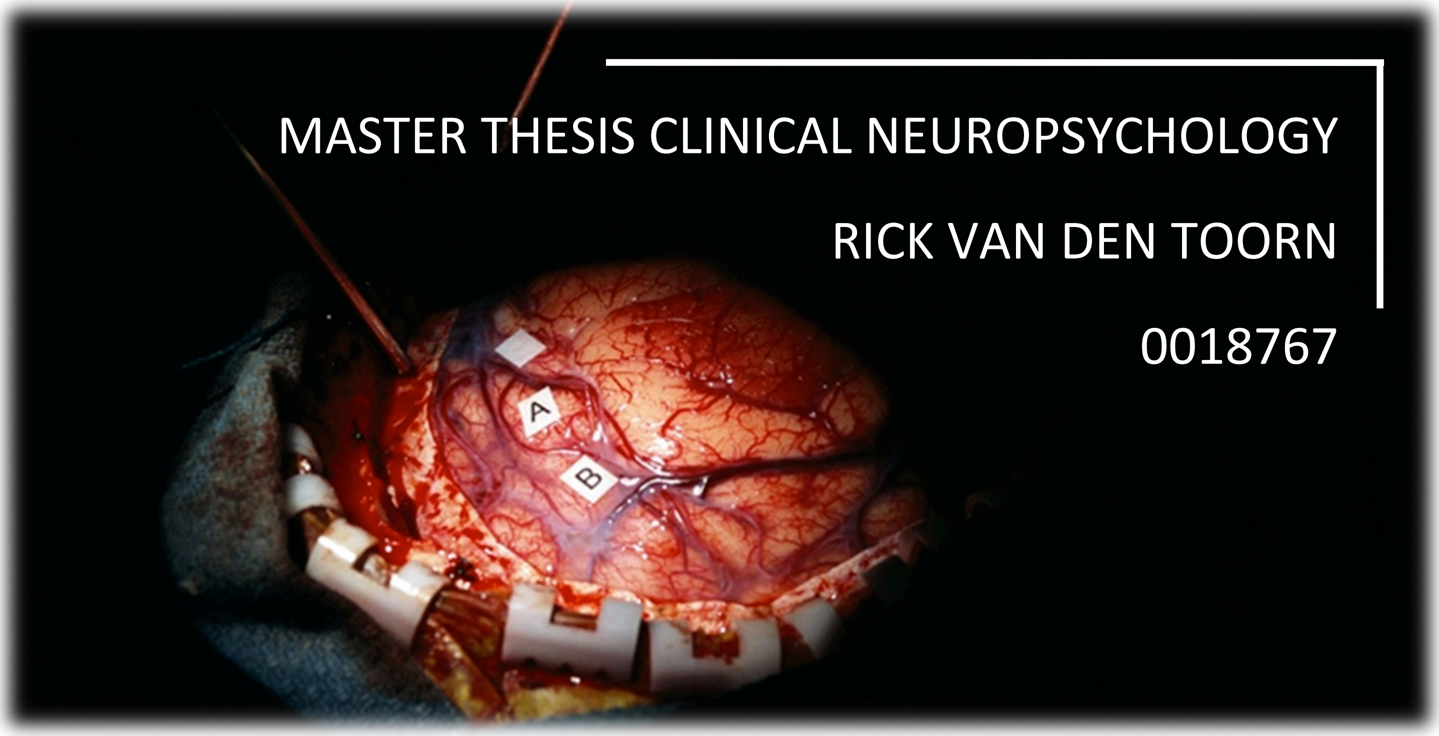

MASTER THESIS CLINICAL NEUROPSYCHOLOGY

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Spatial Attentional Functioning in Adult Brain Tumor Patients

Utrecht University
Master Clinical Neuropsychology

MASTER THESIS

Spatial Attentional Functioning in Adult Brain Tumor Patients

The impact of resective surgery on cognitive functioning by comparing pre- and postsurgical neuropsychological outcome in 24 glioma patients

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Abstract

Background. Cognitive functioning is at risk in patients with gliomas because of the infiltration of healthy surrounding brain tissue. Cognitive changes can be related to direct tumor effects, treatment effects including surgery, radiotherapy, chemotherapy, antiepileptic medication, and corticosteroids, and ultimately, tumor progression. *Objective.* We determined the impact of resective surgery on cognitive functioning by comparing pre- and postoperative neuropsychological outcome specifically focusing on attentional functioning (as measured by the Stroop Color Word Test (SCWT)). *Methods.* 24 adult patients (10 females, median age: 40, range: 20-64) with supratentorial gliomas (WHO II: 17, WHO III: 3 and WHO IV: 4) underwent neurosurgery of which 17 in eloquent brain regions using intraoperative brain mapping. Neuropsychological examination was administered approximately one week before surgery and 9 months thereafter. Outcome was analyzed at the group and individual level. Several predictive factors for potential cognitive deterioration were explored. *Results.* Deterioration following surgery in reading speed (performance on Card 1, SCWT) was observed at group level. The effect of predictive factors and individual analyses showed that more extensive resections (i.e. >80%) and tumors located in language eloquent areas yielded clinically relevant deterioration in reading speed. *Conclusion.* Deterioration in reading speed was found clinically relevant in the predictive dichotomies Extent of Resection (EOR) and language eloquent area. In these patients, both tumor location and location of surgical intervention suggest involvement of the superior longitudinal fasciculus (SLF II). Extra attention should be sought in this particular region during resective brain surgery along with further research in order to map *spatial attention* in a more accurate way.

