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Dyslipidemia among patients with type 2 diabetes mellitus visiting Specialized Center for Diabetes and Endocrinology

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ARTICLE INFORMATION

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ABSTRACT

Background: The most common pattern of dyslipidemia in diabetic patients is increased triglyceride (TG) and decreased HDL cholesterol level, The concentration of LDL cholesterol in diabetic patients is usually not significantly different from non diabetic individuals,
Diabetic patients may have elevated levels of non-HDL cholesterol [LDL+VLDL]. However type 2 diabetic patients typically have apreponderance of smaller ,denser LDL particles which possibly increases atherogenicity even if the absolute concentration of LDL cholesterol is not significantly increased. The Third Adult Treatment Panel of the National Cholesterol Education Program (NCEP III) and the American Heart Association (AHA) have designate diabetes as a coronary heart disease (CHD) equivalent and recommended treatment of LDL-c to < 2.6 mmol\l (<100 mgldl)

Objectives: We assessed the treatment ,type and control of dyslipidemia among adults with diabetes mellitus.

Methods: This is a prospective study conducted in the Neurosurgical Hospital in Baghdad, Iraq, during the period from January 1999 to January 2001. Any patient admitted during the period of the study with clinical history, signs, symptoms, and contrast enhanced MRI suggesting a cerebral glioma and confirmed by postoperative histopathological results of glioma has been included in this study. While multifocal lesions, long-lasting epilepsy, use of antiepileptic therapy, multiple cranial lesions, previous cranial surgery, any chronic illness, and histopathological result of other tumors were exclusion criteria. All patients were at their first operation for brain tumors. Patients were examined by analyzing several functional domains (intelligence, executive functions, memory, language, praxis, gnosis and mood state) in order to establish the effect of tumor and surgery on cognition.

Results:29 patients who fulfilled the selection criteria were included. Mean duration of clinical history was 5 months (range 1-9 months). At baseline, using test- and domain-based criteria, 79% and 38% of patients, respectively, were impaired, the former related to tumor factors such as edema (P <0.05), larger size (P <0.05) and higher grade (P = 0.001). Verbal memory, visuospatial memory and word fluency were the most frequently affected functions, partly associated with depression. Postoperatively, 38% and 55% of patients, respectively, were unchanged, 24% and 21% improved, and 38% and 24% worsened; 24% and 62% of patients were intact, respectively.

Conclusions: The extent of removal did not influence the outcome. Improvement involved previously impaired functions and was correlated with high-grade tumors. Worsening regarded executive functions was related to tumor size and was partly explained by radiological findings on postoperative MRI. This prospective study, focusing on the effects of tumor and surgery, showed that tumor significantly affects cognitive functions, mainly due to the mass effect and higher grading. Surgical treatment improved the functions most frequently affected preoperatively and caused worsening of executive functions soon after operation, leaving the overall cognitive burden unchanged and capable of improvement prospectively.

Introduction:

In recent years, there has been a reappraisal of the clinical setting in brain tumors, after a transient decrease in interest. This reassessment is due to a number of factors such as the possibility of matching deficits to location according to an increasing number of techniques, the possibility of intraoperative clinical monitoring while the patient is awake, and the central role that quality of life (QOL) plays in any treatment choice.

In neurosurgery, for the purposes of obtaining subclinical and objective data, a neuropsychological approach has been widely advocated, but then, unlike the trend in epilepsy surgery, this has been substantially neglected[1]. Preoperative general neuropsychological assessment has seldom been reported, while specific assessment (i.e. language) has been applied only to awake surgery. Postoperatively, clinical settings were even more heterogeneous and neuropsychological evaluation exceptional [2]. Nevertheless, evidence is now emerging to strengthen the rationale for such assessment.

The need for adequate perioperative evaluation to properly interpret follow-up studies has been reinforced by the importance of cognitive assessment for rehabilitation programs and by their significant impact on prognosis [3,4].

Besides the improvements in surgical technique, a great deal of effort has focused on highlighting glioma margins well beyond direct visual impressions in an attempt to improve the quality of resection. Information on tumor extent, acquired both before (MRI, spectroscopy.) and during operation (5-aminolevulinic acid, 5-ALA), has led to larger resection volumes, endangering functioning brain which may be either mixed with the tumor in low-grade variants, or impinged upon by the tumor at its margins in high-grade variants [5].

