A case of bilateral frontal tumors without "frontal syndrome"

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A case of bilateral frontal tumors without "frontal syndrome"

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Abstract

We report the longitudinal case study of a right-handed patient harboring two frontal tumors that benefited from bilateral simultaneous surgery. The tumors were WHO Grade II gliomas located in the left inferior frontal area (including the cingulate gyrus) and the right anterior superior frontal gyrus. The double tumor resection was guided by direct electrical stimulation of brain areas while the patient was awake. Neuropsychological assessments were administered before and after the surgery to analyse how the brain functions in the presence of two frontal gliomas that affect both hemispheres and reacts to a bilateral resection, which can brutally compromise the neuronal connectivity, progressively established during the infiltrating process. We showed that both the tumor infiltration and their bilateral resection did not lead to a "frontal syndrome" or a "dysexecutive syndrome" predicted by the localization models. However, a subtle fragility was observed in fine-grain language, memory and emotional skills. This case study reveals the significance of brain plasticity in the reorganization of cognitive networks, even in cases of bilateral tumors. It also confirms the clinical relevance of hodotopical brain models, which considers the brain to be organized in parallel-distributed networks around cortical centers and epicenters.

Keywords

Frontal syndrome; Executive processing; Neuropsychology; Brain plasticity; Bilateral Grade II gliomas; Neurosurgery.

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INTRODUCTION

The notion of “frontal syndrome” is controversial. According to the classical localizationist view of brain functioning, which is principally based on studies of sudden cerebral damage, frontal lesions generate specific disturbances in language (notably when affecting the dominant left hemisphere), executive, and socioemotional processes (Stuss, Alexander, & Benson, 1997). By contrast, the hodotopical perspective (based on recent findings from diffusion tensor imaging tractography (DTI) and awake surgery under electrical stimulations), suggest that “frontal syndrome” could be absent in cases of slow-growth tumors that progressively infiltrate the frontal lobes or after extensive frontal lobectomy and, conversely, could be generated by the alteration of complex nonfrontal brain networks (Duffau, 2012).

Early descriptions (e.g., De Ajuriaguerra & Hécaen, 1960; Luria, 1978; Luria & Tsvetkova, 1967) of “frontal syndrome” caused by frontal damage report (a) behavioral disorders such as apathy, aboulia, gesture and action apraxia, pseudodepression or euphoria, poor motivation, distractibility, inhibition deficits and perseveration, and (b) cognitive impairments such as memory deficits (working memory and meta-memory), language disorders (especially spontaneous fluency reduction, aphasia, lexical access deficits, and pragmatic deficiencies), visual-spatial disorders (in particular, ocular-motor troubles and unilateral spatial neglect), and impairment of the executive functions (especially attention, control, and planning) (Godefroy, 2003; Stuss, 2011). Patients with frontal lesions are more specifically impaired in novel, conflicting, or complex situations that require goal-directed actions and control functions (Miotto & Morris, 1998; Shallice & Burgess, 1991).

The “dysexecutive syndrome” that affects executive functions has often been confused with “frontal syndrome” and appears in most cases of frontal lesions (Godefroy, 2010; Stuss, 2011; Stuss & Alexander, 2007). Indeed, the executive processes that involve high-level cognitive activities (planning, inhibition, flexibility, and control) and sustain problem-solving and daily life adaptation require frontal activation. However, “dysexecutive syndrome” can be observed in cases of non-frontal lesions (especially subcortical lesions), and conversely, frontal lesions do not obligatorily lead to dysexecutive syndrome (Godefroy, 2003).

The connectionist view of brain functioning is based on data from intraoperative brain mapping during the resection of gliomas under electrical stimulation (Duffau, 2005) and from DTI (Catani, 2006, 2007). These data support a representation of brain organization and lesion effects in terms of wide cortico-subcortical-cortical networks rather than in specialized frontal cortical areas. The areas belonging to the same networks can be disturbed by a localized lesion, regardless of the specialized role of individual brain centers in some functions (e.g., language, memory, attention).

