, 971. https://doi.org/10.1080/02687038.2013.810329

Rose, M. L., Raymer, A. M., Lanyon, L. E., & Attard, M. C. (2013). A systematic review of gesture treatments for post-stroke aphasia. *Aphasiology*, *27*, 1127. https://doi.org/10.1080/02687038.2013.805726

Sanai, N., & Berger, M. S. (2008). Glioma extent of resection and its impact on patient outcome. *Neurosurgery*, *62*, 766. https://doi.org/10.1227/01.neu.0000318159.21731.cf

Satoer, D., Vincent, A., Ruhaak, L., Smits, M., Dirven, C., & Visch-Brink, E. (2018). Spontaneous speech in patients with gliomas in eloquent areas: Evaluation until 1 year after surgery. *Clin Neurol Neurosurg*, *167*, 116. https://doi.org/10.1016/j.clineuro.2018.02.018

Satoer, D., Vork, J., Visch-Brink, E., Smits, M., Dirven, C., & Vincent, A. (2012). Cognitive functioning early after surgery of gliomas in eloquent areas. *J Neurosurg*, *117*(5), 831-838. https://doi.org/10.3171/2012.7.JNS12263

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., & Weiller, C. (2006). Dynamics of language reorganization after stroke. *Brain*, *129*(Pt 6), 1371-1384. https://doi.org/10.1093/brain/awl090

Schellig, D., & Schuri, U. (2009). *NBV. N-Back Verbal*. Schuhfried GmbH.

Scherrer, K., Schrott, K., Bertoni, B., Ska, B., Coté, H., Ferré, P., & Joanette, Y. (2016). MEC Testverfahren. Deutsche Version des kanadischen Protocole Montréal d'Evaluation de la Communication [MEC test. German version of the Montreal evaluation of communication]. In. Köln: Prolog.

Schlegel, U., Westphal, M., Winking, M., & Broich, K. (2003). Klinische Symptomatik und allgemeine Therapie. In U. Schlegel, M. Weller, & M. Westphal (Eds.), *Neuroonkologie* (Vol. 2, pp. 84-113). Thieme.

Schmitt, I., & König, H. (1999). Testrezension: Neglect Test (NET) [Test Review: Neglect Test (NET)]. *Zeitschrift für Neuropsychologie*, *10*, 73. https://doi.org/10.1024//1016-264X.10.1.65
Schneider, B., Wehmeyer, M., & Grötzbach, H. (2012). *Aphasie. Wege aus dem Sprachdschungel* (Vol. 5). Springer.
Shamji, M. F., Fric-Shamji, E. C., & Benoit, B. G. (2009). Brain tumors and epilepsy: pathophysiology of peritumoral changes. *Neurosurg Rev*, *32*, 285. https://doi.org/10.1007/s10143-009-0191-7
Shao, Z., Janse, E., Visser, K., & Meyer, A. S. (2014). What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Front Psychol*, *5*, 772. https://doi.org/10.3389/fpsyg.2014.00772
Shewan, C. M., & Kertesz, A. (1980). Reliability and validity characteristics of the Western Aphasia Battery (WAB). *J Speech Hear Disord*, *45*(3), 308-324. https://doi.org/10.1044/jshd.4503.308
Sollereder, S., & Burtscher, J. (2021). *Studienprotokoll Sprachverarbeitung bei neuro-onkologischen Erkrankungen. Unpublished manuscript* (3).
Sorribes, I. C., Moore, M. N. J., Byrne, H. M., & Jain, H. V. (2019). A Biomechanical Model of Tumor-Induced Intracranial Pressure and Edema in Brain Tissue. *Biophys J*, *116*, 1574. https://doi.org/10.1016/j.bpj.2019.02.030
Spaccavento, S., Craca, A., Del Prete, M., Falcone, R., Colucci, A., Di Palma, A., & Loverre, A. (2014). Quality of life measurement and outcome in aphasia. *Neuropsychiatr Dis Treat*, *10*, 37. https://doi.org/10.2147/NDT.S52357
Sporns, O. (2012). *Discovering the human connectome*. MIT Press.
Statistik Austria. (2020). *Krebserkrankungen in Österreich 2020*. S. Austria. http://www.statistik.at/web_de/services/publikationen/4/index.html?includePage=detailedView&sectionName=Gesundheit&pubId=679
Stemmer, B. (2015). Lateralization of Language as Demonstrated by Brain Imaging Procedures. In J. D. Wright (Ed.), *International Encyclopedia of the Social & Behavioral Sciences* (Vol. 13, pp. 398-409): Elsevier.
Stockert, A., & Saur, D. (2017). Aphasie: eine neuronale Netzwerkerkrankung [Aphasia: A Neuronal Network Disease]. *Nervenarzt*, *88*, 866-873. https://doi.org/10.1007/s00115-017-0356-5
Stuss, D. T. (2011). Functions of the Frontal Lobes: Relation to Executive Functions. *J Int Neuropsychol Soc*, *17*, 289-298. https://doi.org/10.1017/S1355617711000695
Sweet, L. H. (2011). N-Back Paradigm. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of Clinical Neuropsychology* (pp. 1718-1719). New York Springer.
Swinburn, K., Porter, G., & Howard, D. (2005). *Comprehensive aphasia test*. Psychology Press.
Talacchi, A., Santini, B., Savazzi, S., & Gerosa, M. (2011). Cognitive effects of tumour and surgical treatment in glioma patients. *J Neurooncol*, *103*, 549. https://doi.org/10.1007/s11060-010-0417-0
Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain : 3-dimensional proportional system: an approach to cerebral imaging*. Thieme Thieme Med. Publ.
Taphoorn, M. J., & Klein, M. (2004). Cognitive deficits in adult patients with brain tumours. *Lancet Neurol*, *3*(3), 159-168. https://doi.org/10.1016/S1474-4422(04)00680-5
Teixidor, P., Gatignol, P., Leroy, M., Masuet-Aumatell, C., Capelle, L., & Duffau, H. (2007). Assessment of verbal working memory before and after surgery for low-grade glioma. *J Neurooncol*, *81*, 313. https://doi.org/10.1007/s11060-006-9233-y
Tesak, J. (2006). *Einführung in die Aphasiologie* [Introduction to Aphasiology]. (2. aktualisierte Aufl.. ed.). Thieme.
Thagard, P. (2010). Cognitive science.
Thiel, A., Herholz, K., Koyuncu, A., Ghaemi, M., Kracht, L. W., Habedank, B., & Heiss, W. D. (2001). Plasticity of language networks in patients with brain tumors: A positron emission tomography activation study. *Ann Neurol*, *50*, 629. https://doi.org/10.1002/ana.1253
Tremblay, P., & Dick, A. S. (2016). Broca and Wernicke are dead, or moving past the classic model of language neurobiology. *Brain Lang*, *162*, 60-71. https://doi.org/10.1016/j.bandl.2016.08.004
Troyer, A. K., Moscovitch, M., Winocur, G., Alexander, M. P., & Stuss, D. (1998). Clustering and switching on verbal fluency: the effects of focal frontal- and temporal-lobe lesions. *Neuropsychologia*, *36*, 504. https://doi.org/10.1016/S0028-3932(97)00152-8
Tucha, O., Smely, C., Preier, M., & Lange, K. W. (2000). Cognitive deficits before treatment among patients with brain tumors. *Neurosurgery*, *47*(2), 324-333; discussion 333-324. https://doi.org/10.1097/00006123-200008000-00011
Turkstra, L. S., Coelho, C., & Ylvisaker, M. (2005). The use of standardized tests for individuals with cognitive-communication disorders. *Semin Speech Lang*, *26*(4), 215-222. https://doi.org/10.1055/s-2005-922101
Ullman, M. T. (2004). Contributions of memory circuits to language: the declarative/procedural model. *Cognition*, *92*(1-2), 231-270. https://doi.org/10.1016/j.cognition.2003.10.008

Vaidya, A. R., Pujara, M. S., Petrides, M., Murray, E. A., & Fellows, L. K. (2019). Lesion Studies in Contemporary Neuroscience. *Trends Cogn Sci*, *23*, 671. https://doi.org/10.1016/j.tics.2019.05.009

van der Meulen, I., van de Sandt-Koenderman, W. M. E., Duivenvoorden, H. J., & Ribbers, G. M. (2010). Measuring verbal and non-verbal communication in aphasia: reliability, validity, and sensitivity to change of the Scenario Test. *Int J Lang Commun Disord*, *45*, 435. https://doi.org/10.3109/13682820903111952

van Kessel, E., Snijders, T. J., Baumfalk, A. E., Ruis, C., van Baarsen, K. M., Broekman, M. L., . . . Robe, P. A. (2020). Neurocognitive changes after awake surgery in glioma patients: a retrospective cohort study. *J Neurooncol*, *146*, 109. https://doi.org/10.1007/s11060-019-03341-6

