

Parkinson's disease after psychosurgery for the treatment of cocaine addiction

Enfermedad de Parkinson después de la psicocirugía para el tratamiento de la adicción a la cocaína

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In 2018 we published a clinical case (Haro et al., 2018) of a 32-year-old patient who began to use cocaine at the age of 14 and was diagnosed with “limbic dysfunction syndrome” at 17. The treatment recommended by his psychiatrist was psychosurgery. It was performed in two separate interventions in which radiofrequency-induced thermal coagulation lesions were performed with the aim of deactivating the anterior cingulate cortex (AC), disconnecting it from the ventral striatum and the amygdala in both hemispheres. Shortly after the surgery, the patient began to have delusions and was diagnosed with paranoid schizophrenia. At the age of 27, he showed negative psychotic symptoms and cognitive deficits, he scored 27/36 on Tower of London test (Krikorian, Bartok & Gay, 1994) which implied a reduced capacity for problem solving and planning.

With this letter, two years after the first publication of the case, the authors present the evolution of the patient after the appearance of a probable late complication of psychosurgery. New neuroimaging data, neurological evaluation and discussion conducted from a translational point of view are included.

During the last two years, the patient has remained stable within his chronic psychopathology. Daily drug treatment consisted of 30mg of olanzapine, 12mg of paliperidone, 450mg of quetiapine, 1500mg of valproic acid, and 4mg of biperiden. Although dopamine antagonists used as typical antipsychotics (haloperidol, pimozide, etc.) pro-

duce severe motor effects (akinesia and tremor), atypical antipsychotics such as those prescribed here (olanzapine, paliperidone, and quetiapine) act as dopamine receptor antagonists but also of serotonin and / or acetylcholine (biperiden) receptors, and they tend to have fewer motor effects in humans, and even improve tremor in animal models of Parkinson's disease (PD) (Betz, Ishiwari, Wisniecki, Huyn & Salamone, 2005). Thus, after the appearance of tremors in the upper limbs, which also did not remit with reductions in antipsychotic drugs, the patient was referred to the Neurology Department to rule out PD.

On neurological examination, the patient presented moderate hypomimia, mild hypophonia and dysarthria, decreased bilateral arm movement, moderate axial stiffness, moderate and symmetrical upper limb stiffness, bradykinesia in the right hemibody and marked slowness when performing finger tapping and movements alternating with the right hand. He did not show resting tremor or tremor in the lower limbs, maintaining correctly postural stability. In the evaluation of the motor state, using the unified scale for PD (UPDRS III) (Fahn, Elton & Members of the UPDRS Development Committee, 1987), the patient scored 25/68 (mild-moderate motor impairment) and he scored 2,5 (mild bilateral disease with recovery on pull test) on the Hoehn and Yarh scale (Hoehn & Yarh, 1967).

The last MRI performed on the patient revealed abnormal cavities in the right putamen, the left nucleus accumbens (Nacb) and the AC of both hemispheres, together