Awake surgery and non-invasive brain mapping have stimulated translational research in an attempt to properly investigate the brain before resection in individual patients. On moving from intraoperative naming-assisted surgical resection to other language and cognitive tasks, while a multi-staged system of evidence is still needed to control all variables, patient safety must be guaranteed by accurate pre- and postoperative comparative assessment.

Methods:

This study is a prospective study conducted in the neurosurgical hospital in Baghdad, Iraq, during the period from January 1999 to January 2001. Any patient admitted during the period of the study with clinical history, signs, symptoms, and contrast enhanced MRI suggesting a cerebral glioma and confirmed by postoperative histopathological results of glioma has been included in this study. While multifocal lesions, long-lasting epilepsy and/or use of antiepileptic therapy, multiple cranial lesions, previous cranial surgery, any chronic illness, and histopathological result of other tumors (not glioma) were exclusion criteria. All patients were at their first operation for brain tumors. In no case could medical diseases have endangered the operation, as established by preoperative anaesthesiological evaluations. Extent of removal was classified on the basis of postoperative contrast enhanced MRI. Gross total removal was indicated by the absence of either contrast enhancement or hyperintensity on T2-weighted images, depending on how the tumor was documented preoperatively. Subtotal removal was indicated by any residual mass. Postoperative MRI (T1-weighted enhanced, T2-weighted and diffusion) was performed in all cases within the first post-operative week in order to determine the extent of removal and possible additional brain injuries (increased edema or ischemia).

The only pharmacological treatment implemented was corticosteroid therapy (dexamethasone, no more than 16 mg/day). Antiepileptic drugs (carbamazepine) were started as prophylaxis before surgery.

All patients underwent a comprehensive battery of neuropsychological tests consisting in measures of intellectual functions, executive functions, memory, language, praxis, gnosis and mood state for depression and anxiety. Each test was administered using standard procedures and instructions (Table 1). In order to maintain physical comfort while preserving the integrity of the information obtained, the assessment was accomplished in two or three sessions over a period ranging from 1 to 5 days. To avoid the practice effect between pre- and postoperative testing, two different versions of the same cognitive tests were performed. This was not possible only in the case of the Raven test. However, given that we did not provide any feedback on performance and that the test-retest reliability of the Raven test is very high (0.70-0.80), we believe that a practice effect is very unlikely. The postoperative tests were performed in a time window ranging from 3 to 7 days.

Mood variables of patients (depression and anxiety symptoms) were evaluated for two main purposes: first to check the validity of cognitive tests (a highly anxious state or depressive symptoms can reduce the performance at neuropsychological evaluation) and second to establish the patient's psychological characteristics using the Beck Depression Inventory and the State-Trait Anxiety Inventory (STAI) [6,7]. In order to determine the patient's neuropsychological disability (functional impairment), patient data were analyzed by means of two criteria, namely patient performance in each single test, and patient performance in conceptualized neuropsychological domains, including intelligence, executive functions, memory, language, praxis and gnosis (Table 1).

Table 1: Cognitive tests and Psychological questionnaires.

A: Cognitive tests.

Neuropsychological Domains	Neuropsychological Tests
Handedness dominance	Edinburgh Handedness Inventory (EHI) [8]
Intelligence	Raven Colored Matrix (Raven 47)[9]
Executive functions	Word fluency (FAS) [10] Trail Making Test (TMT-A e B)[10]
Memory	Verbal Digit Span (Span) [9] 15 Rey-Osterrieth Word List, immediate recall (ROWL, DR) [9] 15 Rey-Osterrieth Word List, delayed recall (ROWL, DR) [9] Spatial Supraspan Learning (TAS)[11] Rey-Osterrieth Complex Figure (ROCF) [12]
Language	Visual Object Naming (VON) [13]
Praxis	Copy design [11] Limb praxis [11] Orofacial praxis [11]

Gnosis	Body Part Dnomination (BPD) [14] Finger Denomination (FD) [14]

B: Psychological questionnaires.

Affective State	Psychological Questionnaires
Depression	Back Depression Inventory (BDI)[6]
Anxiety	State and Trait of Anxiety Inventory (STAI State and Trait) [7]

Neuropsychological disability was established when at least one test or domain was indicative of impairment. A test was considered impaired if the test score was below a cut-off determined on the basis of results obtained in a sample of normal subjects, adjusted according to age, sex and education, in relation to published Italian normative data [8-14].