In cases of World Health Organization Grade II glioma (LGG) surgery, frontal lobectomy does not cause “frontal syndrome” (Bonnetblanc, Desmurget, & Duffau, 2006; Duffau, Capelle, & Denvil, Sichez, Gatignol, Taillandier, et al., 2003). As these low-growth tumors slowly infiltrate brain areas, they permit plasticity and functional reshaping of the brain to neutralize infiltration effects (Duffau, 2005). To exert efficient compensatory mechanisms, the brain progressively recruits regions near the lesion or in the contralateral hemisphere and activates neural networks in vertical (cortical-subcortical) and horizontal (crosscortical) axes (Desmurget, Bonnetblanc, & Duffau, 2007). Thus, the tumor resection ultimately affects functionally silent areas (Duffau, Capelle, Denvil, Sichez, Gatignol, Lopes, et al., 2003). We sought to evaluate how the brain functions in the presence of two frontal gliomas that affect both hemispheres and reacts to a bilateral resection, which could brutally compromise the neuronal connectivity progressively established during the infiltrating process. Although cases of bilateral thalamic and temporal tumors are well documented, reported cases of resection orbito-frontal gliomas are rare. Turola et al. (2009) reported the case of a 43-year-old woman who had an initial isolated epileptic seizure and subsequent psychiatric symptoms. Magnetic resonance imaging (MRI) showed a bi-frontal Grade IV glioma (large in the right frontal lobe, smaller in the left) associated with apathy, psychomotor slowdown, apraxia and expressive aphasia. The neurosurgeons performed sequential surgical removal of the left and right tumors, and the patient benefitted from radiotherapy. Histological examination demonstrated the presence of a grade IV glioblastoma. Two months later, the patient was able to perform her daily life activities with only mild dysphoria.

In this paper, we report the longitudinal case study of a patient harboring two frontal tumors that benefited from bilateral simultaneous surgery. The tumors were Grade II gliomas (oligodendrogliomas) infiltrating the two frontal lobes; more precisely, these tumors were located in the left inferior frontal area, including the cingulate gyrus and the right anterior superior frontal gyrus. The anterior region of the cingulate gyrus has been implicated in several processes: its medial region has been implicated in response selection, its restrosplenial region has been implicated in memories access, and its posterior region has been implicated in visual-spatial processing (Vogt, 2009). The *pars opercularis* (Brodmann's area 44), *triangularis* (area 45), and *orbitaris* (area 47) of the left inferior frontal gyrus are implicated in verbal working memory (and thus sentence processing), word selection, and articulation (Friederici, 2006). The right superior frontal gyrus, including both dorsal and orbital segments, has an important role in the bilateral control of complex movements, bimanual coordination (Martino et al., 2011; Peraud, Meschede, Eisner, Ilmberger, & Reulen, 2002), and language planning when a left tumor infiltrates this zone in right-handed patients (Duffau, Capelle, Denvil, Sichez, Gatignol, Lopes, et al., 2003).

Although the tumors affected our patients' "eloquent" brain areas, notably responsible for language, motor, executive, social, and emotional skills, the patient did not show deficiencies during the pre-operative neuropsychological assessment, except for fine-grain language, memory, and emotion skills. Two months after the bilateral tumor resection, a similar syntactic impairment was observed, coupled with focal slowness during some tasks—a known effect of the surgery—and mild motor deficits. Through the longitudinal study of the patient's evolution (in the pre-, per-, and postoperative sessions) we explain why and how, in spite of a bilateral frontal lesion, no "frontal syndrome" was observed.

CASE REPORT

The patient, Mr. X. B., was a right-handed 34year-old urbanism project manager. He obtained a vocational training certificate at secondary school, and a certificate of competency (14 years of education). He was married and had two young children. He began rugby when he was 5 years old and had several trainings per week. In June 2010, during training, he suffered from epileptic seizures that started with motor and speech symptoms and then became generalized. The MRI showed two frontal bilateral tumors. In previous years, the patient never experienced any cognitive or mood change; he reported tiredness at the end of the afternoon, which increased after anti-epileptic treatment administration. Thus, he needed to sleep 20 minutes every day. In our experience, such complaint of tiredness is frequent and seems to be a sign (sometimes the single sign) of illness. During his four seizures, which appeared only during physical activity, motor signs were predominant; the right arm raised and bended, speech was blocked, and a general stiffness preceded convulsion.

The patient underwent neurological examination, sequential MRI, and neuropsychological examination, with a delay of 5 months between the two assessments. Two neuropsychologists of the team administered the neuropsychological evaluation pre-operatively and post-operatively. The evaluation included tasks assessing global cognitive efficiency, memory skills (episodic memory, working memory), executive and emotion processing, attention and visuo-constructive capacities, lexical access, and productive/expressive syntactic skills. The patient was expected to benefit from a double tumor resection while awake. The surgery aimed to remove the two tumors as completely as possible, and to prevent severe neurological deficits by respecting the elicited positive motor, cognitive, and language areas. Tasks requiring executive, language, and motor skills were administered during the awaked phase.

