

Demotivating outcome of asymmetrical Nucleus Accumbens disconnection for cocaine related disorder: a translational point of view

Desmotivadora evolución de la desconexión asimétrica del Núcleo Accumbens en el trastorno por consumo de cocaína: un punto de vista traslacional

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Dear Editor,
Neuroanatomical disconnection used in animals reveal that cortico-limbic-striatal circuit involving the medial prefrontal cortex (mPFC), the basolateral amygdala (BLA), and nucleus accumbens (Nacb) mediate decision-making processes (Salamone & Correa, 2012; Salamone, Yohn, López-Cruz, San Miguel & Correa, 2016). BLA projections modulate Nacb activity, and influence the direction of behavior toward relevant stimuli (Floresco, Blaha, Yang & Phillips, 2001). Disruption of activity in both the Nacb and BLA, as well as their communication, reduces preference for more effortful options, increases for riskier ones, with less motivated behavior (Salamone & Correa, 2012; Salamone et al., 2016).

With this letter, the authors present the history of a patient after extensive psychosurgery, including neuroimaging and neuropsychological assessment, and discussion from a translational point of view.

The patient was adopted few days after being born with dystocia. The biological-family history is unknown. His adoptive parents suffered from cocaine and alcohol-related disorder. During childhood, the patient had most symptoms of Attention Deficit Hyperactive Disorder (ADHD). He was described as an aggressive child and had a diagnostic of conduct disorder. At 14, he started cocaine consumption. At 16, he was diagnosed of “non-specified impulse control disorder” and cocaine-related disorder. His intelligence Quotient was 85. At 17, a psychiatrist diagnosed

the patient with a “mental disorder secondary to dystocia”. Magnetic resonance image (MRI) indicated atrophy of the left hemisphere. Positron emission tomography (PET) showed a moderate general reduction in brain metabolism. Based upon last diagnose and neuroimaging study, a neurosurgeon diagnosed the patient from “impulse control dysfunction” and “limbic dysfunction syndrome”, prescribing psychosurgery for the control of aggressiveness.

The neurosurgery consisted in thermal coagulation lesions induced by radiofrequency. The target regions were anterior cingulate (AC), anterior capsula, and stria terminalis of left hemisphere and anterior capsula and the amygdala of right hemisphere. A second surgery extending the lesions in left anterior capsula and right AC was performed two months later given a relapse in aggressiveness.

After psychosurgery, the aggressiveness persisted, and the patient started to have delusions. The patient alternated periods of cocaine and heroin consumption, with periods of permanence in penitentiary centers. He was diagnosed with paranoid schizophrenia without treatment adherence. At the age of 27, he showed predominant cognitive deficits and negative psychotic symptomatology.

Fifteen years after psychosurgery, at 32, a more thorough neuroimage exploration was performed (Figure 1). MRI showed abnormal cavities in right putamen, left Nacb, internal capsule and AC of both hemispheres. Tractography showed major impact on the connections among AC, Nacb and amygdala. Morphological analyses show a

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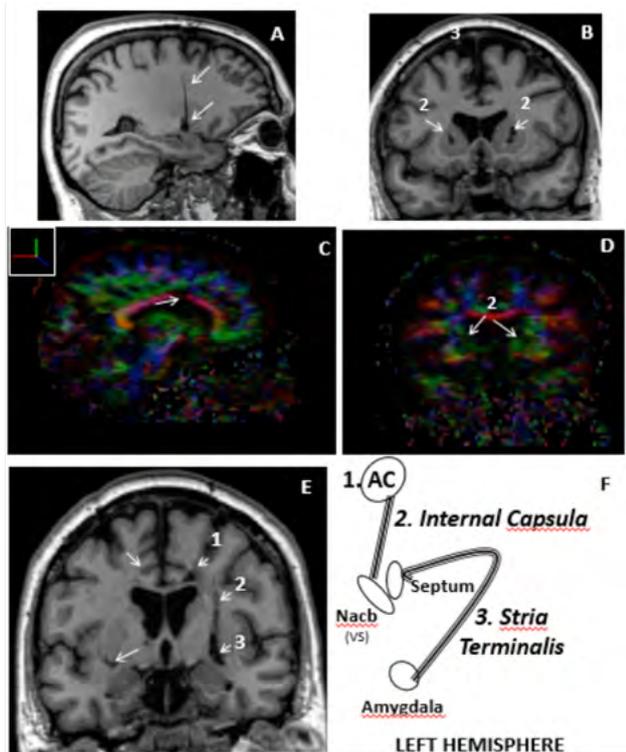