Keywords: Brain tumor – glioma – resective tumor surgery – cognitive functioning – reading speed – spatial attentional functioning - neuropsychological assessment – pre- and postsurgical measurement – health related quality of life (HRQOL) – superior longitudinal fasciculus (SLF) – Stroop Color Word Test (SCWT)

Introduction

Almost 70% of all primary brain tumors, i.e. tumors originating from brain tissue itself, are so called *gliomas*. Gliomas arise from glial cells, which are non-neuronal cells that provide support and nutrition to the brain. Secondary or metastatic brain tumors spread from cancers primarily originating outside the brain and have a much higher prevalence. In this study, the focus will be on gliomas.

Gliomas are known to infiltrate the surrounding healthy brain tissue and, in line with the World Health Organization (WHO) scale (Louis et al., 2007), are graded according to their histological degree of malignancy. High-grade gliomas are classified as either grade III anaplastic astrocytoma, anaplastic oligodendroglioma or anaplastic oligoastrocytoma, or as grade IV glioblastoma (glioblastoma multiforme, GBM). Low-grade gliomas are well differentiated and portend a much better prognosis for the patient (median survival time of 7 - 10 years) than high-grade gliomas, which are undifferentiated and characterized by a median survival of less than 2 years. A glioma ultimately is a devastating disease with a negligible cure rate.

The highly infiltrative nature of both high-grade and low-grade gliomas often prevents curative surgical resection and complicates effective delivery of many kinds of therapy. Treatment primarily focuses on extending life expectancy while maintaining health-related quality of life (HRQOL) as high as possible. Since effective treatment interventions have increased overall survival, there has been greater awareness that many brain tumor patients, despite adequate disease control, experience cognitive dysfunction (Correa, 2006). These cognitive deficits might affect their HRQOL and interfere with the patient's ability to function at premorbid levels, both professionally and socially. In order to make informed treatment choices concerning survival and HRQOL, it is critical to define the factors that can be associated with cognitive decline.

First, *the tumor itself* is an important contributor. Klein and colleagues (2002) found cognitive deficits already present at the time of histological diagnosis (i.e. following surgery, but before subsequent treatment) and could often be related to the location of the tumor with patients with tumors located in the left hemisphere being most affected. Furthermore, fast growing tumors (i.e. WHO grade III and IV) are a predictor of cognitive impairment as well as tumor-related epilepsy (Brown et al., 2006). As a reaction to the disease, but also depending on the tumor location, brain tumor patients may experience feelings of anxiety, depression, and future uncertainty. These mood disturbances can cause deficits in attention and motivation and may subsequently negatively affect cognitive functioning (Heimans & Taphoorn, 2002).

A third important factor is *treatment.* First of all, *surgery* is needed to establish the histological diagnosis and to alleviate neurological symptoms through the reduction of tumor mass effects on the cortex or on the subcortical functional fibers (Taphoorn & Klein, 2004). Although surgery is believed to be beneficial for cognition, it can also cause, mostly transient, neurological deficits by compromising the healthy brain tissue surrounding the tumor (Bertani et al., 2009). Yet, in the months following surgery some recovery often still takes place, reflecting neosynaptogenesis, combined with sprouting of axons and dendrites to loco-regional and remote regions; the main plasticity mechanism in the normal brain (Duffau et al., 2003). New techniques such as pre-operative functional MRI, diffusion tensor imaging and intra-operative electrical stimulation (cortical and subcortical) provides detailed functional information during surgery. The use of these brain mapping techniques improves the extent of resection, while minimizing morbidity and enhancing HRQOL.

Many low-grade glioma patients will take *antiepileptic drugs (AEDs)* during their illness because they experience epileptic seizures. Apart from AEDs, cognitive functioning may also be negatively affected by the seizures themselves (Martin Klein et al., 2003). Furthermore, *corticosteroids* are used to reduce intracranial pressure caused by edema which often will have a positive effect on cognitive outcome. However, corticosteroids may also cause mood disturbances and psychosis which can have a negative effect on cognition as shown previously (Fietta, Fietta, & Delsante, 2009). Besides the factors described above, it is also important to account for *patient-related variables* such as age, gender, performance status, level of education, extent of resection, time since diagnosis and number of recurrences.

As discussed previously, surgery is believed to alleviate neurological symptoms by the removal of tumor tissue and reducing intracranial pressure. However, damage of normal surrounding tissue may also cause mainly transient *focal* neurological deficits, in contrast to more *diffuse* cognitive disturbances caused by radiation and chemotherapy (Scheibel, Meyers, & Levin, 1996; Taphoorn & Klein, 2004). The benefits of surgical resection on cognitive outcome have not been demonstrated yet because retrospective studies show conflicting results and often lack a presurgical baseline (Yoshii et al., 2008). Therefore, the purpose of the present study is to report pre- and postoperative neurocognitive follow-up data to determine the incidence and extent of cognitive deficits following neurosurgery.

Intraoperative language mapping, especially on a cortical level, has received a lot of attention in the past decade (Duffau, Gatignol, Mandonnet, Capelle, & Taillandier, 2008). Less well understood in the process of mapping are cognitive functions such as memory and attention. Attentional functioning is a relatively fundamental cognitive function of which' boundaries overlap with those of many other cognitive processes, including arousal, perception, recognition, memory, and executive function. Accordingly, attentional disturbances may exacerbate impairments in these other domains of cognition. Therefore, the present study specifically aimed at determining the effects of tumor location and location of surgical intervention on attentional functioning in order to get a better understanding of the neuroarchitecture of this important cognitive function. A distinction will be made between *spatial* and *selective attention* as measured by the Stroop Color-Word Test (SCWT) in different conditions (Stroop, 1935).