NEUROPSYCHOLOGICAL ASSESSMENTS BEFORE AND AFTER SURGERY

Pre-operative session

The *global cognitive functioning* assessed with the *Montreal Cognitive Assessment* (*MoCA*; Nasreddine et al., 2005) was average (26/30). Naming, memory, attention, language, abstraction, and orientation were within the normal range, but slight deficiencies appeared in the visual-spatial executive domain (only 4/12 digits were noted on the clock), language (phonemic fluency was restricted to 10 words), abstraction (in the Similarities subtest, the patient did not find the similarity between a watch and a ruler), and memory (he only recalled 4/5 words after a 5-minutes delay). (Table 1)

Language

Spontaneous speech was fluent, coherent, and informative. Word repetition (*Boston Diagnostic Aphasia Examination BDAE*, Mazaux & Orgogozo, 1982) and the *Dénomination 70* (*DO-70*; Petit & Wikramaratna, 2011) and *Dénomination 80* (*DO80*; Deloche & Hannequin, 1997) picture-naming tasks were efficient. The patient spontaneously corrected one naming error (he said “meuble” (“*furniture*”) for “commode” (“*chest of drawers*”)) and produced one perseveration. Written language was correct in the word graphic evocation subtest (*BDAE*, Mazaux & Orgogozo, 1982) and in the *E.Co.S.Se* test (Lecocq, 1996), which requires reading aloud sentences of diverse morphosyntactic complexity.

Oral language comprehension was average in the *Token Test* (De Renzi & Vignolo, 1962) and disturbed in the *E.Co.S.Se* test. The patient was unable to understand relative and embedded sentences, spatial prepositions, and numeral ordinal adjectives. In parallel, he made errors in a morphosyntactic productive test (*Test d’expression morphosyntaxique fineTEMf* ; Bernaert-Paul & Simonin, 2011), which requires producing sentences by matching photographs with given words used in an obligatory presentation order (e.g., “fille – prend – photo”, “*girl – takes – photo*”). The patient could not produce relative sentences with an object and a subject, passive dative sentences, and did not use the correct prepositions.

Memory

Working memory was first assessed with the *Reading span test* (Desmette, Hupet, Schelstraete, & Van Der Linden, 1995), which requires reading aloud a series of sentences before recalling the last word of each sentence; the patient efficiently recalled four elements in order. In the second test, *Letter Digit Sequences*, which requires ordering letters and digits (Wechsler, 2001), he obtained an average standard score (9).

Episodic verbal memory was assessed with the *Hopkins Verbal Learning Test (HVLT*; Rieu, Bachoud-Lévi, Laurent, Jurion, & DallaBarba, 2006). The patient had to learn a list of 12 orally presented words and was then asked to recall them immediately (three trials) and 20 minutes later. Finally, he had to recognize the words mixed with distracters. The patient correctly performed the task (FR 1: 8, FR 2: 10, FR 3: 10, and DLR: 9). Encoding, storage, and recall were good. However, one intrusion error was observed in both free recall and later recall, and the patient produced four perseverations (three during the free recall and one in later recall), which suggests inhibition deficiencies. Moreover, the identification of words among distracters was slightly weak, which suggests consolidation vulnerability.

Episodic visual-spatial memory was assessed with the *10/36 Test* (Dujardin, Sockeel, Cabaret, De Sèze, & Vermersch, 2004), which includes a learning phase of 3 trials (consisting of memorizing the location of 10 stimuli presented during 10 seconds and recalling their location 7 minutes after presentation). The score was weak for the first trial (2/10), but maximal for the second trial. The learning score and the long-term recall (10/10) were average.

Executive processing and attention

The *Stroop test* (Golden, 1978) was average in each condition. The *Trail Making Test* (*TMT*; Reitan & Wolfson, 1995) was average in both conditions A and B. In the two

Verbal Fluency tasks (Cardebat, Doyon, Puel, Goulet, & Joanette, 1990), the patient showed mild lexical evocation difficulty. He showed a 10 second delay during the semantic fluency task (with animals), which suggests verbal initiation latency. His orthographic fluency (with the letter P) was better, but the patient made two perseverations. The patient had average performances in the two tasks of the *Test d'Evaluation de l'Attention* (*TEA*; Zimmermann & Fimm, 1994), i.e., the *Divided Attention task*, which requires processing simultaneous visual and auditory stimuli, and the *Phasic Attention task* of the TEA, which requires quickly detecting visual stimuli with and without an auditory signal.

Visuo-spatial perception

The patient performed excellently on the three tasks of the *Visual Object and Space Perception battery* (Warrington & James, 1991), which require detecting partially masked letters and analyzing cubes, and on the *Beery Visual-Motor-Integration test* (*VMI*; Beery & Beery, 2006), which requires copying gradually complex forms.

Emotional processing

The patient was administered three experimental tasks (Du Boullay, Plaza, Capelle, & Chaby, 2013) that require identifying emotions (neutral, joy, anger, fear, sadness, and disgust) in visual (emotional faces from KDEF; Lundqvist, Flykt, & Ohman, 1998), auditory (emotional voices from Belin database; Belin, Fillion-Bilodeau, & Gosselin, 2008) and cross-modal (faces/voices) conditions. The patient's visual identification of disgust (70%) and his auditory identification of joy (90%) were slightly weak. The reaction times were slow in all conditions for all emotions, but were significantly impaired for joy in all conditions, vocal anger, and all cross-modal emotions. The patient did not show depression or anxiety as assessed by the *Beck Depression Inventory-II* (*BDIII*; Beck, Steer, & Brown, 1996) scale of depression and the *State and Trait Anxiety Inventory* (*STAI*; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1993), respectively.

