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Integrative function of single neurons in the human subthalamic nucleus during checking behavior

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Objective: To study the role of the subthalamic nucleus (STN) in the processing of cognitive information during checking behaviour in patients with obsessive compulsive behaviour (OCD).

Background: Human behavior depends on complex interactions between cognition and emotion. How does the brain combine these two dimensions to make a decision and elaborate a goal-directed action remains unclear. One hypothesis is that such an integrative process might occur owing to the convergence of information through the basal ganglia. Recently, the associative and limbic STN have been proposed as potential targets for deep brain stimulation in patients with medically-resistant form of OCD¹. We took the opportunity of the last study to investigate the role of STN neurons in the processing of cognitive information.

Methods: We used an instrumental task (CT), adapted from a matching to sample-task, that specifically offered the opportunity to verify once one subject has made a choice². Single unit neuronal activity was recorded in the STN whereas patients with obsessive compulsive disorders (OCD) performed the CT.

Results: Among 125 single neurons recorded during task performance, 45 (36%) were task-related. Modifications of activity were observed in relation with: visual information during the study phase (28%), the choice phase (22%), or the checking phase (20%), movement execution during the choice phase (37%), or the checking phase (35%) and during the evaluation phase at the end of the task (56%). We found that STN neurons frequently responded in a polymodal manner to cognitive, premotor and emotional events. Moreover, discharge frequency was influenced by checking behavior.

Conclusions: These results suggest that STN neurons process multiple sources of information in accordance with the model of information convergence within the basal ganglia. They also demonstrate that the STN play a part in the physiology of doubt, a critical feature of OCD pathophysiology. 1. Mallet L, et al. *STOC Study Group. N Engl J Med.* 2008 Nov 13;359(20):2121-34. 2. Rotge JY, et al., *Acta Psychiatr Scand.* 2008 Jun;117(6):465-73.

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Subthalamic neuronal activity in patients with obsessive-compulsive disorders or Parkinson's disease

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Objective: Study the subthalamic (STN) neuronal activity in patients with Obsessive Compulsive Disorders (OCD).

Background: Dysfunction in the basal ganglia circuitry has been implicated in obsessive and compulsive disorder (OCD). In a recent clinical research program, high frequency electrical stimulation of the STN has proved to be efficient in alleviating obsessions and compulsions in OCD patients and permitted to study neuronal activity in this disorder (Mallet et al, 2008).

Methods: Unit neuronal activity of STN neurons were recorded in awake OCD patients at rest and compared to data obtained in patients with Parkinson's disease (PD). The mean firing rate and interspike intervals were calculated for each cell. The firing pattern was classified as regular, irregular or bursting (Kaneoke and Vitek, 1996). Neuronal activity was also sampled for each period and epochs of elevated discharge rate were classified as burst using a Poisson surprise analysis. Spike trains with $S \geq 3$ were considered to be bursts. Percentages of action potentials and duration with $S \geq 3$ and mean S value were calculated for each cell. The precise localization of neuronal activity recordings was performed using a 3-D deformable basal ganglia atlas with a particular reference to STN sub-territories.

Results: 156 STN neurons were isolated in 11 OCD patients and 113 neurons in 10 PD patients. In comparison to PD, the mean discharge frequency of STN neurons was lower in OCD patient (24.1 ± 14.1 Hz vs 32.1 ± 17.7 Hz, $P < 10^{-3}$) with a higher burst type activity ($p < 0.03$). The mean S value was higher in OCD patients (7.0 ± 3.5 vs 5.9 ± 1.9 , $P < 10^{-2}$) with a higher mean percentage of action potentials (39.0 ± 13.5 vs 32.8 ± 14.4 %, $P < 10^{-3}$) and duration with $S \geq 3$ (17.7 ± 4.7 vs 14.9 ± 5.6 %, $P < 10^{-4}$).

Conclusions: In OCD patients, the subthalamic neuronal activity seems abnormal with an increase in the bursting type activity. This is in line with the hypothesis of the role of basal ganglia, and the subthalamic nucleus, in the physiopathology of this disorder. Mallet et al, *N Engl J Med*, 2008 Nov 13;359:2121-34. Kaneoke and Vitek, *J Neurosci Methods*, 1996 Oct;68:211-23.