Methods

Patients

24 adult patients (10 females, median age: 40, range: 20-64) with supratentorial gliomas (WHO II: 17, WHO III: 3 and WHO IV: 4) were recruited from the VU University Medical Center, Amsterdam, The Netherlands. The inclusion criteria were: (1) histologically confirmed glioma (WHO grade II – IV), (2) tumor resection, and (3) able to communicate in the Dutch language. Before patients had neurosurgery, they were tested for their performance on a standard neuropsychological battery. Most patients were tested within a week before surgery. After approximately 9 months, post surgical measurements were obtained. This time window was chosen to assure that transient neurological deficits resulting from surgery would be minimal in the majority of patients and additionally, that adjuvant and/or concomitant therapy (e.g. chemo- and/or radiotherapy) had been completed at the time of testing.

Outcome measures

Comprehensive neuropsychological assessment included evaluation of attentional functioning by means of the Stroop Color-Word Test (SCWT) (Lezak, 1995; Stroop, 1935). The SCWT consists of three cards displaying 100 stimuli each. The first card consists of color words printed in black ink. Card 2 consists of colored patches in one of four basic colors (green, red, yellow and blue). The last card (Card 3) displays color words printed in an incongruous ink color. Patients were instructed to read the words (Card 1), to name the color of the colored patches (Card 2) and to name the ink color of the printed words (Card 3), as fast and as accurately as possible. Performance on Card 1, 2, and 3 was used as dependent variable in the current analyses. Outcome measures were standardized and the relative delay of reading speed during Card 3 (= relative interference), because of interference, was corrected for reading speed on Card 1 and Card 2. The following syntax was used for correction: Compute relative interference score = (Card 3 - .5 * (Card 1 + Card 2)) / (.5 * (Card 1 + Card 2)) * 100. Card 3 measures *selective attention* since an automatic response (reading) has to be suppressed actively while the ink color is named. Card 1 and 2 on the other hand measure *spatial attention*, an orienting kind of attention.

Statistical Analysis

Non-parametric related samples Wilcoxon Signed Ranks Tests were used to evaluate possible changes in cognition before and after surgery. Uncorrected data were analyzed at the group level and subsequently evaluated for the relative contribution of factors potentially affecting cognitive outcome: 1) *gender* (male vs. female) 2) *tumor location* (left vs. right hemisphere) 3) *tumor volume* (< 100 ml vs. > 100 ml) 4) *Extent of Resection* (EOR) (<80% vs. > 80%) 5) *histology* (low-grade vs. high-grade glioma) and 6) *language eloquent area* (language eloquent vs. not language eloquent).

Furthermore, since group analyses can obscure cognitive outcome at the individual level, data were analyzed at the individual level for all the data together as well as for the six factors potentially affecting cognitive outcome. Individual outcome measures were standardized (t-scores, corrected for age, gender and education level) and a cut-off score of $t = 37$ was set for determining a clinically meaningful deficit in cognitive functioning. Thus, cognitive performance prior to surgery was compared with healthy subjects, controlling for age and education.

Regarding cognitive follow-up, patients were classified as follows: 1) *not deteriorated*, pre- and postsurgical measurements were both above the cut-off score of $t = 37$ (i.e. within the normal range of cognitive performance). 2) *deteriorated,* the presurgical measurement was above and the postsurgical measurement was below the cut-off score of $t = 37$. 3) *improved,* the presurgical measurement was below and the postsurgical measurement was above the cut-off score of $t = 37$ and 4) *not improved*, both pre- and postsurgical measurements were below the cut-off score of $t = 37$. For ease of survey, data were visualized. Group mean t-scores were included in the graphs in order to determine the mean outcome in clinical relevance (see table 2).

Imaging

Pre- and postsurgical MRI scans were used in combination with clinically relevant performance on the SCWT in order to get a better understanding of the neuroarchitecture of attentional functioning. Individual delta-scores were placed in one of four groups, as described previously, and their MRI scans were used to find a potential overlap in location. Both tumor location and location of surgical intervention were examined in respectively *not* *improved* and *deteriorated* patients. MRI scans of *improved* and *not deteriorated* patients were used as control.

Results

Performance at the group level

Table 1 lists the sociodemographic and clinical characteristics of the 24 glioma patients in this study. Glioma patients as a group showed a decline in reading speed as evidenced by increased response times on Card 1 of the SCWT (see figure 1 and table 2). However, no differences were found between pre- and postsurgical performance on SCWT Card 2, 3, and relative interference.

