State and trait anxiety and depression in patients with primary brain tumors before and after surgery: 1-year longitudinal study

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Object. The aim in this study was to assess the state and trait types of anxiety as well as current depression before and after surgery in patients affected by brain tumors. The relationships between these affective disorders and the patient’s sex, tumor histology, and laterality of the tumor were also evaluated.

Methods. A total of 72 patients affected by a primary brain tumor were enrolled in the study. Histological grades were assigned according to the World Health Organization classification. State and trait anxiety were assessed using the State and Trait Anxiety Inventory; current depression was assessed using the Zung Self-Rating Depression Scale. Cognitive impairment was assessed using the 10-item Short Portable Mental Status Questionnaire. Psychometric evaluation was assessed before surgery and at 1, 3, 6, and 12 months after surgery.

Results. Before brain surgery, 62.5% of patients showed state anxiety, 50% of patients showed trait anxiety, and 9.7% of patients showed current depression. During the follow-up period there was no significant variation in the percentage of patients with state anxiety (p = 0.416) and trait anxiety (p = 0.7), whereas a significant increase in the percentage of those with current depression was found (p < 0.0001), in particular at 1 month (p = 0.002) and 3 months (p = 0.039) after surgical treatment. The tumor’s laterality and histology showed no correlation with psychometric variables, whereas a relationship between the presence of trait anxiety at the enrollment and current depression after surgery (p < 0.0001) was found.

Conclusions. Patients affected by brain tumors frequently experience affective disorders. After brain surgery, a depressive state can develop. The psychometric assessment could be useful in these patients for quick recognition of psychological disorders. (DOI: 10.3171/JNS/2008/108/2/0281)

Key Words • brain tumor • depression • state anxiety • surgery • trait anxiety

Tumors of the central nervous system represent a risk factor for the development of affective disorders such as depression, anxiety, and panic attacks.11,16,17 In particular, depression is common in patients with central nervous system tumors,23 and the prevalence of depressive symptoms in these patients can vary from 15 to 38%.4,13 Furthermore, recently it has been found that preoperative depression represents a prognostic factor for worse survival rates among patients affected by glioblastoma13 and low-grade glioma.17 Anxiety disorders are also common in patients affected by primary brain tumors, and it seems related to tumor localization,16,20 whereas the type and grade of tumor do not seem to play any role.29 At present, however, there are few studies in which anxiety and depression have been assessed with several repeated measurements over a long period following brain tumor surgery. Moreover, studies evaluating the difference between the state and trait form of anxiety are lacking.

Our aim in the present study was to assess state and trait anxiety and current depression before and after surgical treatment (1 year of follow-up postoperatively) in consecutive patients with intracranial tumors. The assessment of state anxiety, trait anxiety, and current depression was performed during 1 preoperative and 4 postoperative evaluations. Relationships between these affective disorders and the patient’s sex, tumor histology, and tumor laterality were also evaluated.

Clinical Material and Methods

Between February 2005 and November 2006, 114 patients affected by a primary brain tumor and requiring surgery were enrolled in the study. This group consisted of 45 men (39.5%) and 69 women (60.5%) whose mean age was 48.1 ± 17.7 years (range 20–80 years of age). Surgical
treatment was performed at the Department of Neurosurgery of “Casa Sollievo della Sofferenza” Hospital, San Giovanni Rotondo, Italy.

Radiological diagnosis of the brain tumors was made using computed tomography or magnetic resonance imaging; histological grading was attributed according to the WHO classification. The tumors were divided into the following classes: Grade I–II gliomas, Grade III–IV gliomas, and benign tumors (meningiomas, pituitary adenomas, and vestibular schwannomas). A cognitive assessment was performed to verify that patients could understand the test procedures. Cognitive impairment was assessed using the 10-item SPMSQ. The SPMSQ is a widely used, valid, reliable, 10-item questionnaire designed to evaluate orientation, memory, and concentration. The score is evaluated in terms of errors. Patients with 5 or more errors on the SPMSQ were considered to have moderate to severe impairment, and patients with 3–4 errors were considered to have mild cognitive impairment; patients with 0, 1, or 2 errors were classified as having no cognitive impairment. The SPMSQ has a specificity > 90% and sensitivity of 50–82%. The SPMSQs were administered before surgery and at 1, 3, 6, and 12 months after surgery.