Per-operative session

A bi-frontal cranial aperture was performed, allowing observation of the right lesion (specific color and tumefaction of the posterior and median F1). The electrical stimulations of the right F1 and F2 elicited finger, hand, and arm motor reactions. More deep stimulation elicited leg, tongue, and hand reactions and language suspension. These reactions allowed the mapping of sensory-motor functions, determining and delimiting the eloquent and functional zones to be spared. Picture naming tests (DO 70; DO 80) were administered to control language production, and the Stroop and Go No Go Tests to control executive processing. A double task (requiring both naming pictures and moving the arm) allowed the controlling of bimodal activity. These tests were repeated during the time of resection (2 hours). Mr X.B. did not show any difficulties.

The resection concerned F1 and F2 and spared the posterior internal region to avoid a supplementary motor area syndrome. On the left side, the resection concerned the internal and anterior part of the frontal lobe, including the corpus callosum. The left lesion volume in area 32 was 4.9 cc before resection and 0.8 cc after resection; the right lesion volume in areas 8/9 was 8.8 cc before resection and 0 cc after resection. During the 14 months preceding surgery, similar spontaneous growth rates were observed for both tumors (2.4 mm mean tumor diameter/year). **Figure 1** shows the fMRI images of the tumors before resection.

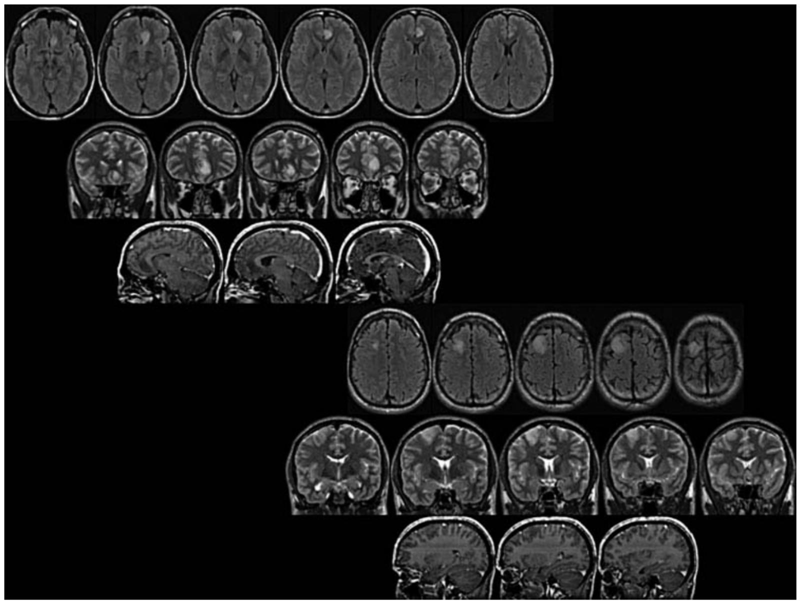

Figure 1. Pre-operative magnetic resonance images of the left (upper) and right (lower) frontal tumors: axial fluid-attenuation inversion recovery, coronal T2-weighted and T1-weighted (after contrast injection) images.

Post-surgical session

Because the patient had bilateral frontal lesions and benefitted from bilateral resection, the post-surgical assessment (realized 64 days after resection) included the tasks administered in the pre-operative session and novel tasks concerning working memory, flexibility, planning, and praxis. The patient reported that, during 2 weeks after surgery, he had difficulty producing appropriate emotions in daily life. He could recognize the facial emotions of others, but his own emotional expressions were not appropriate (e.g., he laughed in sad situations). Thus, he benefitted from cognitive remediation, administered by a neuropsychologist outside the hospital. They worked together on emotion facial recognition from photography, before linking other's emotion identification and the patient's emotional expression.

Global cognitive functioning was average (27/30) in the *MoCA*. However, slight deficiencies were observed in visual-spatial executive skills (hour and minute hands of the clock were not correctly situated, and the patient added the hours before the clock outline), language (he only produced seven words during the orthographic fluency task) and memory (he recalled 4/5 words 5 minutes after presentation). (Table 1)

Language

Spontaneous language was fluent, coherent, and informative. Picture naming was accurate and fast in the *DO-80* and *DO-70* (such as word repetition of *BDAE* and comprehension of sentences in the *Token Test).* In contrast, the patient had difficulty producing the relative sentences subject/object in the *TEMf* ("la femme qui a un bandeau lit", "the woman who has an headband is reading") and object/subject ("les fleurs que cueille la femme sont belles", "the flowers that the woman is picking are beautiful") and he was slow (11 mn 22 sec) in the *E.Co.S.Se*, in which he made errors understanding relative and embedded sentences, although he read the sentences aloud. Written language was normal in both the reading and spelling tasks of *BDAE*.