In order to analyze the neuropsychological domain results, the scores on each selected test for a certain domain were transformed into z-scores according to the mean and standard deviation (SD) of normative data for each specific test. Thus, the score for each of the six domains obtained was the result of the mean of the z-scores for the tests included in a particular domain. A domain was considered impaired if the mean z-score was higher than ±2 SD. Each test or domain was entered in only one paired comparison, resulting in an independent comparison for all, which is why the Bonferroni procedure was not applied.

Patient characteristics and quality of variations between ratings before and after surgery were described in terms of affective and neuropsychological criteria as follows:

1. On the basis of their performance before surgery, patients were divided into two groups: normal versus impaired. The X^2 test was used to analyze differences between groups according to the demographic and tumor variables (age, sex, tumor location, side, histology, edema, size); $P \leq 0.05$ was considered significant;
2. Surgical results were evaluated considering both differences in mean postoperative scores for each neuropsychological measure (test and domain), and improved or worsened patients (Wilcoxon rank-sum test, $P \leq 0.05$). Both improved and worsened patients were then further analyzed according to the demographic, tumor and treatment variables and neuropsychological performance (tests or domains) (X^2, $P \leq 0.05$).
3. In order to rule out any impact of depression and anxiety on the neuropsychological tests, a series of multiple regressions was performed.

Follow-up data were assessed whenever possible 2-3 months postoperatively, using the same evaluation criteria, in patients who did not undergo radiotherapy or chemotherapy.

Results:

During the period of the study, 29 patients were included, who fulfilled the selection criteria. Mean duration of clinical history was 5 months (range 1-9 months). Demographic data and presentingsymptoms are presented in Table 2.

Table 2: Demographic data, clinical variables and presentingsymptoms.

A: presenting symptoms.

Symptom	Patients No. (%)
Headache	4 (14)
Personality change	3 (10)
Confusion	3 (10)
Hyposthenia	3 (10)
Visual disturbance	3 (10)
Dysphasia	2 (7)
Dysphagia	2 (7)
Somatic dysaesthesia	2 (7)

B: Demographic and clinical variables.

Variables		Patients No. (%)
Age (years)	<65	20 (68)
	≥65	9 (32)
Gender	Male	18 (62)
	Female	11 (38)
Histopathology	High grade	17 (58)
	Low grade	12 (42)
Side	Right	13 (45)
	Left	16 (55)
Location	Frontal	11 (38)
	Temporal	7 (24)
	Parieto-occipital	11 (38)
Size (cm)	≤ 3.5	17 (58)
	> 3.5	12 (42)
Edema	Yes	21 (72)
	No	8 (28)
Removal	Gross total	19 (65)
	Subtotal	10 (35)

Affective characteristics:

Outof 29 patients, 8 (28%) complained of depressive mood before surgery, and this state did not change after treatment; 4 patients (14%) presented anxiety before surgery, which decreased to 3 patients (10%) after the operation. On comparing pre- and postoperative mean scores, there were no significant changes in depression ($z = -0.75$, N.S.), while anxiety scores decreased significantly ($z = -2.38$, $P = 0.01$) (Table 3).

Table 3: Time course of patients according to mood disorders.

Questionnaires	BDI	STAI-Y state
Preoperative impaired patients	8	4

Postoperative variations	Unchanged	8	1
	Improved	0	3
	Worsened	0	0
Postoperative impaired patients		8	1
Raw Scores (mean ±SD)	Preoperative	8.8±8.8	46.3±6.6
	Postoperative	7.2±7.3	43.1±6.8
	P value	N.S	<0.01

Anxiety was not significantly related to impaired cognitive scores, tests or domains, before or after surgery. Depression was significantly related to verbal memory (ROWL-IR) before and after surgery (X^2 = 2.06, P<0.05; X^2 = 5.48, P<0.05, respectively) and to word fluency (FAS) before surgery (X^2 = 2.1, P<0.05). In addition, multiple regression with anxiety and depression as predictors of impact failed to show any effect on performance of neuropsychological tests either pre- or postoperatively. These results indicate that, despite the changes in depression and anxiety rates from pre- to postoperative testing, this had no impact on the patients' test performance.

Baseline cognitive characteristics:

Preoperative assessment showed that 6 patients (21%) were normal in all the tests, while 23 patients (79%) showed a deficit in at least one test. Seven patients (24%) had one test below the normal level, one patient (3%) had two tests below the normal level, nine patients (31%) had three tests below the normal level and six patients (21%) had four to six tests below the normal level (Table 4).