Table 1. Sociodemographic and clinical characteristics

Case	Age-Gender	Location	Volume (ml)	Mapping (l/m/s/v)	EOR	Pathology (WHO)	Adjuvant therapy	AED
1	20 F	L temporal	117	l	90%	AA (III)	CH/RT	VPA
2	44 M	L frontal	98	-	62%	OD (II)	-	
3	22 M	R frontotemporal	125	-	68%	A (II)	-	
4	38 F	L frontal	101	l/m	67%	OD (II)	-	
5	24 M	R frontotemporal	36	-	53%	OD (II)	-	
6	56 F	L frontal	150	l/m	67%	OD (II)	-	
7	36 F	L parietal	152	-	50%	OA (II)	RT	
8	41 M	R parietal	22	m	91%	OD (II)	-	
9	31 M	R insular	49	l/m/s	63%	A (II)	-	
10	36 M	L cingulum	94	l/m	78%	OA (II)	-	
11	45 M	R frontal	288	-	63%	AO (III)	RT	
12	40 F	R premotor-frontobasal	41	m	54%	OA (II)	-	
13	40 F	R temporal	140	m	75%	A (II)	RT	
14	51 M	R frontotemporo-insular	102	-	48%	GBM (IV)	CH/RT	
15	54 M	R frontotemporo-insular	27	m	85%	OD (II)	-	
16	35 M	L frontoparietal	81	l/m	49%	GBM (IV)	CH/RT	
17	44 F	L frontal	58	l/m	93%	OD (II)	-	
18	33 M	L parietal	45	l/s	76%	OD (II)	-	
19	64 M	L parietotemporal	16	l	88%	GBM (IV)	CH/RT	
20	26 M	L frontotemporo-insular	131	l/s	76%	A (II)	-	
21	50 F	L precentral	35	m	51%	OD (II)	-	
22	53 M	R frontal	143	-	81%	A (II)	-	
23	25 F	L parieto-occipital	52	l/m/s/v	100%	AA (III)	-	
24	21 F	R parietotemporal	112	l/m/s/v	97%	GBM (IV)	CH/RT	

Age in years, Gender (M = Male, F = Female); Location (L = Left, R = Right); Volume is presurgical tumor volume; Mapping intraoperative (l = language, m = motor, s = sensory and v = vision); EOR (=Extent Of Resection); Pathology of the tumor (AA = Anaplastic Astrocytoma, OD = Oligodendroglioma, A = Astrocytoma, OA = Oligoastrocytoma, GBM = Glioblastoma multiforme) WHO (= World Health Organization, tumor grade II – IV); Adjuvant therapy: CH = Chemo Therapy, RT = Radiotherapy; AED = Anti Epileptic Drug, dose in mg.

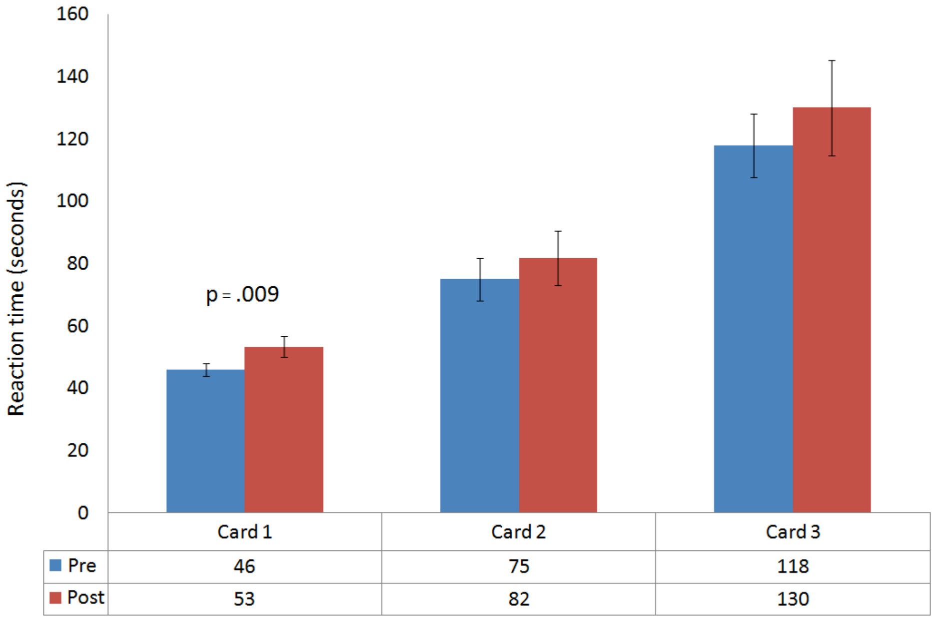

Figure 1. Pre- and postsurgery performance on Card 1, 2 and 3 (SCWT) for *total data* at the group level. Pre- and postsurgery performance on Card 1 differed significantly (p = .009).

The effect of predictive factors

Significant differences were found for *gender*, *hemisphere*, *tumor volume*, *EOR* and *language eloquent area* (see table 2). First of all, males declined in performance on Card 1 (SCWT) whereas women did not. In addition, a decline in performance on Card 1 was found in patients with a tumor located in the right hemisphere. Patients with a tumor in the left hemisphere demonstrated a trend in the same direction. Furthermore, patients with small tumors and extensive resections also deteriorated in reading speed. Lastly, patients with tumors in language eloquent areas were declined in reading speed while patients with tumors located in non-language eloquent areas did not. A noteworthy result is the significant difference found for performance on Card 3 and the relative interference (SCWT) in patients with a right hemisphere tumor.

Performance at the individual level

Patients with a relatively small tumor (<100 ml) had a clinically relevant deterioration in reading speed (Card 1, SCWT) (see figure 2). The same is true for patients with a relatively large EOR (>80%) (see figure 3) and patients where language eloquent areas were found during intraoperative mapping (see figure 4). No clinically relevant deterioration in reading speed was found (group mean) when all individuals (total data) were visualized (see figure 5, red line). Individual delta t-scores are summarized in table 3.

