nous orientent vers une poursuite de l'étude de la connectivité fonctionnelle dans le TOC, et notamment l'analyse de l'influence de différents paramètres cliniques (début des troubles, durée de la maladie, sous-type de TOC) sur cet aspect de la physiopathologie.
Mots clés TOC ; Connectivité fonctionnelle ; Striatum ventral ; ACC ; OFC ; hypoconnectivité

Déclaration d'intérêts Les auteurs déclarent ne pas avoir de conflits d'intérêts en relation avec cet article.

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P021

Translational approach to study flexibility as an endophenotype of obsessive compulsive disorders

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Behavioral flexibility is the ability of a subject to change its behavior according to contextual cues. In humans, Obsessive Compulsive Disorders (OCD) is characterized by repetitive behavior, performed through rigid rituals. This phenomenological observation has led to explore the idea that OCD patients may have diminished behavioral flexibility. To address this question we developed innovative translational approaches across multiple species, including human patients suffering from obsessive-compulsive disorders, and rodent genetic models of OCD to provide original data in the perspective of enlightening the neurocognitive bases of compulsive behaviors. Behavioral flexibility may be challenged in experimental tasks such as reversal learning paradigms. In these tasks, the subject has to respond to either of two different visual stimuli but only one stimulus is positively rewarded while the other is not. After this first association has been learned, reward contingency are inverted, so that the previously neutral stimulus is now rewarded, while the previously rewarded stimulus is not. Performance in reversal learning is indexed by the number of perseverative errors committed when participants maintain their response towards previously reinforced stimulus in spite of negative reward. Unsurprisingly, this behavioral task has been adapted to mice using various response modalities (T-maze, lever press, nose-poke). Using animal models of compulsive behaviors give much more possibilities to study the deficient functions and their underlying neural basis that could lead to pathological repetitive behaviors. Here we present new behavioral set-ups that we developed in parallel in human (i.e. healthy subjects and OCD patients) and mice (i.e. controls and SAPAP3-KO mice) to study the role of the behavioral flexibility as a possible endophenotype of OCD. We observed that the subjects suffering of compulsive behaviors showed perseverative maladaptive behaviors in these tasks. By comparing the results of a similar task-design in humans and mouse models we will discuss the pertinence of such translational approach to further study the neurocognitive basis of compulsive behaviors.
Keywords OCD; Flexibility; Animal models; Subthalamic nucleus; Deep-brain stimulation

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P022

Corpus callosum size may predict late-life depression in women: A 10-year follow-up study

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Background Recent research on late-life depression (LLD) pathophysiology suggests the implication of abnormalities in cerebral white matter [1] and particularly in interhemispheric transfer [2]. Corpus callosum (CC) is the main brain interhemispheric commissure [3]. Hence, we investigated the association between baseline CC measures and risk of LDD.
Methods We studied 467 non-demented individuals without LLD at baseline from a cohort of community-dwelling people aged 80 years or younger (the ESPRIT study). LLD was assessed at year 2, 4, 7 and 10 of the study follow-up. At baseline, T1-weighted magnetic resonance images were manually traced to measure the mid-sagittal areas of the anterior, mid and posterior CC. Multivariate Cox proportional hazards models stratified by sex were used to predict LLD incidence over 10 years.
Results A significant interaction between gender and CC size was found ($P = 0.02$). LLD incidence in elderly women, but not in men, was significantly associated with smaller anterior (HR 1.37 [1.05–1.79] $P = 0.017$), mid (HR 1.43 [1.09–1.86] $P = 0.008$), posterior (HR1.39 [1.12–1.74] $P = 0.002$) and total (HR 1.53 [1.16–2.00] $P = 0.002$) CC areas at baseline in Cox models adjusted for age, education, global cognitive impairment, ischemic pathologies, left-handedness, white matter lesion, intracranial volume and past depression.
Limitations The main limitation was the retrospective assessment of major depression.
Conclusions Smaller CC size is a predictive factor of incident LLD over 10 years in elderly women. Our finding suggests a possible role of CC and reduced interhemispheric connectivity in LLD pathophysiology. Extensive explorations are needed to clarify the mechanisms leading to CC morphometric changes in mood disorders.
Keywords Corpus callosum; Late-life depression; Magnetic resonance imaging; Elderly; Gender; Cohort study

Disclosure of interest The authors declare that they have no conflicts of interest concerning this article.

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