Table 4: Time course of patients according to number of impaired neuropsychological tests

Number of impaired tests	Preoperative impaired patients No. (%)	Post-operative variations			Postoperative impaired patients No. (%)
		Unchanged	Improved	Worsened	
0	6(20.5)	4	0	2	7(24)
1	7(24)	3	1	3	4(14)
2	1(3.5)	0	1	0	5(17)
3	9(31)	2	2	5	3(11)
4	2(7)	1	1	0	4(14)
5	2(7)	1	1	0	4(14)
6	2(7)	0	1	1	1(3)
7	0(0)	0	0	0	1(3)

Visuospatial memory (ROCF), verbal memory (ROWL-DR) and word fluency (FAS) were the most frequently impaired functions (Table 5).

Table 5: Time course and mean scores of neuropsychological test.

A: Time course of impaired neuropsychological tests.

Tests	Pre-operative impaired patients	Post-operative variations			Post-operative impaired patients
		Unchanged	Improved	Worsened	
Raven 47	2	1	1	0	1
FAS	10	8	2	1	9
TMT B	4	3	1	7	10
Verbal span	0	0	0	2	2
ROWL (IR)	7	4	3	4	8
ROWL (DR)	14	11	3	2	13
TAS	4	4	0	1	5
ROCF	17	12	5	1	13
VON	1	0	0	0	1
Copy design	1	1	0	0	1
Limb praxis	0	0	0	1	1
Orofacial praxis	0	0	0	0	0
BPD	1	0	1	1	1
FD	1	1	0	0	1

B: Mean neuropsychological test scores.

Tests	Test Score (Mean±SD)		Cut-off	P value
	Pre-operative	Post-operative		
Raven 47	27.5±5.5	28.17±4.3	18.9	N.S
FAS	24.2±12.5	22.8±12.8	17.4	N.S
TMT B	150.2±88	213.5±127	187	<0.05
Verbal span	5±0.9	4.8±1.2	5	N.S
ROWL (IR)	30.7±10	32.2±9.1	28.5	N.S
ROWL (DR)	5.4±3.3	5.6±3.4	4.7	N.S
TAS	14.7±6.1	16.3±8.3	5.8	N.S
ROCF	14.8±8.5	16.5±8.2	11.2	N.S
VON	61.5±2.8	61.1±3.1	45	N.S
Copy design	12.4±2	12.3±1.8	8	N.S
Limb praxis	19.3±0.8	19±0.43	17	N.S
Orofacial praxis	19.7±0.4	19.7±0.8	18	N.S
BPD	11.4±1.2	10.6±1.95	8	N.S
FD	4.4±1.3	4.1±1.5	3	N.S

Before surgery, on comparing patients with deficits with those without, significant differences were found for tumor characteristics, edema (X^2 = 41.8, P<0.05), histology (X^2 = 49.1, P=0.001) and size (X^2 = 40.5, P<0.05).

With regard to neuropsychological domains, 18 patients (62%) were normal before surgery. The patients with deficits were distributed as follows:

seven (24%) had only one impaired domain and four (14%) had two or more impaired domains (Table 6). The most frequently impaired domain was that of executive functions (Table 7). Prior to surgery, on comparing patients with deficits with those without, no significant correlation with tumor characteristics was found.

Table 6: Time course ofpatients according to number of impaired neuropsychological domains.

Number of impaired domains	Preoperative impaired patients No. (%)	Post-operative variations			Postoperative impaired patients No. (%)
		Unchanged	Improved	Worsened	
0	18(62)	14	0	4	18(62)
1	7(24)	2	3	2	9(31)
≥2	4(14)	0	3	2	2(7)

Table 7: Time course and mean scoresof neuropsychologicaldomains..

A:Time course of impaired neuropsychological domains.

Domains	Pre-operative impaired patients	Post-operative variations			Post-operative impaired patients
		Unchanged	Improved	Worsened	
Intelligence	2	1	1	0	1
Executive function	5	2	3	3	5
Memory	3	1	2	0	1
Language	1	1	0	0	1
Praxis	3	2	1	1	3
Gnosis	1	0	1	1	1

B: Mean neuropsychological domains scores.