Exclusion criteria were as follows: the presence of previous psychiatric disease; alteration of the levels of hypothalamic-pituitary-adrenocortical axis hormones in serum; age < 18 years; and the presence of severe clinical signs of neurological deficits and/or cognitive impairment with an SPMSQ score > 2. Patients affected by neurological and/or cognitive impairment before or after surgery were excluded to avoid bias related to the reduction of the individual’s ability to cooperate with the psychometric test. Written informed consent was obtained from all participants.

Among 114 patients initially enrolled in the study, 10 (8.8%; 3 men and 7 women) died during follow-up, 5 (4.4%; 3 men and 2 women) did not show adherence to the psychometric evaluation at follow-up, 12 (10.5%; 5 men and 7 women) showed a cognitive impairment with SPMSQ score > 2 at follow-up, and 15 (13.2%; 5 men and 10 women) showed severe neurological deficits; all of these patients were excluded from the statistical evaluation. A sample of 72 patients, 31 men (43.1%) and 41 women (56.9%) whose mean age was 45.5 ± 17.3 years (range 20–78 years) were considered for the final statistical analysis.

Psychological Assessment

All the participants were given a questionnaire seeking information on their level of education, socioeconomic, and marital status (Table 1), and containing 2 different self-rating psychometric tests: 1 for the state and trait anxiety and the other for current depression.

State and trait anxiety was assessed using the STAI, made up of 2 axes (y1 for state anxiety and y2 for trait anxiety), both consisting of 20 multiple-choice items; each item has a score from 1 to 4 so that the total point score of y1 and y2 axes can range from 20 to 80. This test was selected on the basis of its simplicity, validity, and reliability. In particular, the STAI test permits a distinction between existing anxiety and predisposition to an anxious reaction as a personality characteristic, as previously described.

State anxiety was assessed using the STAI, made up of 2 axes (y1 for state anxiety and y2 for trait anxiety), both consisting of 20 multiple-choice items; each item has a score from 1 to 4 so that the total point score of y1 and y2 axes can range from 20 to 80. This test was selected on the basis of its simplicity, validity, and reliability. In particular, the STAI test permits a distinction between existing anxiety and predisposition to an anxious reaction as a personality characteristic, as previously described.

Continuous data with normal distribution are given as mean ± standard deviation, and categorical data are expressed as percentages. The normality of data distribution was tested by the Kolmogorov–Smirnov test. The group was examined using the Cochrane Q procedure test for multiple related samples to evaluate how STAI y1, STAI y2, and Zung SDS parameters change at follow-up. The variables with a probability value < 0.10 at univariate analysis were entered in a multivariate logistic regression anal-
Analysis to identify the independent predictors of Zung SDS positivity at 1 and 3 months postsurgery. Categorical data were analyzed using the chi-square test or the Fisher exact test as appropriate. A probability value < 0.05 was considered significant. The data were statistically analyzed using SPSS version 13.0 software (SPSS Inc.).

Results

Sociodemographic characteristics of the sample, the histological type, and localization of the brain tumors are reported in Table 1.

Figure 1 shows the percentage of patients affected by state anxiety, trait anxiety, and current depression before surgery and at the different follow-up intervals. Before surgical treatment, a high percentage of patients affected by state anxiety (62.5%) and trait anxiety (50%) were found among the enrolled patients, whereas the percentage of patients showing current depression was relatively low (9.7%). During the follow-up period, however, there was no significant variation in the percentage of patients with state anxiety (p = 0.416) and trait anxiety (p = 0.7), whereas a significant increase in the percentage of those with current depression was found (p < 0.0001). The percentage of patients with current depression significantly increased at 1 month (p = 0.002) and 3 months (p = 0.039) after surgical treatment, and it continued to increase at 6 months and 1 year after surgical treatment, although without reaching statistical significance (p = 0.72 and p = 0.45, respectively; see also Table 2). The number of patients affected by state anxiety, trait anxiety, and current depression before surgery and at the different follow-up intervals is reported in Table 2.

At analysis, the presence of current depression at 1 month postsurgery was directly correlated to female sex (p = 0.007), trait anxiety (p = 0.0009), and current depression (p = 0.007) before surgery, and with state anxiety (p = 0.003) and trait anxiety (p < 0.0001) at 1 month postsurgery. The logistic regression showed that at 1 month after brain surgery the main determinant of current depression was the presence of trait anxiety (p < 0.0001).