Table 2. Delta (Δ) t-scores for SCWT performance at the group level for different dichotomies and total data

Dichotomies		Card 1	Card 2	Card 3	Relative interference
		Δ t-score (*p*)	Δ t-score (*p*)	Δ t-score (*p*)	Δ t-score (*p*)
Gender	Male (n=14)	-6.6 (.020)*	-4.9 (.423)	-2.7 (.463)	+0.6 (.221)
	Female (n=10)	-5.3 (.241)	-1.3 (.475)	-0.4 (.959)	+4.3 (.445)
Tumor location	Left (n=13)	-7.9 (.055)	-6.0 (.422)	-7.4 (.108)	-1.8 (.600)
	Right (n=11)	-3.8 (.036)*	-0.2 (.725)	+4.9 (.047)*	+6.7 (.006)*
Tumor volume	<100 ml (n=13)	-8.9 (.028)*	-5.3 (.722)	-2.5 (.367)	+1.3 (.552)
	>100 ml (n=11)	-2.6 (.196)	-1.1 (.284)	-0.8 (.929)	+1.1 (.182)
EOR	<80% (n=14)	-3.9 (.187)	-2.1 (.470)	-2.6 (.518)	+0.6 (.605)
	>80% (n=10)	-10.4 (.017)*	-5.9 (.398)	-0.1 (.866)	+5.3 (.263)
Histology	High (n=7)	-9.7 (.127)	-5.9 (.933)	-4.4 (.499)	-0.6 (.866)
	Low (n=17)	-4.5 (.055)	-2.4 (.221)	-0.6 (.897)	+3.2 (.124)
Language eloquent	No (n=13)	-4.4 (.133)	-0.4 (.878)	+3.0 (.433)	+4.4 (.101)
	Yes (n=11)	-8.0 (.033)*	-6.9 (.328)	-7.4 (.266)	-0.5 (.929)
Total data (n=24)		-6.0 (.009)*	-3.4 (.305)	-1.8 (.553)	+2.1 (.209)

*** = significant difference**

WHITE = not deteriorated **BLACK** = deteriorated **DARK GREY** = improved and **LIGHT GREY** = not improved

Coloration shows classification (group level) regarding cognitive follow-up as discussed in the method section.

Finally, the importance in combining individual and group analysis can be made clear by the dichotomy *tumor location*. Patients as a group with tumors in the right hemisphere had a significant decline in performance on Card 1, while patients with left hemisphere tumors did not (although they showed a trend in the same direction). When t-scores were visualized in a graph (see figure 6), the opposite effect was shown; no clinical relevance in patients with right hemisphere tumors (no deterioration) and, although it was still a trend, a clear deterioration in patients with left hemisphere tumors.

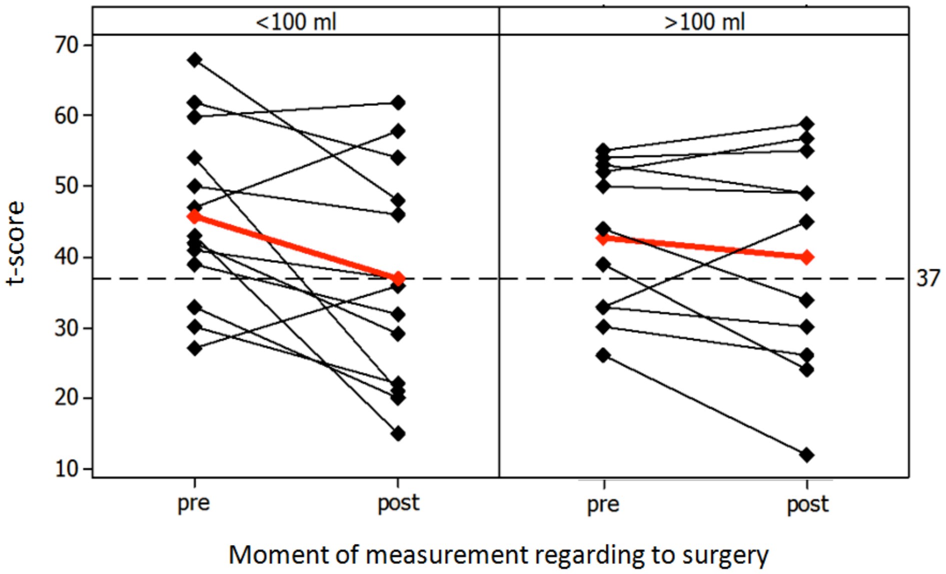

Figure 2. Individual t-scores (pre- and postsurgery) for SCWT performance (Card 1) in dichotomy tumor volume. Small tumors <100 ml (n=13) in left panel, large tumors >100 ml (n=11) in right panel. The cut-off score of t = 37 is marked by the dotted line. The red line shows mean group performance. Small tumors (<100 ml): *Not deteriorated* = 6, *deteriorated* = 4, *improved* = 0 and *not improved* = 3. Large tumors (>100 ml): *Not deteriorated* = 5, *deteriorated* = 2, *improved* = 1 and *not improved* = 3