Domains	Test Score (Mean±SD)		P value
	Pre-operative	Post-operative	
Intelligence	4.24±2.7	4.71±2.2	N.S
Executive function	1.67±3.3	0.86±3.7	N.S
Memory	-0.76±0.7	-0.46±0.7	<0.05
Language	0±1	0±1	N.S
Praxis	0±1.9	0±1.7	N.S
Gnosis	0±1.4	0±1.3	N.S

Postoperative cognitive results:

By test, postoperative mean scores showed a significant deterioration in the TMT-B test (attention, z = -2.24, P<0.05). By domain, a significant difference was found for the memory domain (z = -2.61, P<0.05) (Tables 5 and 7).Patients were classified as unchanged, improved or worsened on comparing the number of impaired tests or domains before and after operation (Tables 4 and 6). Postoperatively, only two patients presented an unchanged number of impaired tests but of different type.

By test, 11 patients (38%) were unchanged, 7 patients (24%) improved and 11 patients (38%) worsened. When postoperative variations were correlated to demographic, tumor and treatment variables, larger tumors were significantly associated with a risk of worsening (X^2 = 50.04, P<0.01) and high-grade histology was significantly associated with improvement (X^2 = 42.1, P<0.05).

By neuropsychological domain, 16 patients (55%) were unchanged, 6 patients (21%) improved and 7 patients (24%) worsened. Variations were found not to be associated with demographic, tumor and treatment variables.

In worsened patients (n= 11), postoperative MRI showed additional edema around the surgical field in three cases and ischemia due to division of a temporal branch in one case.

Worsening was significantly associated with executive functions both when considering single tests (FAS z = -2.52, P = 0.01 and TMT-B z = -2.36, P<0.05) and domains (z = -2.53, P=0.01). On the other hand, improvement was significantly associated with word fluency (FAS z = -2.20, P<0.05), verbal memory (ROWL-RD z = -2.20, P<0.05), visuospatial memory (ROCF z = -2.32, P<0.05) and the memory domain (z = -2.36, P=0.01).

Eight of 12 patients with low-grade gliomas were assessed at early follow-up. In this series, comparing the number of impaired tests with the postoperative phase, we observed improvement in three out of four postoperatively worsened patients, while there was no significant difference in the average test and domain scores

Discussion:

A number of studies provide a basis for suggesting that a prospective neuropsychological approach is needed in neuro-oncology for comprehensive clinical assessment. Hochberg et.al (1980) tried to explain why glioma patients failed to resume active social lives and their pre-morbid employment [15]. Concentration, problem solving and ability to learn were sensitive tests for establishing diffuse damage. It was still uncertain whether the cause was tumor, radiotherapy or surgery [16]. Mackworth et.al (1992) used a QOL self-report measure which was found to be unrelated to high-grade KPS (90-100) [17]. They therefore recommended that more detailed measures of cognitive and mental functioning should be part of the QOL assessment. Taphoorn et.al in the same year, used cognitive measures in addition to questionnaires and found that memory and concentration were not described with self and neurological assessment [18]. Since then other authors have confirmed that mental problems have a greater impact on QOL than physical problems, and that KPS is a measure of physical problems only, demonstrating that neuropsychology is a sensitive tool for analyzing brain performance [19,20]. Klein et.al in 2002 proved that these tools are specific for brain tumors since the latter, rather than any morbidity-related factor, are the original cause of cognitive deficits, as demonstrated by the lower cognitive burden in a group of patients with a comparable prognosis (low-grade hematological tumors) [21].

To date, knowledge of differential cognitive features in brain tumors has been obtained in the postoperative phase, where it proves impossible to distinguish between the objective impact of residual tumor, radiation, chemotherapy and surgical treatment on cognition. In addition, long-lasting epilepsy, seizure frequency and antiepileptic drug use are confounding factors, since they may play a role in cognitive impairment [22, 23]. At low dose, for short periods, the effect of corticosteroid therapy is negligible, and individual variations make it impossible to assess its cognitive impact[24]. Bearing in mind this bias in case selection, there is unlikely to be any correlation between type of deficit and location [18,19,25], but correlations can be found rather between tumor grade and cognitive burden [26-28]. This is substantially different from observations in stroke patients and confirms the specificity of neuropsychological tools, which may be capable of capturing the effect of tumor characteristics (mass effect, edema and tumor infiltration) in patients [29]. The present findings provide a rationale for the choice of a substantial neuropsychological battery and possibly supplementary focal investigations for preoperative brain tumor assessment [30, 31].

Tests and domains were used alternatively to classify cognitive disability. We observed higher sensitivity and accuracy using tests compared with domains even though the number of impaired tests in itself fails to provide quality information and correlation data for daily living activities.