Van Voorhis, C. R., & Morgan, B. L. (2007). Understanding Power and Rules of Thumb for Determining Sample Sizes. *Tutorials in quantitative methods for psychology*, *3*, 50. https://doi.org/10.20982/tqmp.03.2.p043

Vander Heiden, M. G., & DeBerardinis, R. J. (2017). Understanding the Intersections between Metabolism and Cancer Biology. *Cell*, *168*, 669. https://doi.org/10.1016/j.cell.2016.12.039

Varela, F. J. (1996). Neurophenomenology. A methodological remedy for the hard problem. *Journal of Consciousness Studies*, *3*(4), 330-349.

von Cramon, D. Y., & Säring, W. (1982). Störung der Orientierung beim hirnorganischen Psychosyndrom [Impaired Orientation in the Organic Brain Psychosyndrome]. In D. Bente, H. Coper, & S. Kanowski (Eds.), *Hirnorganische Psychosyndrome im Alter: Konzepte und Modelle für die pharmakotherapeutische Forschung* (pp. 38-50). Springer. https://doi.org/10.007/978-3-642-68557-6

Vulchanova, M., Vulchanov, V., Fritz, I., & Milburn, E. A. (2019). Language and perception: Introduction to the Special Issue “Speakers and Listeners in the Visual World”. *Journal of Cultural Cognitive Science*, *3*, 112. https://doi.org/10.1007/s41809-019-00047-z

Wacker, A., Holder, M., Will, B. E., Winkler, P. A., & Ilmberger, J. (2002). Vergleich von Aachener Aphasie- Test, klinischer Untersuchung und Aachener Aphasie-Bedside-Test bei Hirntumorpatienten. [Comparison of the Aachener Aphasia-Test, clinical examination and the Aachener Aphasia-Bedside-Test in brain tumor patients]. *Nervenarzt*, *73*, 765–769. https://doi.org/10.1007/s00115-002-1358-4

Wechsler, D. (1941). *The measurement of adult intelligence* (2. ed.. ed.). Williams & Wilkins.

Weller, M. (2003). [Neurooncology]. *Nervenarzt*, *74*(12), 1139-1149. https://doi.org/10.1007/s00115-003-1645-8

Weller, M., & Schlegel, U. (2012). Hirntumoren [Brain Tumors]. In S. Schwab (Ed.), *NeuroIntensiv*. Springer. https://doi.org/10.1007/978-3-642-16911-3_34

Westphal, M., Schlegel, U., Weller, M., Voges, J., Schramm, R. A., Kristof, D., . . . Sepehrnia, A. (2003). Primäre Tumoren des Gehirns und seine Häute [Primary Tumors of the Brain and its Meninges]. In U. Schlegel, M. Weller, & M. Westphal (Eds.), *Neuroonkologie* (Vol. 2, pp. 182-295). Thieme.

Wiestler, O. D., & Reifenberger, G. (2003). Pathologische Anatomie und WHO-Klassifikation der Tumoren des Nervensystems [Pathological Anatomy and WHO-Classification of Tumors of the Central Nervous System]. In U. Schlegel, M. Weller, & M. Westphal (Eds.), *Neuroonkologie* (Vol. 2). Thieme.

World Health Organization. (2001). *International Classification of Functioning, Disability and Health: ICF*. (92-4-154542-9).

World Health Organization. (2013). *International Classification of Diseases for Oncology (ICD-O)*. Malta: World Health Organization

Ye, Z., & Zhou, X. (2009). Executive control in language processing. *Neurosci Biobehav Rev*, *33*, 1177. https://doi.org/10.1016/j.neubiorev.2009.03.003

Yuan, B., Zhang, N., Yan, J., Cheng, J., Lu, J., & Wu, J. (2020). Tumor grade-related language and control network reorganization in patients with left cerebral glioma. *Cortex*, *129*, 157. https://doi.org/10.1016/j.cortex.2020.04.015

Zambrano-Cruz, R., & Méndez-Ramírez, L. F. (2018). Neuroanatomic Correlates of Anomia: A Scoping Review. *CES Psicol*, *11*, 96. https://doi.org/10.21615/cesp.11.2.8

Zanella, F. E. (2002). Zerebrale Neoplasien des Erwachsenen. In H. D. Böttcher, V. Seifert, M. Henke, & S. Mose (Eds.), *Klinik der hirneigenen Tumoren und Metastasen. Grundlagen, Diagnostik und Therapie*. W. Zuckerschwerdt Verlag.

Zimmermann, N., de Mattos Pimenta Parente, M. A., Joanette, Y., & Fonseca, R. P. (2014). Unconstrained, phonemic and semantic verbal fluency: Age and education effects, norms and discrepancies. *Psicol. Reflex. Crit*, *27*, 63. https://doi.org/10.1590/S0102-79722014000100007

Zucchella, C., Capone, A., Codella, V., De Nunzio, A. M., Vecchione, C., Sandrini, G., . . . Bartolo, M. (2013). Cognitive rehabilitation for early post-surgery inpatients affected by primary brain tumor: a randomized, controlled trial. *J Neurooncol*, *114*, 100. https://doi.org/10.1007/s11060-013-1153-z

Table of Figures

Abstract

Introduction & Research Relevance

Language impairments caused by brain tumors (Taphoorn & Klein, 2004) are heterogenous and mild (Brownsett et al., 2019; Davie et al., 2009) and require standardized language tests for diagnosis and treatment (Miceli et al., 2012b). However, most tests were developed for stroke patients (Anderson et al., 1990b; Miceli et al., 2012) and first evidence suggests that they are insufficient to adequately capture language impairments in individuals with brain tumors (Brownsett et al., 2019; Satoer et al., 2018; Wacker et al., 2002).

Methodology

The aim of the thesis was to answer how language impairments in individuals with brain tumors are characterized and diagnosed. The language abilities of 15 individuals with predominantly frontal and temporal brain tumors were evaluated before and immediately after brain surgery. Parts of the *Aphasie-Check-Liste (ACL)* (Kalbe et al., 2002), *Regensburger Wortflüssigkeits-Test (RWT)* (Aschenbrenner et al., 2000) and *MEC-Testverfahren (MEC)* (Scherrer et al., 2016) were conducted and MR images were acquired.

Results & Interpretation

The study group was more frequently and severely impaired in the ACL color-figure-test, verbal fluency, reading comprehension of words and sentences, RWT category switching task, MEC metaphor and text comprehension and spontaneous speech. Repetition, reading, writing, picture-naming and auditory comprehension of words and sentences in the ACL were less frequently and less severely impaired. In many cases, word-finding was impaired in the spontaneous speech analysis but unimpaired in the picture-naming task.

After tumor resection, a non-significant decline in language abilities was observed. Comparisons of single patients with either left or right hemisphere tumors of the same lobe did not attribute a specific linguistic role of the right hemisphere to pragmatic language. Tumor size and grade were not predictive of more severe language impairments.

Language subtests which require executive functioning were more frequently and severely impaired in the study group. The standardized language tests of this study seemed to be partially suitable for this clinical population.

Limitations & Outlook

The small and heterogenous participant group is the main limiting factor of this thesis. Language impairments caused by brain tumors should be further researched to ensure adequate diagnosis and treatment.

German Abstract

Einleitung & Forschungsrelevanz

Sprachstörungen in Folge von Hirntumoren (Taphoorn & Klein, 2004) werden als heterogen und mild beschrieben (Brownsett et al., 2019; Davie et al., 2009) und benötigen standardisierte Testverfahren für die Diagnostik und Therapie (Miceli et al., 2012). Vorhandene Sprachtests wurden primär für Schlaganfallpatient:innen entwickelt (Anderson et al., 1990; Miceli et al., 2012) und erste Studien weisen darauf hin, dass diese Testverfahren Sprachstörungen bei Hirntumorpatient:innen nicht adäquat erfassen können (Brownsett et al., 2019; Satoer et al., 2018; Wacker et al., 2002).

Methodik

Das Ziel dieser Arbeit ist zu beantworten, wie Sprachstörungen bei Personen mit Hirntumoren charakterisiert sind und diagnostiziert werden. Aus diesem Grund wurden 15 Personen mit hauptsächlich frontalen oder temporalen Hirntumoren vor und unmittelbar nach einer Tumorresektion untersucht. Teile der *Aphasie-Check-Liste (ACL)* (Kalbe et al., 2002), des *Regensburger Wortflüssigkeits-Test (RWT)* (Aschenbrenner et al., 2000) und des *MEC-Testverfahrens (MEC)* (Scherrer et al., 2016) sowie ein MRT wurden durchgeführt.