Memory

Episodic verbal memory skills were excellent in the *HVLT*, with a maximal score in each trial (12/12). Episodic visual memory was slightly weak in *Rey Figure reproduction* (Form 2), with omission and imprecise reproduction of elements (49/72, C25). Time processing was slow (243 sec, C75–C90), and strategy was efficient. Working memory was efficient in *Digit span* (NS = 13) (Wechsler, 2001) and limited in *Letter-Digit Sequence* (NS = 9). The patient used a phonological loop, needing a delay between trials, because the digits sounded in his head, the latter interfering with the former.

Executive processing and attention

Executive functioning was variable. The *Batterie Rapide d'Efficience Frontale* (*BREF* ; Dubois, Slachevesky, Litvan, & Pillon, 2000), which includes semantic similarities, lexical evocation, motor sequences, conflictual sequences, and Go/No Go, was administered to complement the *MoCA*. The patient obtained an average score (17/18), with a mild deficiency in fluency. A novel version of the *Stroop Test* was administered (Chatelois, 1993), including a fourth flexibility condition (reading words or naming their colors); the patient struggled with this task. The patient showed greater deficiency in the B-condition (alternating digits and letters) of the *TMT* test than he did before surgery (TMT-B: 141 sec). The patient did not correctly seriate both letters and digits. The verbal fluency tasks were slightly restricted (16 words, with a phonemic constraint and 28 with a semantic constraint). A 5-second delay was observed, suggesting initiation latencies. Attention was assessed with two novel tasks, the sustained visual attention *Test D2* (Brickenkamp, 1998) and the sustained auditory attention test Paced Auditory Serial Addition Task (*PASAT*; Naegele & Mazza, 2003). The patient showed global accuracy during *D2*, but he omitted one line and did not select all cues (the letter/d/) at the end of the test, saying "I don't see anything, there are/d/everywhere." During the *PASAT*, he committed one addition, four omissions, and three telescoping errors.

Visuo-spatial perception

The visual-spatial constructive skill was assessed with the *Figure de Rey* Copy (Wallon & Mesmin, 2009). The patient's performance was low (69/72 < C2) and slow. In fact, X.

B. used a good planning strategy, but a gestural imprecision did not allow him to control figure realization. Praxis, assessed with gesture imitation and production of gesture sequences, were in the normal range.

Emotional processing

Emotion identification was accurate for all emotions in each condition. The reaction times were slow in all conditions and for all emotions, especially for joy and cross-modal processing. The patient did not show depression or anxiety, as measured by the *Beck Depression* (*BDI-II*) and anxiety (*STAI*) scales. Table 1 (pre and postoperative neuropsychological assessments) summarizes the patient's results.

DISCUSSION

We reported the case study of a patient who suffered from two bilateral frontal gliomas and who was administered various neuropsychological and language tasks preand post-operatively. Damage to the frontal lobes can cause a variety of symptoms, including those affecting attention and concentration, mental flexibility and spontaneity, language production and reception, speech, perceptions regarding risk-taking and rule abiding, socialization, sexual habits and interest, creativity and problem solving skills, and also integration of olfactory perceptual evidence (e.g., Bowman, Kording, & Gottfried, 2012). However, in cases of slow-growth tumors, the brain is able to compensate for cell infiltration using plasticity and connectivity mechanisms, which can prevent a frontal lesion from causing frontal lesion and frontal/dysexecutive syndrome. We questioned whether such documented compensatory mechanisms are also present in cases of bilateral frontal gliomas and bilateral simultaneous resection.

BRAIN PLASTICITY IN BILATERAL LESIONS

LGGs are the most common slow-growth cerebral tumors. They often occur in young people (medial age: 35 years) and systematically evolve into high-grade gliomas, with a median of approximately 7–8 years for anaplastic transformation. Surgery prevents the progression of LGG to a malignant and eventually fatal form (Bonnetblanc et al., 2006). The slow progression of LGG triggers a large functional reorganization within cerebral structures. The following three parameters may enable cerebral plasticity and efficient reorganization in LGG: (1) the intervention of crucial subcortical connectivity (lesions of the white matter tracts may result in cognitive impairments); (2) the timing of the lesion, although compensatory mechanisms could be more efficient in cases of slow-growth tumors than in acute lesions such as strokes; and (3) plasticity affects complex functions (language, memory, and emotion) more than sensorymotor functions most likely because of their respective maturation course. Brain plasticity can be induced pre-operatively by progressive tumor growth, and the surgical act itself might contribute to functional remapping post-operatively. The mechanism leading to neuronal reorganization is partially intralesional, depending on the recruitment of perilesional and ipsi-hemispheric regions and recruitment from contralesional homologous areas (Bonnetblanc et al., 2006; Duffau, 2012).

