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Answer to the Comment by Lévêque et al. on 'Bilateral Cingulotomy and Anterior Capsulotomy Applied to Patients with Aggressiveness'

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We appreciate a lot the interest in our paper 'Bilateral cingulotomy and anterior capsulotomy applied to patients with aggressiveness' published in *Stereotactic and Functional Neurosurgery* [1]. However, Lévêque et al. wrote the title as 'Bilateral anterior capsulotomy and cingulotomy applied to patients with aggressiveness' [2]. We think that mistake could be caused by the special interest in the effect of capsulotomy. We have read all the issues by Lévêque et al. in order to try answering.

We have published a very similar series of cases entitled 'Evaluación de la cingulotomía bilateral y la capsulotomía anterior en el tratamiento de la agresividad' [3] in 2011. This paper involved similar patients with aggressiveness because the Unit of Stereotactic, Functional Neurosurgery and Radiosurgery has attended this kind of cases since 1994. Both series correspond to a bigger cohort that included around 36 patients. Initially, we had to elaborate a scientific and ethical process to diagnose and propound a method of treatment for these subjects. In the first series reported [3], 12 patients underwent bilateral anterior capsulotomy and cingulotomy and were evaluated by the Mayo-Portland Adaptability Inventory and Global Assessment Functioning Scale because those were the accessible instruments at that moment. A year later, a second series [1] was treated with the same surgery procedure but studied by the Overt Aggression Scale and Global Assessment of Functioning Scale. Those series have 4 cases in common (No. 1, 5, 7 and 8 from the second series). We must state several differences between them:

(1) The first series was followed up for only 6 months owing to the fact that the patients came from different states of Mexico and from the metropolitan area. Those of the second series came mainly from the metropolitan area.

(2) The first series was evaluated in the follow-up period by 3 psychiatrists; they applied the Mayo-Portland Adaptability Inventory. The second series was evaluated only by a single psychiatrist (J.J. Bustamante) who applied the Overt Aggression Scale.

(3) The first series was followed up for 6 months and the second series for 4 years.

According to the points below, the following information should be considered:

(A) There are no patients omitted in the series because they are different.

(B) Four patients were involved in both series and they were evaluated by the Mayo-Portland Adaptability Inventory and the Overt Aggression Scale. They were followed up for 6 months and 4 years. The first paper was published in March/April 2011, i.e. during the period of evaluation of the second paper (from July 2010 to May 2011).

(C) Side effects are not the same because they came from different series. Of course, we can observe a similarity between the two because the same procedure was used.

(D) The image of capsulotomy shows a representative lesion of fibers in the internal capsule and some part of the striatum is involved in this area. Although, the main target of the leucotomy is in the anterior limb of the internal capsule. That observation suggests another small series only with anterior capsulotomy that has not been published. We present here two different slices of axial MRI where bilateral anterior capsulotomy is shown at the 4-year follow-up (fig. 1).

Fig. 1. Two axial slices show bilateral capsulotomy in a patient after 4 years of follow-up.

Fig. 2. Distribution of age for the two different series of patients who underwent bilateral anterior capsulotomy and cingulotomy.

(E) The follow-up was not the optimum but more importantly this kind of proceedings should report the results and the side effects, and this is probably the most extended report. Neuroaggressive disorder is one of the most frequent psychiatric illnesses reported by psychiatric centers, psychiatrists or relatives. Since the beginning, we had formed a specific team of specialists consisting of a neurologist, psychiatrist, neuropsychologist and neurosurgeon. The entire process has been entered into a proceedings manual monitored and supervised by the Ethics Committee and Medical Direction of the Mexico General Hospital. The only death not related to the surgery was observed during the operative period of the study. In 6 months of follow-up, no death was recorded; the clinical condition improved and the side effects resolved in the first month. We would like a more extended period of follow-up but no severe side effect was observed during the study time.

(F) Informed consent is an ethical procedure in order to assure the patient's autonomy when he or she decides to accept a specific treatment. Neuroaggressive disorder is a condition which prevents perfect understanding. However, we tried to explain when that was possible. That ethical situation was faced considering the risks and benefits in every case by the 2 teams who reviewed all requests of the treatment psychiatrist. One of them consisted of 1 psychiatrist, 1 neurologist, 1 neuropsychologist and 2 neurosurgeons who analyzed the clinical condition. The second team was an ethics group who assessed the environmental conditions in his or her family or in the hospital. Two principal objectives were looked for: to prevent physical damage to the patient and others and to improve quality of life. In all cases one member of the family received a complete explanation of the risks and the benefits of the procedure. We consider that this study was driven to improve daily life for the patient. Obviously, deep brain stimulation should be a better option but the cost of devices makes it not an accessible alternative. It is very

easy to argue for it but all patients were evaluated individually by at least 2 independent psychiatrists and were considered medically intractable. Besides, the institutional review board evaluated each case individually and considered surgery justified. Before the surgical treatment, most patients were isolated and restrained due to the risk of physical aggression against other patients and personnel of the Mental Institution as well as self-aggressive behavior. As for the concern of the authors for lesions in the brain in functional neurosurgery, at present, ablative procedures are still in use for epilepsy, and other more refined (but less effective) lesioning, such as radiosurgery, have been proposed as alternative in epilepsy and obsessive-compulsive disorder. We fully agree that treatment of aggressive disorders and addiction is controversial, and ideally reversible methods such as deep brain stimulation should be employed. However, we would refer authors to the report on psychosurgery delivered to the National Commission for the Protection of Human Subjects of Medical and Behavioral Research [4]. This detailed report was elaborated by distinguished neuroscientists and legislators during the years of highest criticism of psychosurgery in 1977. The report concluded that, in spite of an ill-defined psychiatric disorder in most patients, surgery was beneficial to most of them. It is not to say we should remain at the same level as treatments in the past, however: better diagnosed cases, evaluated by proper scales, by ethical and research committees, selected as medically intractable cases, and with modern stereotaxis, should provide better results.

(G) In figure 2 we show the specific distribution of every series and it is evident that there are differences between them.

(H) The rationale for this procedure was to interrupt the fibers coming from the hypothalamus to the frontal cortex into the anterior limb of the internal capsule. Cingulotomy and anterior capsulotomy have been applied to treat psychiatric patients with less morbidity than those treated by hypothalamotomy. Besides, we would like to quote the third paragraph in chapter I, page 17, of the report mentioned above: '...the types of psychiatric disabilities for which lesions of medial or lateral limbic structures are likely to be most beneficial have been established. Lesions of the medial frontal area, the anterior cingulate region, or closed related fiber systems, are most effective in syndromes characterized by psychic hyperactivity such as seen in patients suffering from tension, anxiety, restlessness, and obsessive behavior' [4].

(I) Finally, in 'Bilateral cingulotomy and anterior capsulotomy applied to patients with aggressiveness' [1], the Discussion section has a special paragraph where we accept the necessity to create a specific forum to review this ethical issue. Probably, other authors consider psychosurgery as a no-safety procedure for aggressive behavior or as a social control manner, but our professional group is formed by highly specialized psychiatrists, functional neurosurgeons and neuropsychologists. We are monitored by several institutional review boards, and the final goal of this protocol was to improve the quality of life of the patients and their relatives. We expect that in the future deep brain stimulation will be accessible for this kind of patients but right now their treatment is a very special issue as was commented on in the paper 'Scientific and ethical issues related to deep brain stimulation for disorders of mood, behavior and thought' [5].

References

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