Figure 1.

MRI test performed 15 years after surgery (A, B and E). Tractography images showing impact on corpus callosum (C) and internal capsule fibers (D). (F) Schematic with the neurosurgery targets. The goal of the surgery was to inactivate AC and to disconnect it from ventral striatum (VS) and amygdala in both hemispheres, as well as to produce a lesion of the amygdala in the right hemisphere and disconnect amygdala output fibers in the left hemisphere.

marked reduction in the volume of parietal cortices and medial PFC, including ventromedial and orbital cortex. Furthermore, neuropsychological assessment (BIS-11, LSRP, IOWA gambling task and Tower of London) showed impairment of planning processes, difficulties in cost/benefit decision-making, psychopathic traits and high motor impulsivity.

Combined unilateral lesions of the mPFC and the Nacb in opposite hemispheres (disconnection) in animals reduced selection of effortful options and produced perseveration of behavior without integrating information from affective feedback (Salamone & Correa, 2012; Hauber & Sommer, 2009). Moreover, disconnection between mPFC and other striatal regions (e.g. medial caudate-putamen) impairs aspects of attentional function and habit-based memories (Phillips & Carr, 1988; Packard, Hirsh & White, 1989). In humans, functional connectivity between the AC and the Nacb, as well as, between AC and amygdala is relevant for decision-making and reward anticipation, respectively (Cohen, Heller & Ranganath, 2005; Marsh, Blair, Vythilingam, Busis & Blair, 2007). In addition, non-routine tasks, which require constant monitoring of new information to plan appropriate responses, are particularly susceptible to PFC damage. The patient has been reported to

have difficulties in acquiring new habits and shows difficulties in sustaining attention. Furthermore, neuropsychological assessment suggests impairment of planning processes and difficulties in cost/benefit decision-making. Hence, these behavioral patterns are consistent with the lesions performed during the surgery and the resulting damage observed in the recent images.

Barcia et al (2007) and Leiphart & Valone-III (2010) recognized that the most frequent psychosurgeries are anterior capsulotomy, which have been shown beneficial for general anxiety and obsessive-compulsive disorders, and anterior cingulotomy, which have shown improvements for depression, bipolar and schizoaffective disorders. However, addiction and schizophrenia had the lowest reported improvements, and there is evidence that combining more than one brain target may make the outcomes worse.

In this letter, we suggest that “impulse control dysfunction” and “limbic dysfunction syndrome” when the patient was adolescent could have been better defined as ADHD, conduct and cocaine-related disorders. These disorders have specific and effective non-surgical treatments. Fifteen years after psychosurgery, he developed Schizophrenia and aggressiveness persists. Furthermore, the patient presents increased choice of riskier options, an inability to integrate information related to affective feedback (punishment or reward), difficulties in acquiring new habits, and difficulties in sustaining attention. Taking into account the animal models, these functional impairments are partly due to the psychosurgery, which suggests an irreversible and demotivating prognosis.

Conflicts of interest

There are no conflicts of interest. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The Fundación de investigación del Hospital Provincial de Castellón has supported the open access. All authors contributed equally.

Ethical aspects

The ethical committee of Castellón Provincial Hospital Consortium approved the study, and an informed consent was obtained from the legal tutor and from the participant for experimentation (neuroimages and neuropsychological tests) and publication.

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