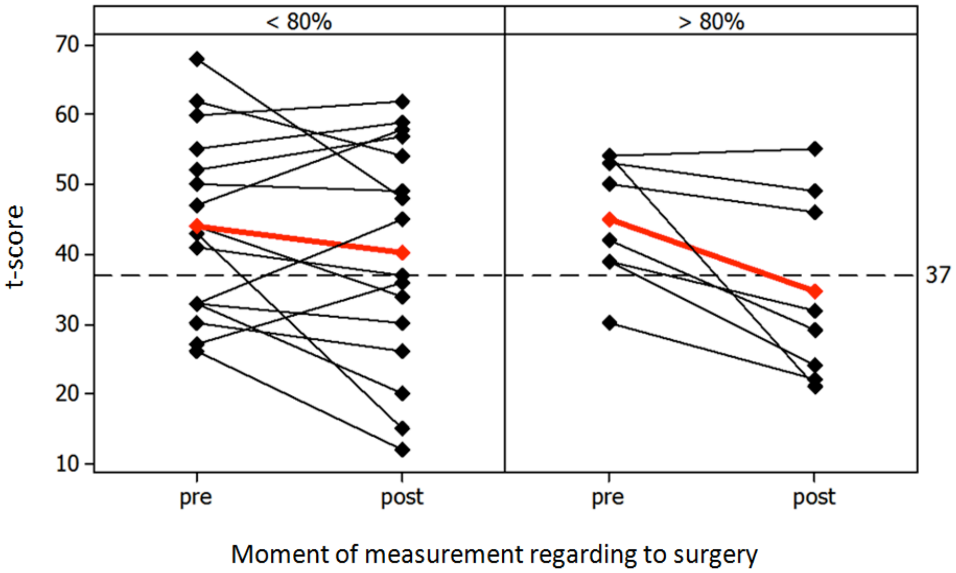

Figure 3. Individual t-scores (pre- and postsurgery) for SCWT performance (Card 1) in dichotomy EOR. Small EOR <80% (n=16) in left panel, large EOR >80% (n=8) in right panel. The cut-off score of t = 37 is marked by the dotted line. The red line shows mean group performance. Small EOR (<80%): *Not deteriorated* = 8, *deteriorated* = 2, *improved* = 1 and *not improved* = 5. Large EOR (>80%): *Not deteriorated* = 3, *deteriorated* = 4, *improved* = 0 and *not improved* = 1

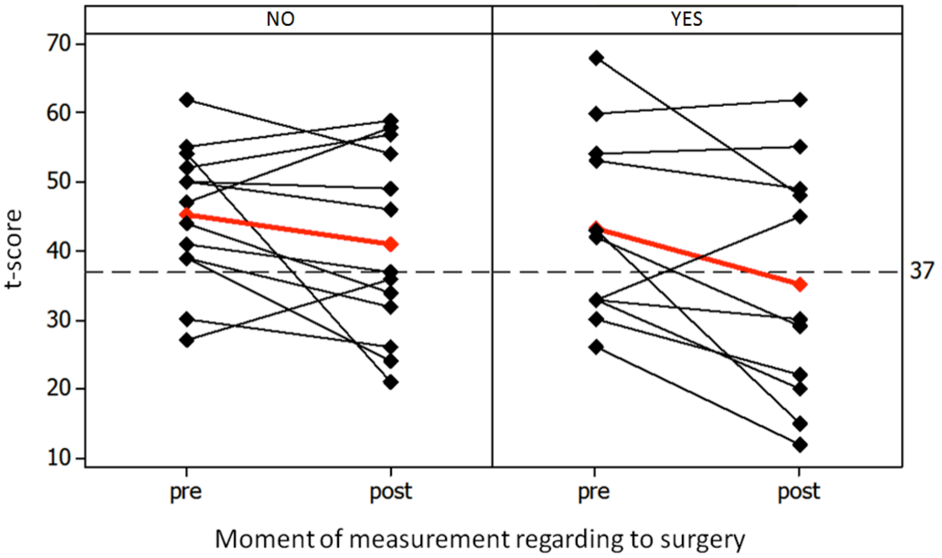

Figure 4. Individual t-scores (pre- and postsurgery) for SCWT performance (Card 1) in dichotomy Language eloquent area. NO (n=13) in left panel, YES (n=11) in right panel. The cut-off score of t = 37 is marked by the dotted line. The red line shows mean group performance. NO: *Not deteriorated* = 7, *deteriorated* = 4, *improved* = 0 and *not improved* = 2. YES: *Not deteriorated* = 4, *deteriorated* = 2, *improved* = 1 and *not improved* = 4