Brain tumor patients are known to have a higher level of psychological distress (i.e., depression and anxiety) than the normal population. In this special setting (hospitalized patients, awaiting operation) we observed a 28% rate for depression and a 14% rate for anxiety, in line with previous studies [32,33]. Of interest is the fact that depression was stable before and after operation and correlated with impaired functions in both phases, with verbal memory always and with word fluency in the postoperative phase, but without influencing functional assessment. Anxiety, on the other hand, improved in the postoperative phase and was not correlated with any of the tests. The same trend, for both depression and anxiety, was found by Grant et al. [34], while Pringle et al. found a postoperative reduced rate of about 50% for both [32].

We observed that 79% of patients presented impaired cognition in at least one test, 24% in one test, 3% in two tests, 31% in three tests, and 21% in four or more, and this was correlated with edema, tumor grade and size. Visuospatial memory, verbal memory and word fluency were the most frequently affected functions. The deficit rate decreased when adopting domain-based criteria (24% had one impaired domain and 14% two or more) and was not correlated with demographic and tumor factors. Executive function was the most frequently impaired function.

Using a comparable comprehensive neuropsychological battery, Tucha et al. found deficits in 91% of cases in at least one of the nine cognitive areas explored, and 71% in three areas. Executive functions and memory were the most frequently affected domains (78% and 64%, respectively) in a large series with mixed frontal and temporal tumors, affected by intracranial hypertension syndrome in an undefined number of cases. The authors stated that ‘‘undisturbed memory and attentional processes require the functioning of a variety of brain regions’’ to justify the lack of correlation between site and function [31].

For perioperative cognitive evaluation, Yoshii et.al used only one test, a modified Mini Mental State Examination (MMSE), which to date has never been proved specific for these patients [30].

In the present series, which is unique in its aim to correlate pre- and postoperative neuropsychological findings using a comprehensive battery, we found an acceptable rate of worsened patients (38%) over a wide range of explored functions and a 24% rate of improved patients, using very strict criteria (one additional impaired test). Worsening correlated with executive functions, and improvement with memory function. It seems that the volume of the operated area (tumor size) rather than the location is important for postoperative worsening, but release of the mass effect, which is typical of quickly developing masses (high grade), may have positive consequences. This is confirmed by the type of improvement which is significantly associated with memory function, the most frequently observed deficit before surgery. Only in a minority of worsened cases (4 out of 11) did postoperative MRI show increased edema or ischemia which may be correlated with clinical features. Situations such as head injuries and cardiac surgery offer a key to further interpretation since they occur acutely, present similar impairments and typically show a transient effect [35,36]. In particular, head injuries share the same pathogenesis, the mechanical effect, generalized rather than focal, possibly due to deliquoration and manipulation of large areas and/or widely distributed networks. In addition, it is worth mentioning that improvement is of greater clinical importance since it is more likely to be permanent, while acute impairment is more likely to be transient[37]. On the whole, using sophisticated tools, we observed an unchanged cognitive burden in the acute postoperative phase, which suggests a highly probable improvement in early follow-up once the acute deficits have subsided, as we have observed in a limited number of patients.

Teixidor et al. and Giovagnoli et al. used a focal battery in series selected by site and histology. In low-grade gliomas in the temporal lobe and in language areas, they found divergent findings with regard to memory, global memory and working memory, respectively, the only explored function[19,38]. In Teixidor et al.’s series, immediate postoperative worsening was found for neurological deficits in 65% of cases and for working memory in 96% of cases, while the KPS remained 70 or higher. Giovagnoli et al. found that mean postoperative scores for all tests were not significantly lower than the preoperative scores. This difference may be explained by the different surgical technique adopted: awake mapping guiding resection in the first series, versus selected extended resection for tumors inducing epilepsy in the second series. Impairment subsided completely over 3 months in the first series. These results suggest that the reliability of studies aimed at measuring the effect of tumor before starting radiotherapy, in the first month after surgery, is limited because of either a lack of preoperative data or persistence of the effect of surgery [25-27]. In our experience, additional focal impairment is unlikely, and provides no rationale for considering studies in this period to test focal dysfunction. Even greater limitations are presented by those studies that try to assess the impact of surgery on cognition some months later, during follow-up, since, meanwhile, a number of confounding treatments may have been given (antiepileptic drugs, corticosteroids, radiotherapy, chemotherapy) [4, 39].