The presence of current depression at 3 months postsurgery was directly correlated to female sex (p = 0.001), trait anxiety before surgery (p = 0.003), state anxiety (p < 0.0001), trait anxiety (p < 0.001), and current depression (p < 0.0001) at 1 month postsurgery, and state anxiety (p < 0.0001) and trait anxiety (p < 0.0001) at 3 months postsurgery. The logistic regression showed that at 3 months after brain surgery the main determinant of current depression was the presence of current depression at 1 month after surgery (p < 0.0001) and state anxiety at 3 months after surgery (p < 0.0001).

When we evaluated patients divided by sex, no significant variation in the percentage of state and trait anxiety was found in either women or men, whereas the percentage of patients with current depression significantly increased during the follow-up period in both women and men (Table 3). In women compared with men, however, a significantly higher percentage of state anxiety, trait anxiety, and current depression was found before surgery and at the different follow-up intervals (Table 4).

No significant correlation between right laterality of the tumor and state anxiety (p = 0.36), trait anxiety (p = 0.24), and current depression (p = 0.75) was found. Moreover, the left laterality of the tumor showed no correlation with state anxiety (p = 0.95), trait anxiety (p = 0.46), and current depression (p = 0.75).

![Bar graph showing the percentage of patients affected by state anxiety (STAI y1), trait anxiety (STAI y2), and current depression (Zung SDS) before surgery and at the different follow-up intervals. During the follow-up period there was no significant variation in the percentage of patients with state anxiety (p = 0.416) and trait anxiety (p = 0.7), whereas a significant increase in the percentage of current depression was found (p < 0.0001). The percentage of patients with current depression significantly increased at 1 month (p = 0.002) and 3 months (p = 0.039) after surgical treatment, and it continued to increase at 6 months and 1 year after surgical treatment, although without reaching statistical significance (p = 0.72 and p = 0.45, respectively; Cochrane Q procedure test for multiple related samples).](image-url)
However, data concerning affective disorders after surgery are still controversial. In particular, although some authors found a regression of anxiety, coupled with worse psychological profiles. The relationship between sex and affective disorders in such patients is still controversial. Some authors found no sex difference, whereas others showed high levels of anxiety, or depression in female patients before surgery, and a high risk for depression and for a decrease of quality of life at 1 year after surgery. According to these last data, our findings showed that state anxiety, trait anxiety, and current depression are present in a significantly higher percentage of female patients compared with male patients both before and after neurosurgery. Moreover, our data are supported by epidemiological evidence showing that the prevalence of depression in female patients is approximately twice that in male individuals in the general population, and by data showing that, among patients with cardiac diseases, females show higher levels of anxiety and depression, coupled with worse psychological profiles.

There were no significant differences in anxiety and depression at different follow-up intervals in the study.

### Discussion

The presence of affective disorders such as anxiety and depression is common in patients affected by primary brain tumors before surgery. However, data concerning affective disorders after surgery are still controversial. In particular, although some authors found a regression of anxiety and depression after surgery, others showed an increase of the depression at these patients' follow-up evaluations.

Nevertheless, it is difficult to differentiate the role played by the neurophysiological effects of the tumor per se and the role played by the patient’s knowledge of being affected by a cerebral disease. Moreover, most of the studies assessed anxiety and depression only a few times during the follow-up after surgery.

In the present longitudinal study, state and trait anxiety and current depression were evaluated before and after brain surgery in several testing sessions in a cohort of patients affected by primary brain tumors. A high percentage of patients affected by state and trait anxiety was found among the enrolled patients before brain surgery. These results could be due to a psychological reaction to several factors (such as the diagnosis of a brain lesion; the fear of surgical intervention and/or anesthesia; or the risk of death, coma, or neurological and physical deficits after surgery) other than to the hospitalization.

During the follow-up period, although state and trait anxiety did not significantly change in our sample, an increase in percentage of current depression was found, particularly at 1 and 3 months after the surgical procedure, although it tended to increase also at 6 months and 1 year after surgery. These data are in line with recent findings by Litofsky and coworkers, who showed increased levels of depression at 6 months after tumor surgery.

At univariate analysis, several factors showed a direct correlation with the increase of current depression at 1 and 3 months after surgery; these were female sex, trait anxiety, and current depression before surgery. However, at the logistic regression the main determinant for the increased current depression was the presence of anxiety, as a trait before surgery and as a state after surgery. Also, the presence of current depression at 1 month postsurgery was the main determinant of current depression during the remaining follow-up period. These data could indicate that patients with brain tumors who exhibit anxiety should be strictly followed after surgery because of the risk of developing current depression in a short time, with its tendency to increase.