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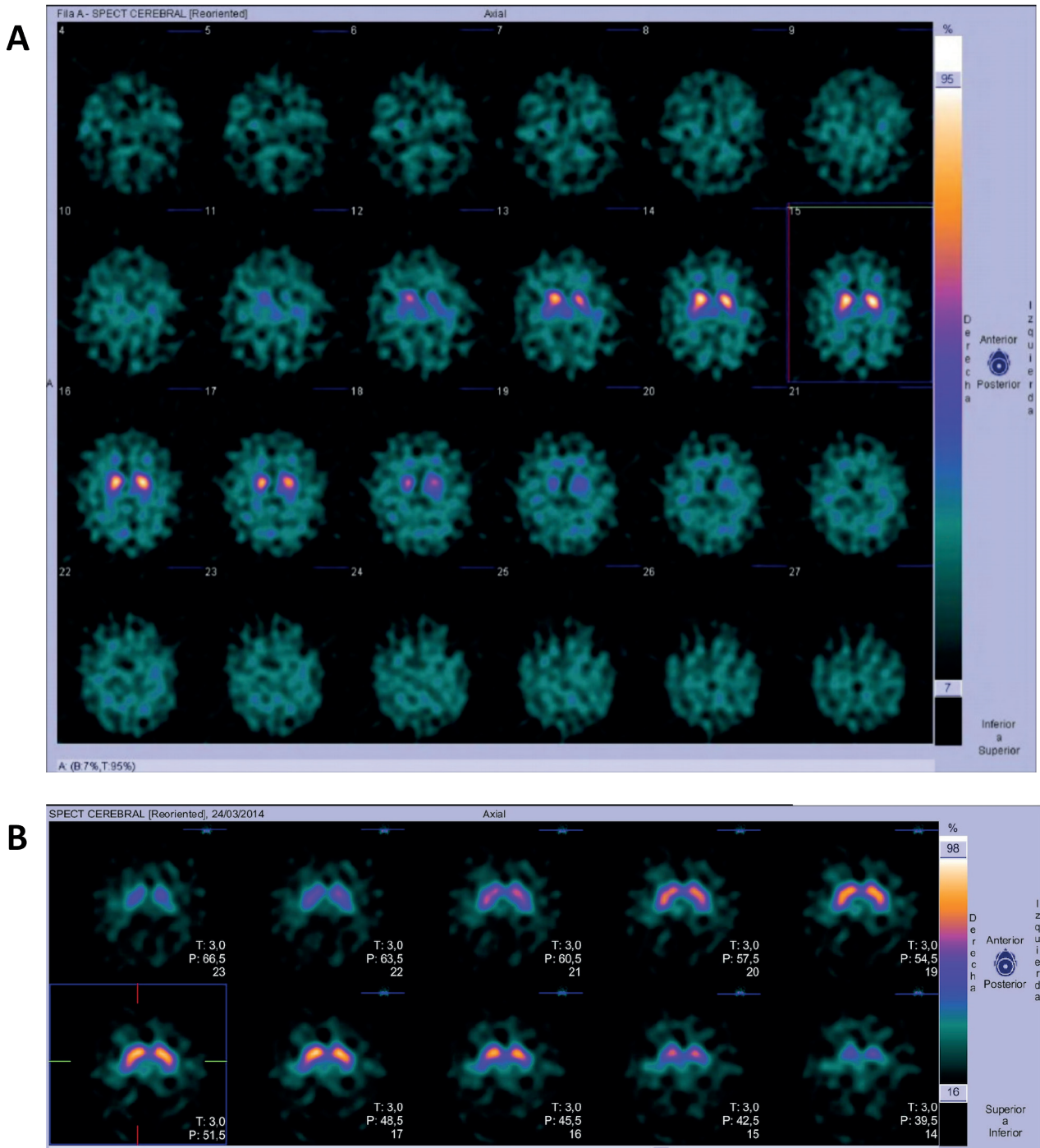


Figure 1. Axial view of SPECT with DaTscan A) performed on the patient in which a moderate decrease in the right putamen and a severe decrease in the left one of dopamine transporters, or B) performed on a patient of similar age without alterations in the basal ganglia.

with a marked reduction in the volume of the parietal and medial prefrontal cortices (mPFC), including orbital and ventromedial cortex. Thus, a monophotonic computed tomography (SPECT) of dopamine transporters (DAT) with Ioflupane-123 (DaTscan) was requested, in which a decrease in DAT was observed bilaterally in the presynaptic neurons of putamen, being moderate in the right and severe on the left (Figure 1), thus confirming the diagnosis of PD (de la Fuente-Fernandez, 2012) as a consequence of the structural changes produced by psychosurgery and

the subsequent neuroadaptations. After diagnosis, 60mg of propranolol per day was added to his usual treatment, showing slight improvement in tremors.

Although no association between psychosurgeries and PD has been described (most studies analyze postsurgical periods of 6 months to 2 years), side effects such as bradykinesia or gait alteration have been described in surgeries that have affected the dorsal striatum (putamen) (Yampolsky & Berdensky, 2014). On the other hand, a possible outcome of Nacb disconnection is a hypodopaminergic

state such as the one described here with the decrease in DAT, which has been associated in animal models with abnormal corticostriatal oscillations that can alter the striatal dopaminergic balance resulting in the release of alpha-synuclein whose accumulation plays a fundamental role in the pathogenesis of PD (Sharott, Vinciati, Nakamura & Magill, 2017). In addition, a neurodegeneration of the cerebral cortex such as that detected in the patient would be compatible with the hypothesis proposed by Foffani and Obeso (2018) which indicate that the origin of the prodromal focal motor symptoms, such as those observed in the patient, could be in a retrograde nigrostriatal degeneration initiated in the corticostriatal fibers.

In this letter we suggest that the extensive psychosurgery for cocaine addiction that the patient underwent not only had medium-term repercussions such as schizophrenia, but in the long term (15 years later) may also have triggered or contributed to an early and irreversible neurodegenerative process such as PD. It is unclear the extent to which the extensive cocaine abuse may also have contributed to the vulnerability of the dopamine neurons, or interacted with the other factors present. In the authors' opinion, surgery for behavioral disorders should be limited to exceptional cases due to the significant sequelae that can occur even after years; PD could be included among them.

Conflicts of interests

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Ethical aspects

Informed consent was obtained from the legal guardian and the patient for experimentation (neuroimaging) and publication.

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