Conclusions:

We measured the effects of tumor and surgical treatment on cognitive functions. The present findings suggest that: (a) analysis using an extensive neuropsychological and mood battery is strongly advised; (b) at baseline, patients' cognitive functions are often impaired (79%), memory and to some extent executive functions being those most frequently affected by the tumor, influenced by the mass effect (size and edema) and by higher tumor grading; (c) the immediate postoperative findings showed an unexpected low incidence of additional deficits (38%) and a considerable rate of early improvement (24%), correlated with tumor size and histology, respectively.

Thus, the tumor effect rather than the surgical effect seems to be more prevalent in the early postoperative period. Postoperative worsening seems to be due to a generic mechanical effect and to manipulation/removal of tumor periphery rather than to discrete focal injury, as demonstrated by the occurrence of executive function impairment. The results of this study furnish a basis for advocating a safety framework to improve surgical attempts to remove increasingly large amounts of tumor-infiltrated brain. In addition, whenever the limits of functional brain are approached and reached, awake monitoring could be employed using new paradigms. For these reasons, neuro-psychological assessment is a valid tool to be introduced in routine neurosurgical practice and also constitutes the ideal premise for prospective longitudinal evaluations.

References:

1. Meyers CA, Brown PD Role and relevance of neurocog-nitive assessment in clinical trials of patients with CNS tumors. J ClinOncol (2006) 24(8):1305-1309.
2. Sanai N, Mirzadeh Z, Berger MS Functional outcome after language mapping for glioma resection. New Engl J Med (2008) 358(1):18-27.
3. Sherer M, Meyers CA, Bergloff P. Efficacy of post acute brain injury rehabilitation for patients with primary malignant brain tumor. Cancer (1997)80(2):250-257.
4. Bosma I, et al. The course of neurocognitive functioning in high-grade glioma patients. Neuro-Oncol (2007)9:53-62.
5. Stummer W, Pichlmeier U, Meinel T, Wiestler OD, Zanella F, Reulen HJ, ALA-Glioma Study Group Fluorescence-guided with 5-aminovenulinic acid for resections of malignant glioma--a randomised controlled multicentre phase III trial. Lancet Oncol (2006)7(5):392-401.
6. Beck TA Depression causes and treatment. University of Pennsylvania Press, Philadelphia (1972).42-44.
7. SpielbergerCD STAI state-trait anxiety inventory Forma Y. OrganizzazioniSpeciali, Florence (1970).25-29.
8. Oldfield RC. The assessment and analyses of handedness: the Edinburgh inventory. Neuropsychologia (1971) 9:97-113.
9. Caltagirone C, Perri R, Musicco M La fasepreclinicadellamalattia di Alzheimer. Cortical Medicine, Roma (2001).101-112.
10. Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laicona M, Capitani E Trail making test: normative values from 287 normal adult controls. Int J NeurolSci (1996) 17:305-309.
11. Spinnler H, TognoniG Standardizzazione e taraturaita-liana di test neurologici. Ital J NeurolSci (1987) 7(suppl. 8):1-120.
12. Rey AReattivodellafiguracomplessa. ManualeOrga-nizzazioniSpeciali, Florence (1983).65-70.
13. Laiacona M, Barbarotto R, Trivelli C, Capitani E Disso-ciazionisemanticheintercategoriali: descrizione di unabatteriastandardizzata e datinormativi. Archivio di Neurologia, Psichi-atria e Psicologia (1993) 54:209-248.
14. Bisiach E, Cappa S, Vallar G Guidaall'esameneuropsi-cologico. Raffaello Cortina, Milano (1983).87-91.
15. Hochberg FH, SlotnickB Neuropsychologic impairment in astrocytomas survivors. Neurology (1980) 30(2):172-177.
16. Archibald YM, Lunn D, Ruttan LA, Macdonald DR, Del Maestro RF, Barr HWK, Pexman JHW, Fisher BJ, Gaspar LE, Cairncross JG Cognitive functioning in long term survivors of high-grade glioma. J Neurosurg (1994) 80:247-253.
17. Mackworth N, Fobair P, Prados M. Quality of life self-reports from 200 brain tumor patients: comparisons with Karnofsky performance scores. J Neuro-Oncol (1992) 14:243-253.
18. TaphoornMJ,et al. Assessment of quality of life in patients treated for low-grade glioma: a preliminary report. J NeurolNeurosur Psychiatry (1992) 55:372-376.
19. Giovagnoli AR, Boiardi A. Cognitive impairment and quality of life in long-term survivors of malignant brain tumors. Ital J NeurolSci (1994) 15:481-488.
20. Palson A, Ek L, Ahlstro¨m G, SmitaA Pitfalls in the assessment of disability in individual with low-grade gliomas. J Neuro-Oncol (2003) 65:149-158.
21. Klein M, et al. Effect of radiotherapy and other treatment related factors on mid-term to long-term cognitive sequelae in low-grade gliomas: a comparative study. Lancet (2002) 360(2):1361-1368.
22. Klein M, Engelberts NHJ, van der Ploeg HM, Kasteleijn-NolstTrenite` DGH, Aaronson NK, Taphoorn MJB, Baijen H, Vandertop WP, Muller M, Postma TJ, Heimans JJ Epilepsy in low-grade gliomas: the impact on cognitive function and quality of life. Ann Neurol (2003) 54:514-520.
23. Correa DD, DeAngelis MM, Shi W, Thaler HT, Lin M, Abrey LE Cognitive functions in low-grade gliomas: disease and treatment effect. J Neurooncol (2007) 81(2):175-184.
24. Starkman MN, Giordani B, Berent S, Schork A, SchteingartDE Elevated cortisol levels in Cushing's disease are associated with cognitive decrements. Psychosom Med (2001) 63:985-993
25. Jagaroo V, Rogers MP, Black McLPAllocentricvisuo-spatial processing in patients with cerebral gliomas: a neuro-cognitive assessment. J Neuro-Oncol (2000) 49:235-248
26. Hahn CA, Dunn RH, Logue PE, King JH, Edwards CL, Halperin EC Prospective study of neuropsychologic testing and quality of life assessment of adults with primary malignant brain tumors. IJRB (2003) 55(4):992-999
27. BudrukkarA,et al. Prospective assessment of quality of life in adult patients with primary brain tumors in routine neurooncology practice. J Neuro-Oncol (2008)90(3):413-419.
28. Costello A, Shallice T, Gullan R, Beaney R. The early effects of radiotherapy on intellectual and cognitive functioning in patients with frontal brain tumors: the use of a new neuro-psychological methodology. J Neuro-Oncol (2004) 67:351-359.
29. Taphoorn MJB, Klein M Cognitive deficits in adult patients with brain tumors. Lancet Neurol (2004) 66(3):159-168.
30. Yoshii Y, et al. Cognitive function of patients with brain tumor in pre- and postoperative stage. SurgNeurol (2008) 69: 51-61.
31. Tucha O, Smely C, Preier M, Lange KW Cognitive deficits before treatment among patients with brain tumors. Neuro-surgery (2000) 47:324-333.