Ergebnisse & Interpretation

Häufigere und schwerere Beeinträchtigungen wurden in der Studiengruppe im ACL Farb-Figur-Test, Wortflüssigkeit, Lesesinnverständnis von Wörtern und Sätzen, RWT Kategorienwechsel, MEC Metaphern- und Textverständnis sowie der Spontansprache gefunden. Nachsprechen, Lesen, Schreiben, Benennen und das auditive Sprachverständnis von Wörtern und Sätzen in der ACL waren seltener und geringer betroffen. In vielen Fällen wurde eine Wortfindungsstörung in der Spontansprachanalyse, jedoch nicht im Untertest Benennen festgestellt.

Nach der Tumorresektion war eine nicht signifikante Verschlechterung der Sprache zu verzeichnen. Einzelfallvergleiche von Tumoren der linken oder rechten Hemisphäre suggerieren, dass die rechte Hemisphäre keine spezifische linguistische Rolle hinsichtlich pragmatischer Sprachverarbeitung innehat. Tumorgröße und -grad waren nicht prädiktiv für den Schweregrad der Sprachstörung.

In Testverfahren, welche die Beteiligung exekutiver Funktionen bedingen, war die Studiengruppe häufiger und schwerer beeinträchtigt. Die verwendeten Tests scheinen zumindest zum Teil für die klinische Gruppe geeignet.

Limitationen & Aussicht

Größe und Heterogenität der Proband:innengruppe sind limitierende Faktoren dieser Studie. Zukünftig sollten Sprachstörungen bei Hirntumoren weiter erforscht werden, um adäquate Diagnostik und Therapie zu garantieren.

Appendix

Part 1: Proceedings and number of results of the literature research

data base	keywords	results	included abstracts	included articles
PubMed	brain tumor AND language	20	6	2
	brain tumor AND aphasia	8	0	0
	brain tumor AND communication	28	0	0
	brain tumor AND cognition	195	12	2
	brain tumor AND cognitive functioning	159	3	0
PsycINFO	brain tumor AND language	57	7	1
	brain tumor AND aphasia	21	1	0
	brain tumor AND communication	37	0	0
	brain tumor AND cognition	36	3	0
	brain tumor AND cognitive functioning	16	2	0
Cochrane	brain tumor AND language	48	2	0
	brain tumor AND aphasia	20	3	1
	brain tumor AND communication	5	1	0
	brain tumor AND cognition	9	1	0
	brain tumor AND cognitive functioning	7	1	0
total				6

Part 2: Summary of studies on language impairments following brain tumors

language / study	expressive					receptive					
	SPS[1]	PN[2]	VF[3]	W[4]	R[5]	WR[6]	NWR[7]	RHY[8]	AC[9]	RC[10]	P[11]
(Bartha et al., 2000)	NA	NA	T1: +, T2: +, T3: +	T1: +, T2: +, T3: +	T1: +, T2: +, T3: -	T1: +, T2: +, T3: +	NA	NA	T1: +, T2: +, T3: -	NA	NA
(Tucha et al., 2000)	T1: -	NA	NA	T1: +	T1: +	NA	NA	NA	NA	NA	NA
(Chakraborty et al., 2012)	NA	T1: ++	NA	NA	NA	NA	NA	NA	NA	NA	NA
(Satoer et al., 2012)	NA	NA	T1: ++, T3: ++	T1, T3: -	T1, T3: -	T1, T3: -	NA	NA	T1: -, T3: +	NA	NA
(Morrison et al., 2016)	NA	NA	T1: +	NA	NA	NA	NA	T1: +		NA	NA
(Faulkner et al., 2017)	NA	T1: ++	T1: ++	NA	NA	T1: ++	T1: ++	NA	T1: ++	NA	NA
(McCarron et al., 2017)	T1: ++, T2: ++, T3: ++	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
(Arcara et al., 2018)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	T1: ++
(Rofes et al., 2018)	T1: +	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
(Satoer et al., 2018)	T1: ++, T2: ++, T3: ++	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

(Brownsett et al., 2019)	NA	**T3: ++**	T3: +	T3: +	T3: +	T3: +	T3: +	NA	T3: +	**T3: ++**	NA
(Bette et al., 2020)	NA	NA	**T3: ++**	NA	NA	NA	NA	NA	NA	NA	NA
(Piai et al., 2020)	NA	T1: -	NA	NA	NA	NA	NA	NA	NA	NA	NA

Language: [1]SPS = spontaneous speech; [2]PN = picture-naming; [3]VF = verbal fluency; [4]W = writing; [5]R = reading; [6]WR = word repetition; [7] NWR = non-word repetition; [8]RHY = rhyming judgement; [9]AC = comprehension; [10]RC = reading comprehension; [11]P= pragmatic language

Significance: ++ = significant impairment or difference; + = non-significant impairment or difference; - = no impairment

Time: pre-treatment (T1); immediately post-surgically (T2); long-term post-surgically (T3)

Assessment: standardized (green), non-standardized (orange)

Other: NA = not assessed; **bold** = significant AND standardized

Part 3: Overview of participants at T1 and T2 (n=6)

participant	test[9]	subtest[10]	impairment T1[11]	impairment T2
1 nr.5	ACL	CFT	mild	mild
		RC	mild	moderate
		AC	none	none
		PN	none	mild
		VFS	none	none
		VFL	none	none
		R	none	none
		W	none	none
		REP	none	none
	RWT	SCS	PR 1	PR 37
		LCS	PR 99	PR 95
	MEC	TC1	x[12]	x
		TC2	yes	yes
		TC3 questions	yes	yes
		MC	none	yes
		SPS	yes	yes
impaired subtests			5	7
moderate and severe impairments			0	1
2 nr.11	ACL	CFT	mild	mild
		RC	moderate	moderate
		AC	none	none
		PN	mild	none
		SVF	none	moderate
		LVF	moderate	moderate
		R	none	none
		W	none	moderate
		REP	none	none
	RWT	SCS	PR 85	PR 25
		LCS	PR 23	PR 1
	MEC	TC1	x	x
		TC2	none	none
		TC3	yes	yes
		MC	yes	yes
		SPS	yes	yes
impaired subtests			7	8
moderate and severe impairments			2	4
3 nr.15	ACL	CFT	mild	moderate
		RC	moderate	mild
		AC	none	none
		PN	mild	none
		SVF	moderate	mild
		LVF	severe	moderate
		R	none	none
		W	none	none
		REP	none	none
	RWT	SCS	PR 61	PR 51
		LCS	PR 67	PR 40
	MEC	TC1	x	x
		TC2	none	yes
		TC3	none	yes
		MC	yes	yes
		SPS	yes	yes
impaired subtests			7	8
moderate and severe impairments			3	2
4 nr.23	ACL	CFT	mild	mild
		RC	none	none
		AC	none	none
		PN	none	none

[9] ACL = Aphasie-Check Liste, RWT = Regensburger Wortflüssigkeits-Test, MEC = MEC Testverfahren

[10] RC = reading comprehension, AC = auditory comprehension, PN = picture-naming, R = reading, W = writing, REP = repetition, CFT = color-figure test, TC1 = text comprehension text parts, TC2 = text comprehension complete text, TC3 = text comprehension questions, MC= metaphor comprehension, SPS = spontaneous speech, VFL = verbal fluency lexical, VFS = verbal fluency semantic, SCS = semantic category switching, LCS = lexical category switching

[11] none vs. mild to severe in the ACL; percentile rank (PR) in RWT, yes/no MEC

[12] no conversion to impairment or grade available

		SVF	none	mild
		LVF	moderate	moderate
		R	none	none
		W	none	none
		REP	none	none
	RWT	SCS	PR 17	PR 36
		LCS	PR 2	PR 2
	MEC	TC1	x	x
		TC2	none	none
		TC3	none	none
		MC	yes	yes
		SPS	yes	yes
impaired subtests			4	5
moderate and severe impairments			1	1
5 nr.29	ACL	CFT	mild	mild
		RC	moderate	mild
		AC	mild	none
		PN	mild	none
		SVF	mild	none
		LVF	mild	none
		R	none	none
		W	severe	none
		REP	none	none
	RWT	SCS	PR 3	PR 19
		LCS	PR 13	PR 100
	MEC	TC1	x	x
		TC2	yes	yes
		TC3	none	none
		MC	yes	yes
		SPS	none	none
impaired subtests			9	4
moderate and severe impairments			2	0
6 nr.31	ACL	CFT	mild	none
		RC	mild	none
		AC	none	none
		PN	none	none

		SVF	mild	moderate
		LVF	moderate	moderate
		R	none	none
		W	none	none
		REP	none	none
	RWT	SCS	PR 23	PR 1
		LCS	PR 56	PR 10
	MEC	TC1	x	x
		TC2	none	yes
		TC3	none	yes
		MC	none	yes
		SPS	none	yes
impaired subtests			4	6
moderate and severe impairments			1	2