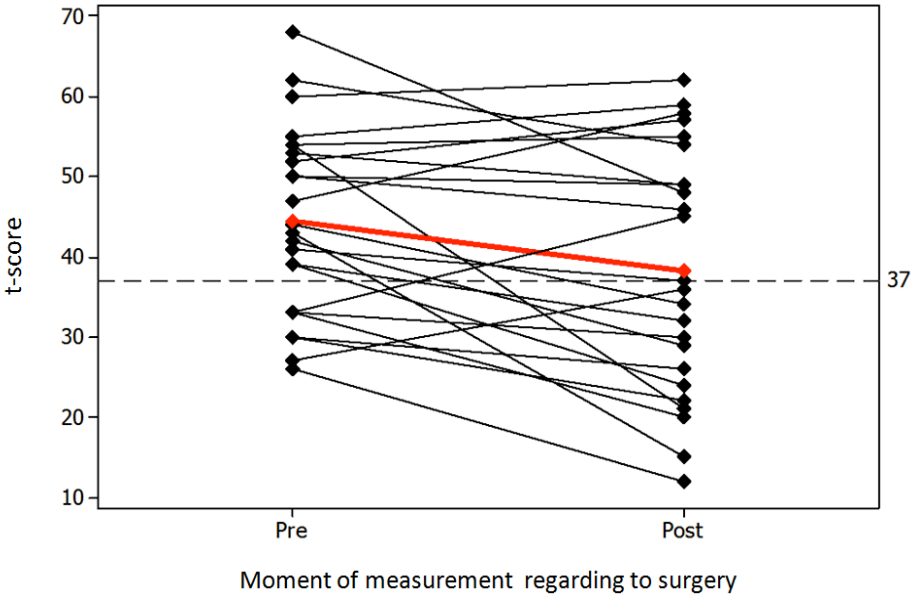

Figure 5. *Individual t-scores* (pre- and postsurgery) in 24 glioma patients for SCWT performance (Card 1) . The cut-off score of t = 37 is marked by the dotted line. The red line shows mean group performance. Total data: *Not deteriorated* = 11, *deteriorated* = 6, *improved* = 1 and *not improved* = 6.

Table 3. Individual delta t-scores for SWCT performance

Case #	Card 1	Card 2	Card 3	Relative interference
1	+1	+4	0	-2
2	+11	+9	+7	+1
3	+4	0	+4	+4
4	-3	-13	-9	-6
5	-4	0	0	0
6	+12	+27	-6	+5
7	-4	-5	-4	-1
8	-4	0	0	+1
9	+2	+3	+5	+5
10	-13	-9	-8	-3
11	+5	+6	+4	+1
12	-8	+2	+22	+26
13	-10	-1	-4	-3
14	-1	+2	+14	+16
15	-7	-1	+2	+4
16	-28	-21	-31	-23
17	-13	-11	+10	+22
18	-20	-28	-22	-6
19	-8	-3	-7	-5
20	-14	-19	-11	0
21	+9	+13	+2	-7
22	-15	-7	+5	+13
23	-33	-23	-13	+2
24	-4	-6	+2	+7

WHITE = not deteriorated **BLACK**= deteriorated **DARK GREY**= improved and **LIGHT GREY** = not improved

Coloration shows classification (individual level) regarding cognitive follow-up as discussed in the method section

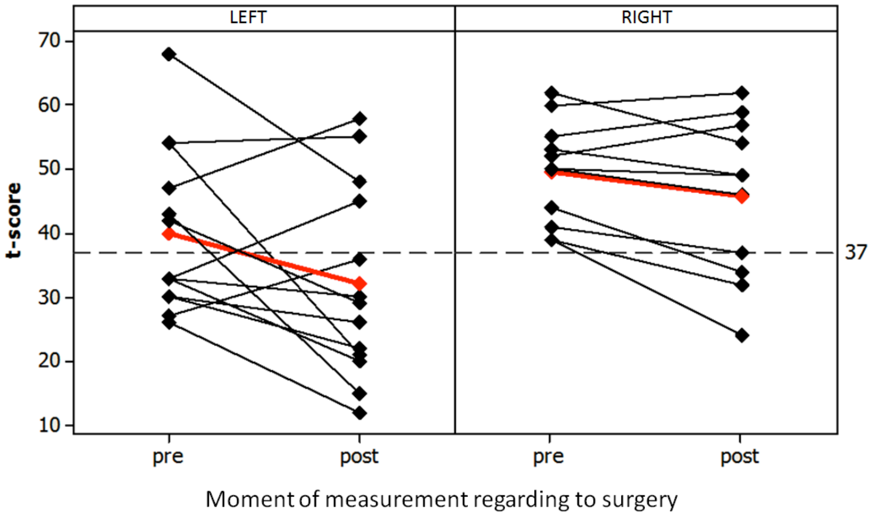

Figure 6. Individual t-scores (pre- and postsurgery) for SCWT performance (Card 1) in dichotomy tumor location LEFT (n=13) in left panel, RIGHT (n=11) in right panel. The cut-off score of t = 37 is marked by the dotted line. The red line shows mean group performance. LINKS: *Not deteriorated* = 3, *deteriorated* = 3, *improved* = 1 and *not improved* = 6. RIGHT: *Not deteriorated* = 8, *deteriorated* = 3, *improved* = 0 and *not improved* = 0

Imaging

Both pre- and postsurgical MRI scans of *deteriorated* and *not improved* patients on Card 1 (SCWT) were examined because of their clinical relevancy (for an example, see figure 7). Although an overall overlap in area SLF II was found, some tumor positions did not fit this location. For example, patient number 15 had deteriorated in reading speed, but his tumor was located in another part of the brain (see table 1). The postsurgical measurement however took place only 3.5 months after surgery and so, transient neurological deficits resulting from surgery could still take place. Furthermore, patient number 13 has had RT as adjuvant treatment, where others in his group did not. This could again explain the more global cognitive deficits while tumor/surgery location did not match.

Most patients within the *not deteriorated* and *improved* groups were showing a tumor location outside the area of SLF II. In two patients the tumor was located near the SLF II, however, they did not deteriorate on reading speed: In patient number 24 it was difficult to determine the language dominant hemisphere, suggesting that the tumor was not in a language eloquent area, explaining why reading speed did not deteriorate. Furthermore, patient number 18 was not categorized as deteriorated, while tumor and surgery location was close to SLF II. It turned out that performance was very good before surgery: Although he did deteriorate a lot (delta score = -20), postsurgical measurement was not below the cut-off score of t = 37 indicating that he was still within the normal range of cognitive performance (see table 3).