The processes of slow tumor infiltration and brain reorganization explain why the presence of LGG within *one* frontal lobe, even if it is located in “eloquent” areas, does not lead to the severe impairments predicted by the localization models that assign a significant role in language and cognitive processing to the left frontal lobe, notably Broca’s area. Duffau, Capelle, Denvil, Sichez, Gatignol, Lopes, et al. (2003), Duffau, Capelle, Denvil, Gatignol, et al. (2003), Duffau, Capelle, Denvil, Sichez, Gatignol, Taillandier, et al. (2003), and Duffau, Gatignol, Mandonnet, Capelle, and Taillandier (2008) reported numerous cases of patients with low-grade gliomas located in the left dominant frontal lobe near or within the premotor cortex (PMC). Pre-operative language testing was normal in the majority of these cases. Plaza, Gatignol, Leroy, and Duffau (2009) described, in a case report, that Broca’s area can be removed without inducing a language disorder. However, a subtle fragility was observed in the patient’s language ability to construct relative clauses, which is related to minor working memory deficits. Together, these results confirm the efficient intervention of compensatory mechanisms in cases of slow-growth tumors.

In our case study, preand post-operative assessments revealed efficient cognitive skills, suggesting that plasticity and changes in connectivity occurred despite *bilateral* lesions. Neuronal connectivity can be progressively established during the infiltrating process of the two frontal gliomas, and the bilateral simultaneous resection did not compromise these compensatory mechanisms.

BI-FRONTAL LESION WITHOUT “FRONTAL SYNDROME”?

Before surgery, XB had a normal life without cognitive or mood dysfunction. Neither “dysexecutive syndrome” nor “frontal syndrome” was found during the pre-operative neuropsychological assessment. After resection of the two gliomas, XB was able to return to a normal social and professional life, without permanent post-surgical deficits. Language, cognitive, and emotional assessments were quite similar to the pre-operative assessments. These results suggest, in accordance with a plastic and dynamic view of brain organization, that extensive *bilateral* frontal gliomas can occur without generating a “frontal syndrome” and that their bilateral resection does not induce a “frontal syndrome”. Duffau (2012) has described mild or absent “frontal symptoms” in cases of unilateral frontal gliomas. Our observation shows that *bilateral* frontal gliomas can occur without generating a “frontal syndrome”.

ROLE OF FRONTAL AREAS IN THE MINOR DEFICIENCIES OF PATIENT XB

Although the patient’s neuropsychological assessment was globally normal, slight and fine-grain impairments were observed in language, memory, and emotion processing. Notably, in pre-operative and post-operative assessments, lexical evocation was weak, productive and receptive morphosyntactic skill was slightly impaired and verbal episodic memory was fragile. Additionally, XB showed atypical difficulty in recognizing “joy”. Furthermore, perseverations were noted in the pre-operative assessment, and flexibility problems were observed in the post-operative assessment. Although slight, the patient's impairments appeared to be linked to the frontal tumor location.

XB's language impairments concerned lexical and syntactic skills, which recruit diverse frontal areas and networks, as shown by data from surgery under electrical stimulation (Duffau, Capelle, & Denvil, Gatignol, et al., 2003; Duffau, Capelle, Denvil, Sichez, Gatignol, Lopes, et al., 2003; Duffau, Capelle, Denvil, Sichez, Gatignol, Taillandier, et al., 2003; Kho et al., 2007; Tomasino, Werner, Weiss, & Fink, 2007; Vidorreta, Garcia, Moritz-Gasser, & Duffau, 2011) and neuroimaging (Fiebach & Friederici, 2004; Friederici, 2006; Inubushi, Iijima, Koizumi, & Sakai, 2012; Tyler & Marslen-Wilson, 2008; Vigneau, Beaucousin, & Herve, 2006).

In the post-operative session of the TMT B, which requires switching between letters and digits, the patient needed more time (141 sec) and he did not correctly order both letters and digits. This flexibility difficulty is often observed in individuals with frontal lobe damage (Baldo & Shimamura, 1998), when they are administered executive tests requiring judgment, inhibition, and cognitive flexibility, which activate prefrontal networks (e.g., Miyake, Friedman, Emerson, Witzki, & Howerter, 2000; Plaza, Gatignol, Cohen, Berger, & Duffau, 2007; Stemme, Deco, Busch, & Schneider, 2005).

Concerning emotion processing, XB did not recognize joy as easily as expected for his age. This atypical result could be linked to the fact that frontal areas are activated during facial emotional processing (Gunning-Dixon et al., 2003; Vytal & Hamann, 2010). Notably, in an audiovisual condition, joy induces specific activity in the superior frontal gyrus (BA8) and the middle frontal gyrus (BA46, 10 and 9) (Pourtois, de Gelder, Bol, & Crommelinck, 2005).