Part 4: Overview of left (LH) and right hemisphere (RH) patient pairs with frontal (F), parieto-occipital (PO) or temporal (T) lobe tumors at T1 and T2

pair	test[13]	sub-test[14]	impairment[15]	
			PO-LH[16]	PO-RH[17]
2 at T1 nr.5 +29	ACL	CFT	mild (object-pointing in incorrect order)	mild (self-corrections)
		RC	moderate (choice of semantic distractors)	mild (insecurity about semantic distractor)
		AC	mild (semantic distractor and delay)	none (no mistakes)
		PN	mild (semantic paraphasia and incomplete sentence)	none (incomplete sentence)
		VFS	mild (low number of words)	none (repetitions)
		VFL	mild (low number of words)	none (repetitions)
		R	none (no mistakes)	none (no mistakes)
		W	severe (lexical paragraphia and no reactions)	none (necessity to repeat instruction)
		REP	none (no mistakes)	none (repetition of wrong case of one word)
	RWT	SCS	PR 1 (insecurity about already named words and repetition)	PR 3 (several breaches of rules)
		LCS	PR 8 (some breaches of rules)	PR 50 (several repetitions and breaches of rules)
	MEC	TC1	x[18] (omission of information)	x (omission of information)
		TC2	yes (omission of information, short retelling)	yes (omission of information, wrong chronology)
		TC3	none (unrelated title in the beginning, wrong answers)	none (wrong answers)
		MC	yes (repetition of metaphors, imprecise explanations)	none (missing details)
		SPS	none (no mistakes)	yes (conduit d'approche, lexical and semantic paraphasia, wrong choice of words, imprecise speech, extensive and repetitive talking, accelerated speech)
impaired subtests			9	4
moderate and severe impairments			2	0
			PO-LH	PO-RH
2 at T2 nr. 5+29	ACL	CFT	mild (wrong choice with syntactically complex sentence)	mild (wrong choice with syntactically complex sentences)
		RC	mild	moderate

[13] ACL = Aphasie-Check Liste, RWT = Regensburger Wortflüssigkeits-Test, MEC = MEC Testverfahren

[14] RC = reading comprehension, AC = auditory comprehension, PN = picture-naming, R = reading, W = writing, REP = repetition, CFT = color-figure test, TC1 = text comprehension text parts, TC2 = text comprehension complete text, TC3 = text comprehension questions, MC= metaphor comprehension, SPS = spontaneous speech, VFL = verbal fluency lexical, VFS = verbal fluency semantic, SCS = semantic category switching, LCS = lexical category switching

[15] none vs. mild to severe in the ACL; percentile rank (PR) in RWT, yes/no MEC

[16] PO-LH = parieto-occipital left hemisphere

[17] PO-LH = parieto-occipital right hemisphere

[18] no conversion to impairment or grade available

			(self-correction and delay)	(self-correction, delay and semantic distractor)
		AC	none (no mistakes)	none (self-correction)
		PN	none (incomplete sentence)	mild (self-correction and incomplete sentence)
		SVF	none (no mistakes)	none (proper names and generic terms)
		LVF	none (no mistakes)	none (proper name)
		R	none (no mistakes)	none (no mistakes)
		W	none (no mistakes)	none (no mistakes)
		REP	none (no mistakes)	none (no mistakes)
	RWT	SCS	PR 19 (breach of rule)	PR 37 (breaches of rules, category errors)
		LCS	PR 100 (no mistakes)	PR 95 (repetitions and semantic neologism)
	MEC	TC1	x (omission of information)	x (omission of information)
		TC2	none (omission of information)	none (addition of information, change in chronology)
		TC3	none (title without inference and wrong answer)	yes (wrong answers)
		MC	yes (imprecise explanations)	none (repetition of metaphor, references to literal meaning, addition of information)
		SPS	none	yes

[19] T-LH = temporal left hemisphere

			(no mistakes)	(choosing wrong words, imprecise speech,topic deviation, extensive and repetitive talking, accelerated speech)
impaired subtests			3	5
moderate and severe impairments			0	1
			T-LH[19]	T-RH[20]
3 at T1 nr.14+19	ACL	CFT	severe (choice of wrong objects, self-correction, repetition of instruction)	mild (wrong choice with syntactically complex sentence)
		RC	severe (wrong choice of pictures, pointing towards two pictures, unsolicited picture-naming)	none (no mistakes)
		AC	severe (insecurity about distractor, pointing towards two pictures)	none (no mistakes)
		PN	severe (delay, imprecise descriptions and word finding difficulty)	mild (self-correction, semantic paraphasia, incomplete sentence)
		SVF	severe (naming of zero words)	moderate (repetition and naming generic terms)
		LVF	severe (naming of zero words)	moderate (reduced number of named words)
		R	severe (addition of words, incompletely read sentences)	none (no mistakes)
		W	severe (lexical paragraphia)	none (no mistakes)
		REP	severe	none

[20] T-RH = temporal right hemisphere

			(repetition of instruction, addition of words)	(no mistakes)
	RWT	SCS	PR 1 (naming one word)	PR 19 (insecurity about already named words, breach of rule, self-correction)
		LCS	PR 1 (naming zero words)	PR 4 (breach of rule)
	MEC	TC1	x (inability to retell text parts)	x (omission, additions or changes of information)
		TC2	yes (inability to retell whole text)	none (omission or addition of information)
		TC3	yes (inability to answer questions)	none (no mistakes)
		MC	yes (missing explanations, commenting the metaphors)	yes (addition or imprecise explanation, reference to literal meaning)
		SPS	yes (word-finding difficulty, missing corrections after wrong word choice, imprecise thoughts, topic deviation, repetition, extensive talking, comprehension problems, interruption of communicative partner)	yes (monotone, slowed speaking)
impaired subtests			13	6
moderate and severe impairments			9	2
			T-LH	T-RH
3 at T2 nr.14+19	ACL	CFT	drop-out	drop-out

[21] F-LH = frontal left hemisphere

			F-LH[21]	F-RH[22]
1 at T1 nr.2+8	ACL	CFT	none (repetition of instruction, delay and self-correction)	none (self-correction)
		RC	none (no mistakes)	mild (self-corrections)
		AC	none (self-correction)	NA
		PN	none (content wise wrong description)	none (unclear description)
		SVF	mild (naming generic terms)	moderate (semantic neologism)
		LVF	moderate (naming very few words)	moderate (naming very few words)
		R	none (change of case of one word)	none (self-corrections)
		W	none (no mistakes)	none (no mistakes)
		REP	none (no mistakes)	none (no mistakes)
	RWT	SCS	PR 39 (repetitions)	PR 0 (repetition)
		LCS	PR 7 (breaches of rules, proper names)	PR 2 (repetitions, proper names)
	MEC	TC1	x (omission of information)	x (omission of information)
		TC2	none (omission of information)	none (omission of information)
		TC3	none (no errors)	yes (long title, wrong answers, incorrect assessment of a situation and feeling)
		MC	yes	none

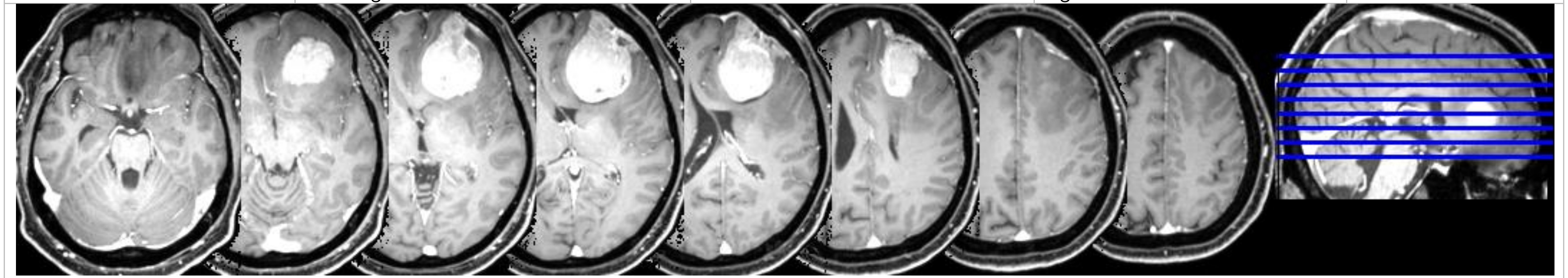
[22] F-RH = frontal right hemisphere

			(addition of information, several references to literal meaning)	(addition of information, reference to literal meaning)
		SPS	yes (word-finding difficulty, incorrect choice of words)	yes (repetition of already said, interruptions of communicative partner)
impaired subtests			4	5
moderate and severe impairments			1	2
			F-LH	**F-RH**
1 at T2 nr.2+8	ACL	CFT	mild (delayed reaction and wrong choice in syntactically complex part)	mild (wrong choice in syntactically complex part)
		RC	NA	none (no mistakes)
		AC	none (no mistakes)	none (no mistakes)
		PN	none (no mistakes)	none (incomplete sentence)
		SVF	moderate (frequent use of generic terms)	moderate (repetititions and insecurity about already named words)
		LVF	moderate (repetitions)	moderate (repetititions and insecurity about already named words)
		R	NA	none (no mistakes)
		W	mild (delayed responses and self-corrections)	none (no mistakes)
		REP	none (no mistakes)	none (no mistakes)
	RWT	SCS	PR 30 (repetitions, breach of rule and category perseveration)	PR 0 (repetition)

