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Is Awake Brain Surgery in Glioblastoma Patients with Severe Aphasia Feasible? Four Case Reports

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Introduction

Glioblastomas (GBM) are malignant primary brain tumors associated with a limited median survival. Traditionally, surgical treatment is performed under general anesthesia but some recent studies revealed that awake surgery in GBM resulted in better outcomes (Gerritsen, Arends, Klimek, Dirven, & Vincent). However, as severe aphasia is common in GBM-patients (Noll, Sullaway, Ziu, Weinberg, & Wefel), the intraoperative distinction between pre-existent aphasia and direct electrical stimulation (DES) or surgery induced paraphasias becomes a challenge.

Methods

We present four cases (A1, B2, C3 and D4) elected for awake surgery with GBM in eloquent language areas (frontal, temporal and/or parietal lobe) and with severe aphasia. Pre- and postoperatively, an extensive test-protocol was administered at different linguistic levels (phonology, semantics and syntax) and modalities (comprehension, production and reading). Intraoperative language tasks for DES and resection were selected from the Dutch Linguistic Intraoperative Protocol (De Witte et al.) and adapted to patients' preoperative level.

Results

Preoperatively all patients had severely impaired scores ($z \leq -2.00$) on TT, BNT, verbal fluency and DIMA Sentence Completion (A1, D4). DIMA Repetition was mildly (A1) to severely impaired (C3, D4). Repetition was only screened in B2 (raw score 12/15). DIMA Semantic odd-picture-out was mildly (A1) to severely impaired (C3, D4), but feasible in C3 presented without time constraints (odd-picture/word-out) and via the graphemic input route. For intraoperative monitoring, DuLIP-tasks were simplified by selecting high-frequency words, diminished phonological complexity and/or presentation via dual input routes (auditory and visually). Functional boundaries were successfully detected by occurrence of new paraphasias, neologisms or perseverations. Postoperatively, there was full recovery from a severe aphasia (all tests $z > -1.50$, apart from letter fluency $z = -1.50$) in A1. Although B2 and C3 improved on TT ($\Delta z \geq 1.50$), they remained severely impaired ($z \leq -2.00$). BNT recovered to normal scores in C3 ($z > -1.50$). Category and letter fluency remained severely impaired

(z≤-2.00) in B2 and C3 although administration of Letter fluency was now possible in B2. DIMA Repetition deteriorated in C3 (administration was not possible anymore). The ABC was below the cut-off score, with errors in comprehension (B2) and production (B2, D4). C3 remained stable on semantic-odd/picture out tasks (without time constraints), sentence completion recovered (z≥-1.5).

Conclusions

We demonstrated for the first time that awake surgery in severely aphasic GBM-patients was well feasible without further deterioration of aphasia. Almost full recovery was present in A1 and naming recovered in C3. The degree of postoperative improvement could be influenced by preoperative aphasia severity including the level of phonology (repetition) as shown in earlier studies (El Hachioui et al., 2013; Sierpowska et al.).

For adequate intraoperative monitoring of severely aphasic patients, extensive preoperative neurolinguistic examination of different in- and output routes (i.e. auditory, visual, graphemic) is necessary, including an error analysis. Subsequently, the linguist can intraoperatively focus on the intact linguistic levels and modalities thereby facilitating reliable interpretation of further language deterioration during DES and surgery. As this only concerns case-descriptions, the added value of awake surgery in GBM remains to be demonstrated with an RCT (Gerritsen et al.).

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	A1		**B2**		**C3**		**D4**	
	Pre	**Post (7 w)**	**Pre**	**Post (3 m)**	**Pre**	**Post (3 m)**	**Pre**	**Post (1 d)**
Shortened Token Test (TT)	**-5.74**	-0.32*	**-13.60**	**-6.75***	**-15.08**	**-12.05***	**-5.23**	
Boston Naming Test (BNT)	**-2.89**	-0.07*	**-5.70**		**-2.37**	-0.62*	**-9.60**	
Category fluency animals	**-3.20**	-0.60*	**-3.80**	**-3.20**	na	na	**-3.20**	
Category fluency professions	**-3.30**	-1.20*	**-3.30**	**-2.90**	na	na	**-3.30**	
Letter fluency	**-2.70**	-1.50	na	**-2.50**	na	na	na	
DIMA Repetition (DIMA-R)	-1.91	0.25*			**-14.29**	na	**-7.29**	
DIMA Semantic odd-picture-out (under time pressure)	-1.96	-0.69*			**-5.77**	**-5.77**	**-5.77**	
DIMA Sentence completion (auditory presentation)	**-4.14**	-0.63*			na	na	**-4.14**	
DuLIP Repetition – shortened version			12/15^{Raw}					
DuLIP Semantic odd-picture-out (without time constraints)					> 0			
DuLIP Semantic odd-word-out (without time constraints)					> 0	> 0		
DuLIP Sentence completion (visual presentation)					-1.50	>-1.50		
Aphasia Bedside Check (ABC): (comprehension + production; cut-off = 12)				11^{Raw} (5+6)				12^{Raw} (7+5)

Table 1: Pre- and postoperative neurolinguistic test-protocol (z-scores). Severely impaired scores (z=≤2.00) **in bold**, mildly impaired scores (z=≤-1.50) underlined, d = days. w = weeks. m = months. * = significant improvement pre- versus postoperatively (Δz≥1.5). na = not administered due to aphasia severity. ^{Raw} = raw score. Grey marked tests were not administered due to different protocol or lack of additional intraoperative value.