XB slowly processed all cross-modal emotions, which traditionally recruit the bilateral posterior superior temporal sulcus (STS) (Calvert, 2001; Campanella & Belin, 2007). The observed slowness did not appear as a *general* deleterious effect because his timed responses in picture naming*, TMT A, STROOP* words and colors, and the *Rey figure* copy were all average. It can be hypothesized that the patient was able to integrate emotional information between visual and auditory modalities, but did so more slowly. If STS plays a key role in the integration of audio-visual signals, then emotional face–voice integration is a complex process that recruits various brain regions. In an EEG study, Pourtois, Debatisse, Despland, and de Gelder (2002) found a contribution of the anterior cingulate cortex in face–voice pairing, at approximately 220 ms, and Peelen, Atkinson, and Vuillermier (2010) revealed that one of the two clusters that show significant supramodal emotion information is located in the rostral medial prefrontal cortex, MPFC.

Furthermore, cross-modal integration requires simultaneous perceptual information integration and cognitive voluntary control of interference. In an *f* MRI study, Heekeren, Marrett, Bandettini, and Ungerleider (2004) observed the recruitment of prefrontal regions (especially the left dorsolateral prefrontal cortex, DLPFC) in decision-making functions and in the planning of responses to environmental stimuli requiring multimodal information. Electrical stimulation of the DLPFC generates errors in incongruent visuo-verbal judgment (Plaza et al., 2007). In our paradigm, emotional pairs were congruent, and the patient made only one error in the pre-operative test and no error in post-operative test. XB was able to integrate emotional information between visual and auditory modalities, but did so more slowly than the controls. In accordance with the literature (Driver & Spence, 2000; Pourtois et al., 2002), we can hypothesize that regardless of whether the cross-modal processes sustained by STS (i.e., automatic and early auditory-visual integration and feedback toward unimodal sensory areas) were preserved, the decision-making process between the two modalities sustained by the frontal areas was disturbed and led to an increase in the response time.

After surgery, the response time increased in the cross-modal condition, as previously observed by du Boullay et al. (2013), which demonstrated that there was a weak benefit of cross-modality in GBG patients after surgery compared to controls.

CONCLUSION

The efficiency of most skills in our patient shows the significance of brain plasticity intervention in the reorganization of cognitive networks, also in cases of bilateral lesion, when the slow tumor development allows the brain to compensate for progressive cellular infiltration and cognitive alteration (De Benedictis & Duffau, 2011). The slight deficiencies observed in the patient confirm the relevance of hodotopical brain models, which consider the brain organized in parallel-distributed networks around cortical centers and epicenters (Catani et al., 2012). Finally, the case report confirms that the relationships between dysexecutive syndrome and frontal lesions are neither obligatory nor systematic.

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TABLE 1
Pre- and post-operative neuropsychological assessments

	Pre-operative session	*Post-operative session*
Global cognitive functioning		
MoCA	$26/Z = -.63$ Visuo-spatial/Executive: 4/5 Picture naming: 3/3 Attention: 6/6 Language: 2/3* *(Fluency: 10 words in 1 minute)* Abstraction: 1/2 Memory: 4/5 (Free recall: *4* words + *1 word with cueing help)* Orientation: 6/6	$27/Z = -.18$ Visuo-spatial/Executive: 4/5 Picture naming: 3/3 Attention: 6/6 Language: 2/3* *(Fluency: 7 words in 1 minute)* Abstraction: 2/2 Memory: 4/5 *(*Free recall*: 4* words + *1 word with cueing help)* Orientation: 6/6
Language		
Picture naming DO-80	$79/Z = +.25$	$79/Z = +.25$
Picture naming DO-70	$69/Z = +.08$	$68/Z = -.751$ min $54/Z = +1.81$
E.Co.S.Se (Reading and comprehension of sentences)	86/92* 8 min 40	87/92* 11 min 22
TEMf Oral production of sentences	Active sentences: 15/15, percentile 90 Passive sentences: 15/15, percentile 90 Dative sentences: 9/10, $Z = -8.25$* Dative passive sentences: 15/20, $Z = -14$* Relative subject/objectsentences: 25/25, $Z = +.31$ Relative object/subjectsentences: 9/30, $Z = -3.60$*	Active sentences: 15/15, percentile 90 Passive sentences: 15/15, percentile 90 Datives entences: 10/10, $Z = +.08$ Dative passive sentences: 20/20, $Z = +.28$ Relative subject/objectsentences: 17/25, $Z = -2.66$* Relative object/subjectsentences: 9/30, $Z = -3.60$*
BDAE word repetition task	$10/Z = +.86$	$10/Z = +.86$
BDAE word reading task	$30/Z = +1.02$	$29/Z = +.93$
BDAE word spelling task	$10/Z = +1.36$	$9/Z = +1.1$
Token test	$36/Z = +1.29$	$36/Z = +1.29$
Executive processing		
FAB		$17/18/Z = -.37$ Similarities: 3/3 Lexical fluency: 2/3* *(9 words in 1 minute)* Motor sequences: 3/3 Conflicting rules: 3/3 Go No Go: 3/3 Gripingbehavior: 3/3
TMT-A	26 sec$/Z = -.25$	23 sec$/Z = +.5$
TMT-B	58 sec$/Z = +.09$	141 sec$/Z = -3.68$* 1 error$/Z = -3.41$*
TMT B – A	32 sec/OK	118 sec/> 70sec*
Stroop color	$T = 51/Z = +.1$	$T = 36/Z = -1.4$
Stroop word	$T = 49/Z = -.1$	$T = 45/Z = -.5$
Stroop inhibition	$T = 57/Z = +.7$	$T = 47/Z = -.3$
Stroop flexibility		$Z = -1.8$* 3 corrected color errors, $Z = -.47$
Lexical fluency «P»	$19/Z = -.75$ (percentile 25) 1 perseveration	$16/Z = -1.21$(percentile 10–25)
Semantic fluency *« Animals »*	$26/Z = -1$ (percentile 10–25)	$28/Z = -.75$ (percentile 25)
Attention		
TEA phasic alertness (without alert)	Percentile 43	