		LCS	PR 0 (repetition, breaches of rules)	PR 31 (repetition, breach of rule)
	MEC	TC1	x (omission of information)	x (omission of information)
		TC2	none (omission and changes of information)	none (omission of information)
		TC3	none (phonological paraphasia)	yes (changes of information)
		MC	yes (focus on less essential aspects)	none (imprecise explanations, repetitions)
		SPS	none (word-finding difficulty)	none (imprecise expression of thoughts, excessive talking, repetitions)
impaired subtests			5	4
moderate and severe impairments			2	2

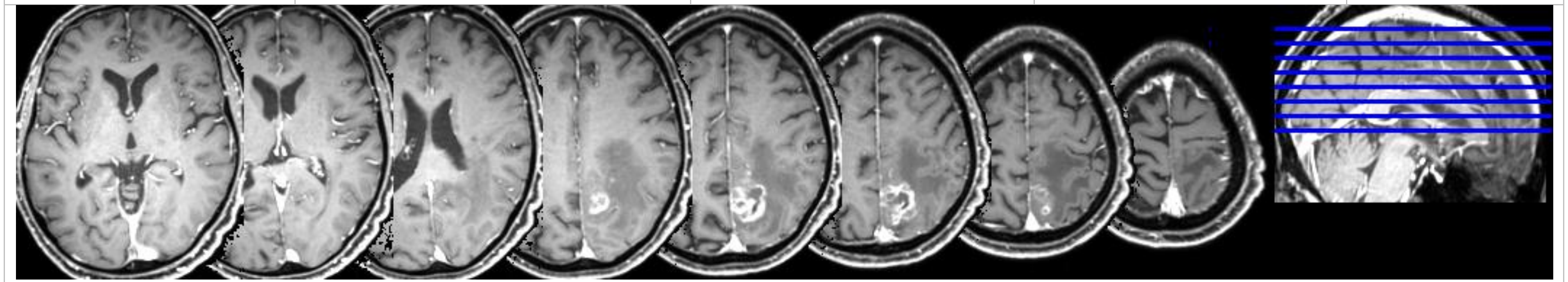
Part 5: Multislice MR Images of all Subjects

participant	tumor type	lobe	hemisphere	WHO grade
1	meningeoma	frontal	right	II



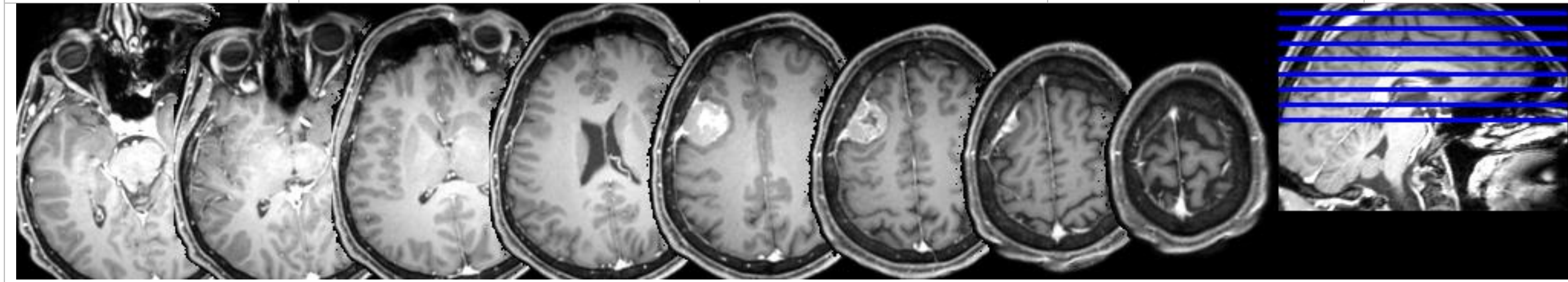
Affected areas:
Cingulate Gyrus (anterior division), Frontal Medial Cortex, Frontal Orbital Cortex, Frontal Operculum Cortex, Frontal Pole, Inferior Frontal Gyrus with Pars Opercularis and Pars Triangularis, Middle Frontal Gyrus, Paracingulate Gyrus

2	glioblastoma	parieto-occipital	right	IV



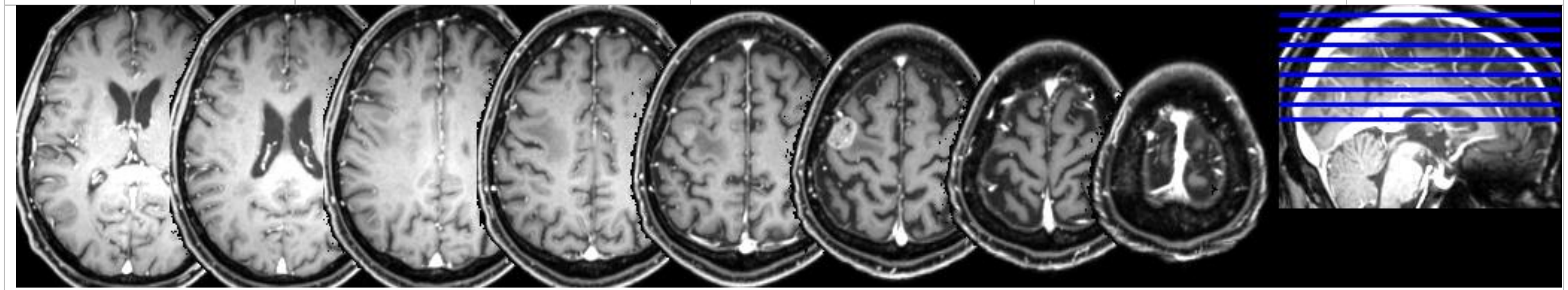
Affected areas:
Cingulate Gyrus (posterior division), Cuneal Cortex, Lateral Occipital Cortex (superior division), Precuneus Cortex, Superior Parietal Lobule

3	meningeoma	frontal	left	I



Affected areas:
Middle Frontal Gyrus, Precentral Gyrus, Superior Frontal Gyrus

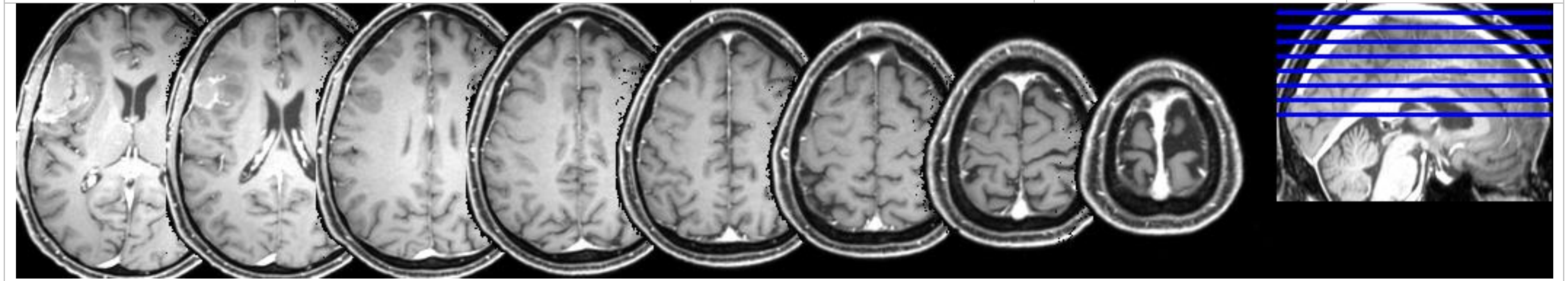
4	metastasis	frontal	left	-



Affected areas[23]:
Middle Frontal Gyrus, Pars Opercularis of the Inferior Frontal Gyrus

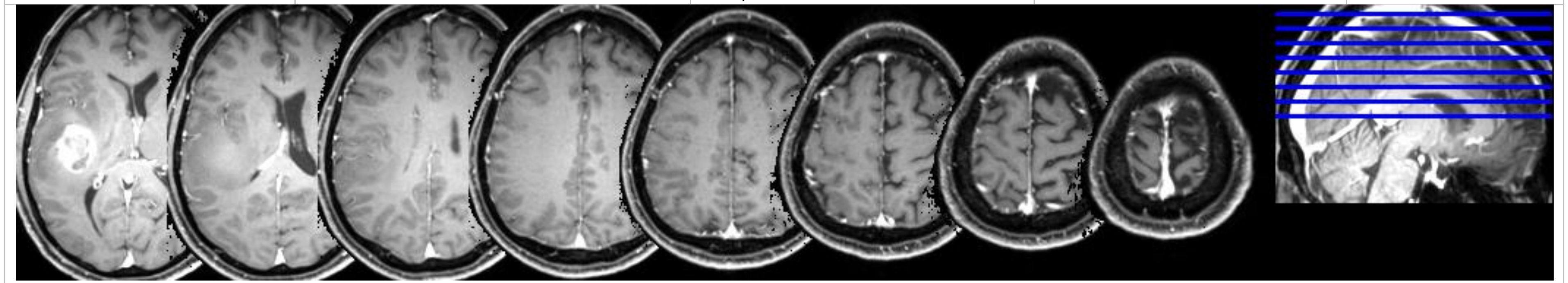
[23] Affected areas of this participant are based on the post-surgical MR image.