The relationship between sex and affective disorders in such patients is still controversial. Some authors found no sex difference, whereas others showed high levels of anxiety, or depression in female patients before surgery, and a high risk for depression and for a decrease of quality of life at 1 year after surgery. According to these last data, our findings showed that state anxiety, trait anxiety, and current depression are present in a significantly higher percentage of female patients compared with male patients both before and after neurosurgery. Moreover, our data are supported by epidemiological evidence showing that the prevalence of depression in female patients is approximately twice that in male individuals in the general population, and by data showing that, among patients with cardiac diseases, females show higher levels of anxiety and depression, coupled with worse psychological profiles.

### Table 2

Variation in number and percentage of patients affected by state anxiety, trait anxiety, and current depression at different follow-up intervals in the study.

<table>
<thead>
<tr>
<th>FU Interval</th>
<th>STAI y1</th>
<th>STAI y2</th>
<th>Zung SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>preop</td>
<td>45 (62.5)</td>
<td>36 (50)</td>
<td>7 (9.7)</td>
</tr>
<tr>
<td>1 mo postop</td>
<td>41 (56.9)</td>
<td>36 (50)</td>
<td>20 (27.7)</td>
</tr>
<tr>
<td>3 mos postop</td>
<td>41 (56.9)</td>
<td>40 (55.5)</td>
<td>26 (36.1)</td>
</tr>
<tr>
<td>6 mos postop</td>
<td>39 (54.2)</td>
<td>37 (51.4)</td>
<td>28 (38.8)</td>
</tr>
<tr>
<td>1 yr postop</td>
<td>40 (55.5)</td>
<td>38 (52.7)</td>
<td>32 (44.4)</td>
</tr>
</tbody>
</table>

* FU = follow-up; y1 = state anxiety; y2 = trait anxiety.
† Statistical comparisons were made using the Cochrane Q procedure test for multiple related samples.

### Table 3

Variation in number and percentage of female and male patients affected by state anxiety, trait anxiety, and current depression at different follow-up intervals in the study.

<table>
<thead>
<tr>
<th>FU Interval</th>
<th>No. of Female Patients (%)</th>
<th>No. of Male Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STAI y1</td>
<td>STAI y2</td>
</tr>
<tr>
<td>preop</td>
<td>31 (75.6)</td>
<td>28 (68.3)</td>
</tr>
<tr>
<td>1 mo postop</td>
<td>32 (78)</td>
<td>28 (68.3)</td>
</tr>
<tr>
<td>3 mos postop</td>
<td>31 (75.6)</td>
<td>30 (73.2)</td>
</tr>
<tr>
<td>6 mos postop</td>
<td>29 (70.7)</td>
<td>29 (70.7)</td>
</tr>
<tr>
<td>1 yr postop</td>
<td>30 (73.2)</td>
<td>29 (70.7)</td>
</tr>
</tbody>
</table>

* Statistical comparisons were made using the Cochrane Q procedure test for multiple related samples.
by a brain tumor is not adequately taken into account. Patients with brain tumors frequently exhibit affective disorders such as anxiety, depression, or panic, and these symptoms often continue to be present after surgical treatment. During the diagnostic period, the physician–patient interaction is generally focused on issues such as diagnosis of the tumor, treatment options, long-term prognosis, and neurological assessment, but evaluation of psychological assessment seems not to have a high priority. Symptoms of depression and anxiety often mimic those commonly found in patients with brain tumors (that is, tiredness and fatigue), but usually the neurosurgeon focuses his or her attention only on the organic features. For these reasons the psychometric evaluation gains great importance in the global evaluation of patients affected by brain tumors, to recognize and treat psychological disorders quickly, thus improving the quality of life of these patients. In this context, our data led us to hypothesize a potential beneficial role of antianxiety and/or antidepressant drug therapy and/or psychological support counseling in patients affected by primary brain tumors. Further studies are needed to evaluate the most effective treatment in these patients.

**Conclusions**

Patients suffering from brain tumors frequently show affective disorders. After brain surgery a depressive state can develop. Psychometric assessments could be useful in these patients to recognize psychological disorders quickly.

**References**

10. Grillon C, Ameli R, Fouth M, Davis M: Fear-potentialized startle:
relationship to the level state/trait anxiety in healthy subjects. Biol Psychiatry 33:566–574, 1993

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