	Pre-operative session	*Post-operative session*
TEA phasic alertness (with alert)	Percentile 42	
TEA phasic alertness (Alert index)	Percentile 42	
TEA Vis. divided attention	Percentile 60	
TEA Audit. divided attention	Percentile 43	
TEA Vis. + Audit. divided attention	Percentile 43	
Visual attention		
D2 rapidity		Percentile 46
D2 precision		Percentile 50–75
D2 regularity		Percentile 50–75
D2 concentration		Percentile 54
Auditive attention		
PASAT total correct responses		52 (percentile 10–25) Part 1: 3 errors/$Z = -.8$ Part 2: 2 errors/$Z = -.1$ Part3: 3 errors/$Z = -.8$
PASAT telescoping errors		$3/Z = -1.3$
PASAT calculation errors		$1/Z = +.1$
PASAT no-response		$4/Z = -.4$
Working memory		
Digit span		SS = 13 Forward span = 7 Reward span = 5
Letter digit sequence	SS = 9	SS = 9
Reading span	Recall: 4 words in order	
Episodic verbal memory		
HVLT free recall 1	$8/Z = +.79$	$12/Z = +3.8$
HVLT free recall 2	10/OK	$12/Z = +1.4$
HVLT free recall 3	$10/Z = -.8$ (1 intrusion: "lynx")	$12/Z = +1.2$
HVLT learning score	$28/Z = +.06$	$36/Z = +2.6$
HVLT delayed recall	$9/Z = -.70$ (1 intrusion: "lynx")	$12/Z = +1$
HVLT recognition	$11/Z = -1.45$	$12/Z = +.4$
Episodic visual memory		
10/36 Free recall 1	2	
10/36 Free recall 2	10	
10/36 Free recall 3	10	
10/36 learning score	$22/Z = +.70$	
10/36 Delayed recall	$10/Z = +1.18$	
Rey figure (Recall)		49/percentile 25 243 sec/percentile 75–90 Type I
Visuo-spatial perception		
VOSP forms	$20/Z = +.24$	
VOSP uncompleted letters	$20/Z = +.87$	
VOSP cubes	$10/Z = +.58$	
Rey figure (Copy)		69/< percentile 2* 100 sec/percentile 5–10 Type I
Emotions		
Faces	Sadness 80% ($Z = -.57$) Anger 100% Disgust 70% ($Z = -.69$) Neutral 100% Happiness 100% Fear 100%	Sadness 80% ($Z = -.57$) Anger 90% ($Z = +.25$) Disgust 70% ($Z = -.69$) Neutral 100% Happiness 100% Fear 90% ($Z = +.35$)

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	Pre-operative session	*Post-operative session*
Voices	S 100%	S 100%
	A 80% ($Z = +1.36$)	A 90% ($Z = +1.99$)
	D 100%	D 100%
	N 100%	N 100%
	H 90% ($Z = -2.58$)*	H 100%
	F 90% ($Z = +.52$)	F 80% ($Z = -.12$)
Faces/Voices	S 100%	S 100%
	A 90% ($Z = +.68$)	A 100%
	D 100%	D 100%
	N 100%	N 100%
	H 100%	H 100%
	F 100%	F 100%
Questionnaire		
Mac Nair Khan	$19/Z = +1.13$	$22/Z = +.9$
STAI-Form Y		
State	T = 35 (very low)	T = 35 (very low)
Character trait	T = 35 (very low)	T = 32 (very low)
BDI-II	1 (no depression)	1 (no depression)

*Significant difference in average scores; SS = Standard score; $Z < -1.65$ or score < C5: Pathological score.