5	meningeoma	frontal	left	I



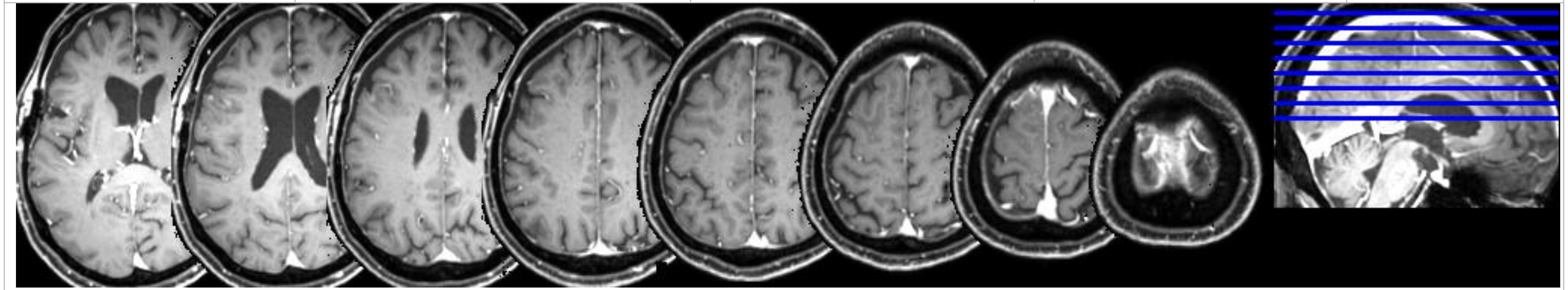
Affected areas:
Central Opercular Cortex, Frontal Orbital Cortex, Frontal Operculum Cortex, Inferior Temporal Gyrus (anterior division), Insular Cortex, Middle Temporal Gyrus (anterior division), Pars Opercularis of the Inferior Frontal Gyrus, Precentral Gyrus, Planum Polare, Superior Temporal Gyrus (anterior division), Temporal Pole

6	cavernoma	temporal	left	-



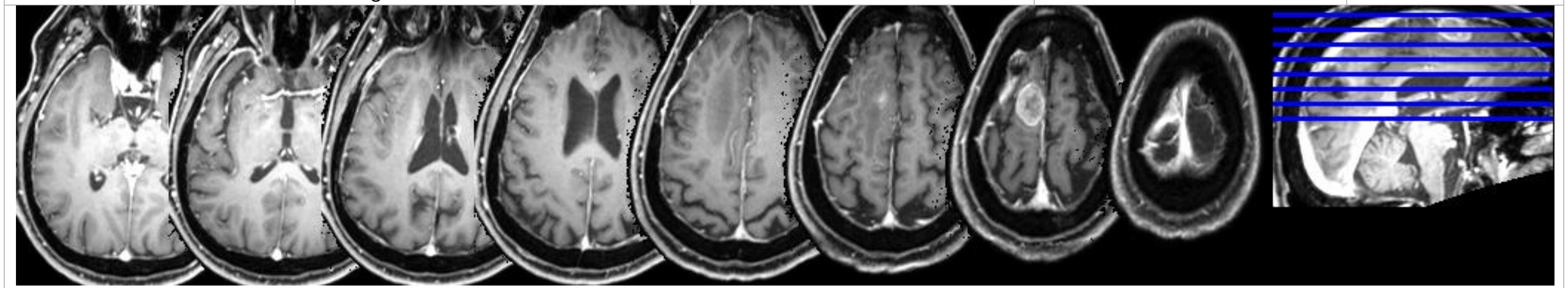
Affected areas:
Central Opercular Cortex, Heschl's Gyrus (H1 and H2), Inferior Temporal Gyrus (anterior division), Insular Cortex, Middle Temporal Gyrus (anterior division), Parahippocampal Gyrus (anterior division), Planum Polare, Superior Temporal Gyrus (anterior division), Temporal Fusiform Cortex (anterior division), Temporal Pole

7	metastasis	frontal	left	-



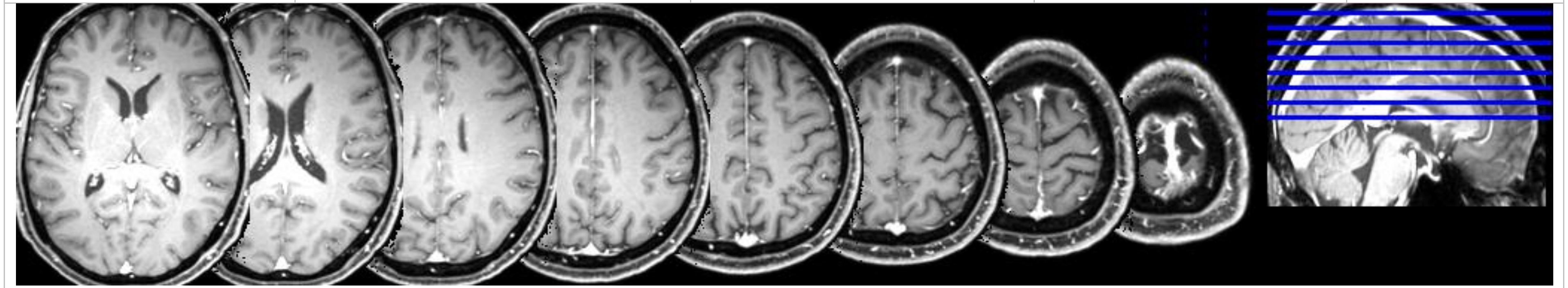
Affected areas:
Middle Frontal Gyrus, Postcentral Gyrus, Precentral Gyrus

8	meningeoma	frontal	left	II



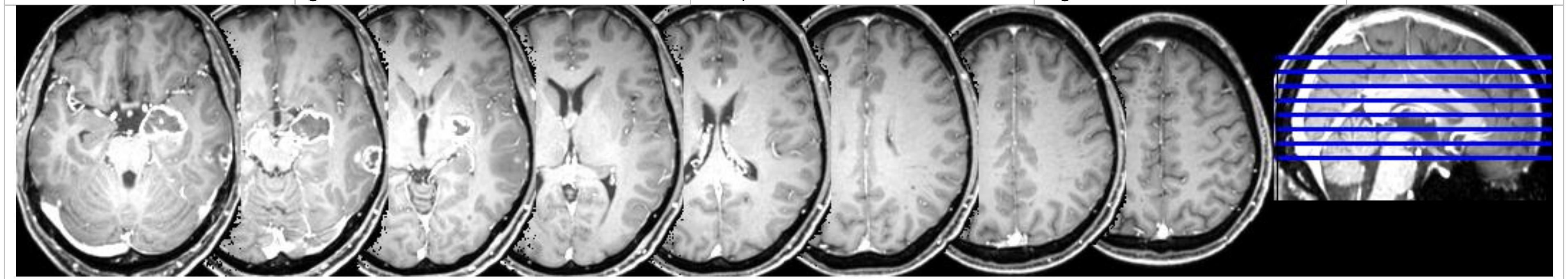
Affected areas:
Juxtapositional Lobule Cortex (former: Supplementary Motor Cortex), Superior Frontal Gyrus