32. Pringle A-M, Taylor R, Whittle JR Anxiety and depression in patients with an intracranial neoplasm before and after tumor surgery. Br J Neurosurg (1999) 13(1):46-51.
33. Anderson SW, Damasio H, Tranel D. Neuropsychological impairments associated with lesions caused by tumor or stroke. Arch Neurol (1990) 47:397-405.
34. Grant R, Slattery J, Gregor A, Whittle IR. Recording neurological impairment in clinical trials of glioma. J Neuro-Oncol (1994) 19:37-49.
35. Broglio PS, Puetz TW. The effect of sport concussion on neurocognitive function, self-report symptoms and postural control. Sports Med (2008) 38(1):53-67.
36. Keith JR, Puente AE, Malcolmson KL, Tartt S, Coleman AE Assessing postoperative cognitive change after cardio-pulmonary bypass surgery. Neuropsychology (2002) 16(3):411-421.
37. Duffau H, Lopes M, Arthuis F, Bitar A, Sichez JP, Van Effenterre R, Capelle L Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985-96) and (1996-2003) functional mapping in the same institution. J NeurolNeurosurg Psychiatry (2005) 76:845-851.
38. Teixidor P, Gatignol P, Leroy M, Aumatell C, Capelle L, Duffau H Assessment of verbal working memory before and after surgery for low-grade glioma. J Neuro-Oncol (2007) 81:305-313.
39. Kaleita TA, Wellish DK, Cloughesy TF, Ford JM, Freeman D, Belin TR, Goldman J Prediction of neurocognitive out¬come in adult brain tumor patients. J Neuro-Oncol (2004) 67:245-253.