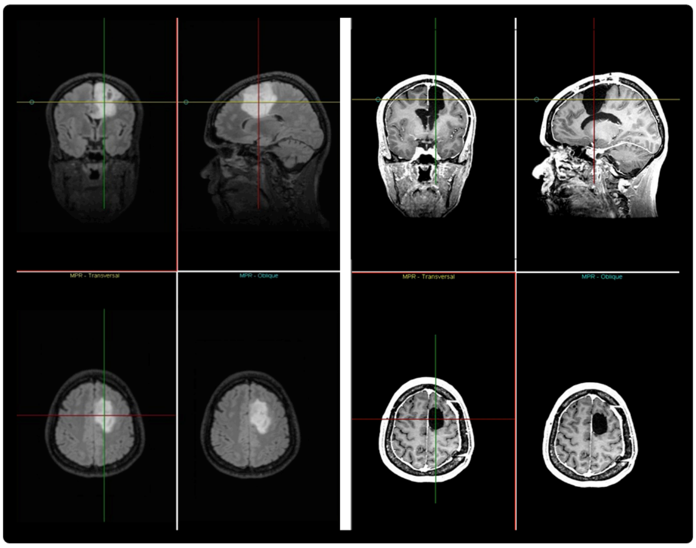

Figure 7. MRI scans of patient #17. Left scan was made pre-surgery (tumor location) and right scan was made post-surgery (location of surgical intervention).

Discussion

The aim of the present study was to assess the impact of resective glioma surgery on cognitive deficits by comparing pre- and postoperative neuropsychological outcome. The majority of studies in brain mapping research have assessed language, whereas attention is less well understood. Therefore, the main focus of this study was on *attention*. In order to get a better understanding of the neuroarchitecture of attention, both tumor location and location of surgical intervention were linked to clinically relevant cognitive outcomes (as measured by the Stroop Color Word Test (SCWT)).

The current findings suggest that, overall, reading speed (Card 1, SCWT) deteriorated at the group level. This is particularly true in relation to the predictive factors *tumor volume*, *EOR* and *language eloquent area,* which demonstrated a significantly clinical effect. These cognitive outcomes were subsequently linked with MRI-scans of both tumor location and location of surgery intervention. An overlap was found in location and deterioration in reading speed and likely to be associated with one specific part of the Superior Longitudinal Fascicle (SLF): SLF II.

Reading speed was found to be deteriorated when a larger area was resected. Intraoperative mapping allows larger extents of resection, but not every function can be mapped yet (De Benedictis, Moritz-Gasser, & Duffau, 2010). Particularly attention is difficult to map because it merely consists out of networks across the brain as well as there is a large overlap with many other cognitive processes. A distinction should be made here between *spatial attention* (Card 1, SCWT), which was found to be deteriorated, and *selective attention* (Card 3, SCWT), which was not changed. Tumors located in language eloquent areas were showing a decline in reading speed as well. Reading aloud and understanding a written word (e.g. Card 1, SCWT) is a complex task that requires a number of cognitive processes, some of which are shared by verbal language (Hillis, 2008).

The finding that patients with small tumors had deteriorated in reading speed is not directly understandable. In this study, categorization in tumor volume (small and large tumors) was done relatively to the median. However, almost all tumors were relatively large in comparison with other brain tumor studies and a real distinction between small and large tumors is therefore hard to make (Dijkstra et al., 2009). The distinction found in tumor volume is most likely influenced by tumor location, although additional work is necessary to resolve this issue.

Involvement of the SLF II has been hypothesized after linking performance on Card 1 (SCWT) with pre- and postsurgical MRI scans. This white matter bundle connects the prefrontal cortex to the caudal inferior parietal cortex which controls spatial attention and visual and oculomotor functions. This suggests the SLF II provides the prefrontal cortex with parietal cortical information regarding perception of visual space. Since these bundles are bi-directional, working memory in the prefrontal cortex may provide the parietal cortex with information to focus spatial attention and regulate selection and retrieval of spatial information (Makris et al., 2005).

Furthermore, evidence is growing that the Frontal Eye Field (FEF), located in the premotor cortex, plays a key role in covert orienting (Thompson, Biscoe, & Sato, 2005). With this ability, visual information can be selected and acquired preferentially within a locus of peripheral vision without shifting gaze. Thompson and Bichot (2005) suggest that the spatially selective activity observed in FEF visual responses functions as a visual salience map that identifies potential saccade targets for eye movements. This implies that the functional link between *attention* and *eye movements* is gated within the FEF, which is in line with the fact that patients did not *lose* their capability of reading itself but rather showed a *decline* in reading speed.

Since this study included only 24 glioma patients, future research is needed to establish the effects of neurosurgery on cognitive functioning. However, gliomas are not as common as many other forms of neuropathology, therefore it is difficult to obtain large homogenous samples for research. Furthermore, besides neuropsychological assessments, it is important to document the patients' mood. As described previously in the introduction, mood disturbances do have a potential negative effect on cognition and should be taken into account (Poppelreuter et al., 2004). The same is true for fatigue (Calvio, Feuerstein, Hansen, & Luff, 2009).

To conclude, reading is increasingly important in both social and professional life. Communication via e-mail, internet shopping, paying bills through web sites and searching for information on the internet are all common daily activities requiring intact attentional processes. Therefore, studies like the present add to our understanding of the neuroarchitecture of attentional functioning. This study will continue with larger patient samples, in order to draw more definite and detailed conclusions. Expectedly, this endeavor will lead to a more sophisticated way of intraoperative mapping and consequently to an improvement of HRQOL in brain tumor patients.

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