9	glioblastoma	temporal	right	IV



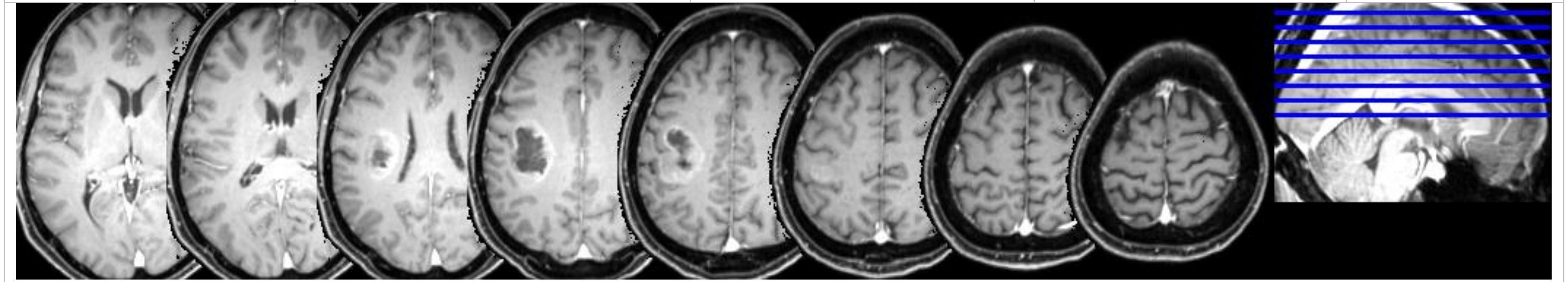
Affected areas:
Insular Cortex

10	glioblastoma	temporal	right	IV



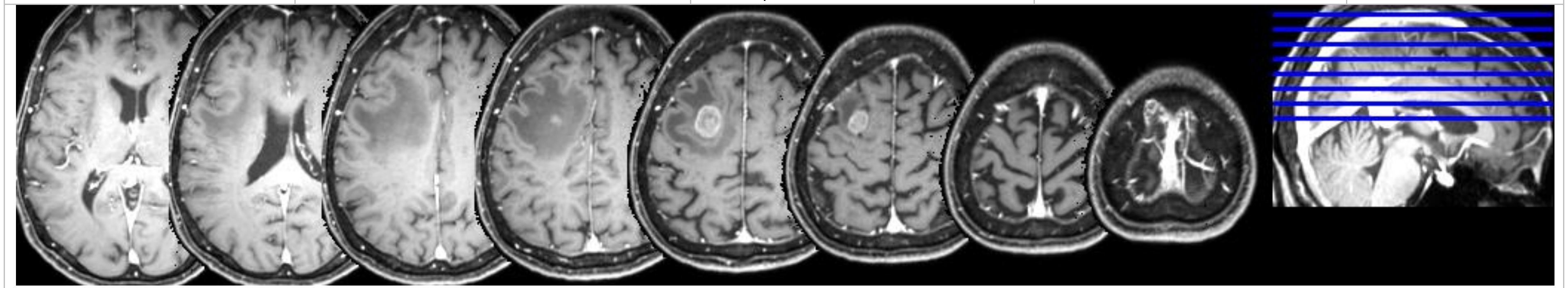
Affected areas:
Tumor 1 (left): Frontal Orbital Cortex, Insular Cortex, Parahippocampal Gyrus (anterior division), Planum Polare, Temporal Fusiform Cortex (posterior division)
Tumor 2 (right): Middle Temporal Gyrus (temporo-occipital part), Temporal Gyrus (posterior division)

11	glioblastoma	frontoparietal	left	IV



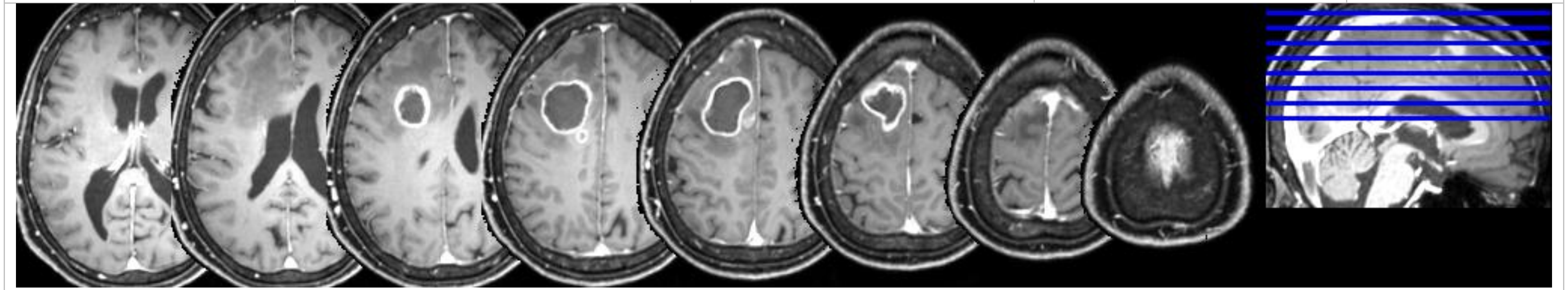
Affected areas:
Angular Gyrus Cingulate Gyrus (posterior division), Parietal Operculum Cortex, Precentral Gyrus, Postcentral Gyrus, Superior Parietal Lobule, Supramarginal Gyrus (anterior division)

12	metastasis	frontoparietal	left	-



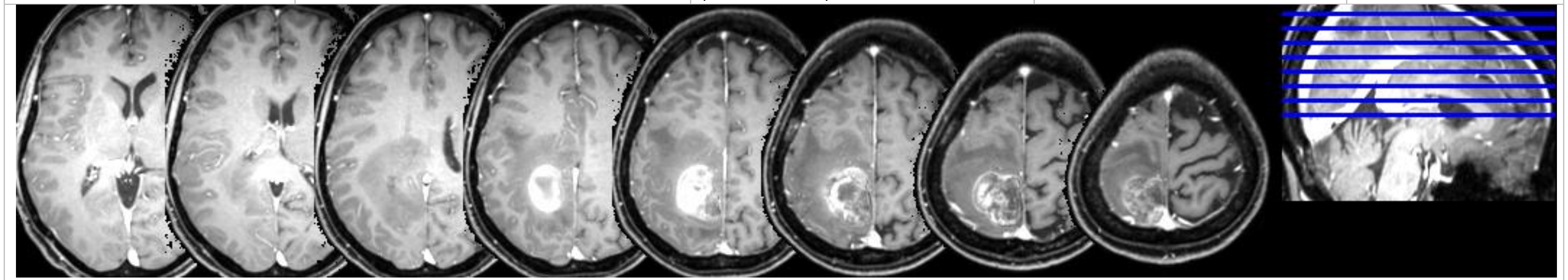
Affected areas:
Middle Frontal Gyrus, Precentral Gyrus, Superior Frontal Gyrus

13	glioblastoma	frontal	left	IV



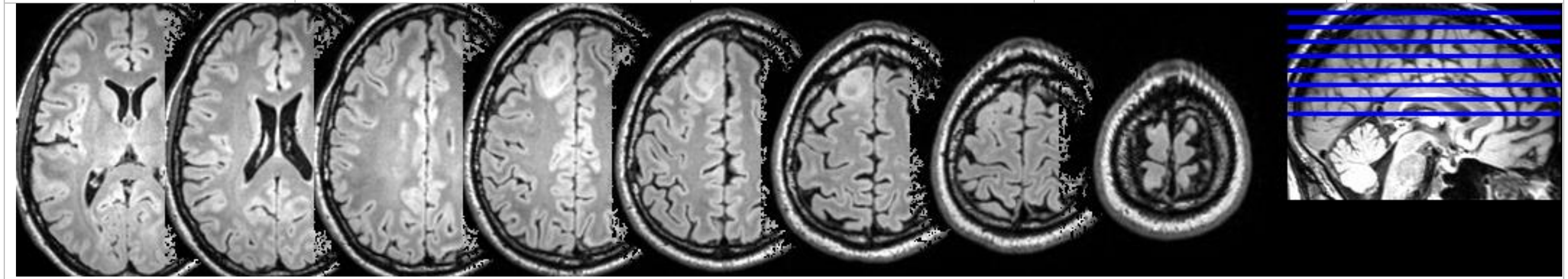
Affected areas:
Cingulate Gyrus (anterior division), Juxtapositional Lobule Cortex (former Supplementary Motor Cortex), Middle Frontal Gyrus, Paracingulate Gyrus, Precentral Gyrus, Superior Frontal Gyrus,

14	metastasis	parieto-occipital	left	-



Affected areas:
Lateral Occipital Cortex (superior division), Postcentral Gyrus, Precuneous Cortex, Supramarginal Gyrus (posterior division) Superior Parietal Lobule

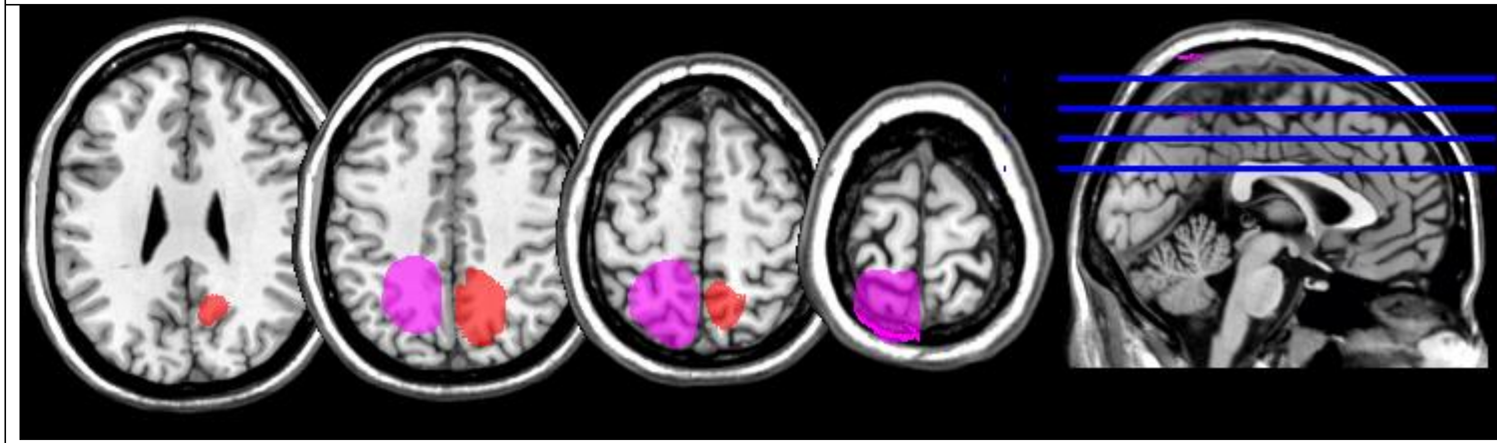
15	astrocytoma	frontal	left	II



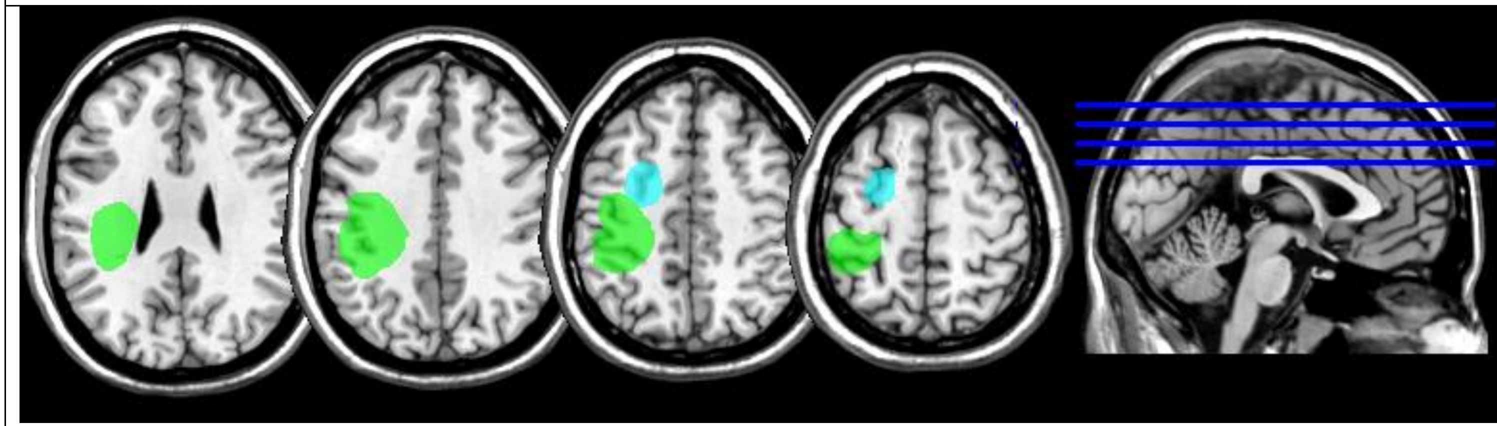
Affected areas:
Frontal Pole, Middle Frontal Gyrus, Paracingulate Gyrus, Superior Frontal Gyrus

Part 5: Multislice MR Images of Lesion Overlay According to Lobe

Lesion overlay of parieto-occipital brain tumors (two subjects)[24]:

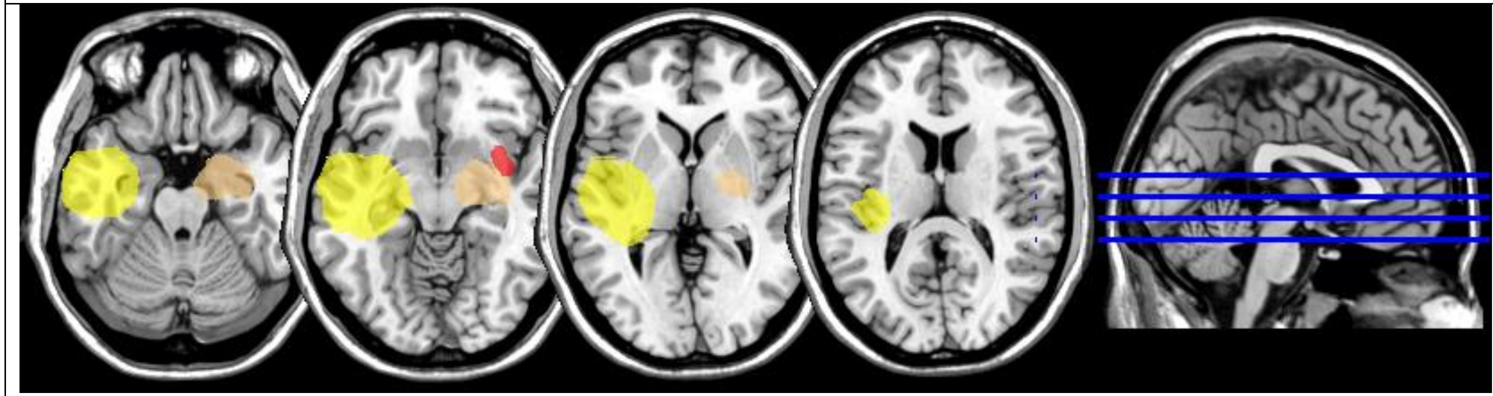


Lesion overlay of fronto-parietal brain tumors (two subjects):

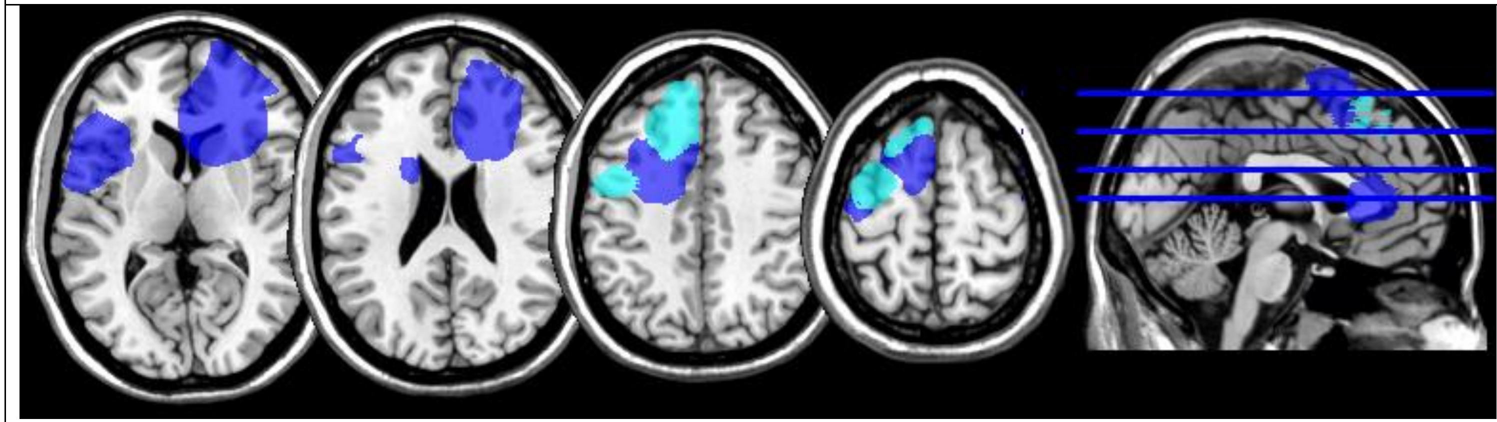


[24] Note that the sagittal plane displays only the very edge of the lesion in red and pink so that it appears to be non-continuous

Lesion overlay of temporal brain tumors (three subjects):



Lesion overlay of frontal brain tumors (eight subjects)[25]:



[25] Note that the sagittal plane displays only the very edge of the lesion in turquoise so that it appears to be non-continuous.