Title of the thesis	**fMRI-based closed-loop neurofeedback to relieve drug-resistant hallucinations in schizophrenia**
Acronym	NEUROFEEDBHAL
Reference number	006

Hosting institution	**Employer**
Université de Lille Website: https://www.univ-lille.fr/home/	INSERM Website: https://www.inserm.fr/en
Hosting research unit 1	**Hosting research unit 2**
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Thesis information

Keywords	Hallucinations, drug-resistance, fMRI capture, neurofeedback, brain-computer interface
Abstract	Neuropsychiatric disorders are the leading causes of disability and health costs in developed countries. Altogether, the direct and indirect costs of mental disorders amount to 199 M$ of health spending worldwide (WHO, 2008). Schizophrenia (SCZ), the most devastating neuropsychiatric disorder, is characterized by the presence of hallucinations, delusions, and cognitive deficits. More than 25% of SCZ patients show no or incomplete responses to current pharmacological or psychological remediation therapies for hallucinations. Refractory hallucinations have a deep impact on autonomy, life achievements and medical use, with complex multi-level social consequences. But after five decades without any significant therapeutic breakthrough, pharmaceutical industries have cut down their research investments on neuropsychiatric disorders while the medical needs remain unmet. On the other hand, non-invasive neuromodulation recently proved to be a safe and effective treatment for drug-resistant hallucinations. In this context, the NEUROFEEDBHAL project takes a translational stance to create and validate an innovative non-pharmacological therapy for intrusive pathological mental states in psychiatry. Real-time functional magnetic resonance imaging (rt-fMRI) is a novel brain imaging approach allowing for online feedbacks derived from mean brain activity in a priori regions. This technology, known as neurofeedback, already demonstrated its ability to alleviate chronic pain by training patients to voluntarily suppress brain activity in

	key regions. Hence, rt-fMRI and neurofeedback represent a significant step toward effective fMRI-based neurofeedback strategies to relieve invalidating subjective symptoms, such as psychotic symptoms by enhancing patient's ability to control over intrusive thoughts. However, intrusive thoughts emerge from complex and transient patterns of activity distributed brain-wide, which are not captured by conventional neurofeedback approaches. The NEUROFEEDBHAL project plans to address this issue by adapting multivariate decoding techniques to rt-fMRI, through developing and validating a robust real-time multivariate decoding algorithm for hallucinations during fMRI acquisitions and assess its therapeutic benefits and tolerance in Schizophrenia patients. The primary objective of the PhD project is to validate a classification algorithm for hallucination-related functional patterns achieving both robustness and high performances (Year 1 of the PhD). We already acquired fMRI data from SCZ patients (DSM-IV-TR) with frequent hallucinations to benchmark candidate classifiers. Three clinical groups have been recruited: those with auditory hallucinations (n=20, AH sample), those with audio-visual hallucinations (n=20, A+VH sample), and those without hallucinations (n=20, noH sample). Each above-mentioned category (AH, A+VH and noH), will be split into training and testing samples to compute leave-one-out cross-validated decoding performance estimates for several selected classifiers. During years 2 and 3 of the PhD, we will use the discriminative maps obtained from the classifiers to train SCZ patients with drug-resistant hallucinations to sustain the brain network associated with the H- condition. We will not only provide feedback on the brain states associated with H-/TRANS/H+/END periods but will also provide appropriate “coping strategies” to the participant, on a screen facing the subject head within the MRI scanner. To assess the efficacy of strategies, we will carry out a double-blind randomized controlled trial. The outcome measures will be scores on hallucinations and quality of life scales.
Expected profile of the candidate	The candidate must have a Master degree in Cognitive Psychology, Neuroscience, Computer Science or Artificial Intelligence with expertise in at least one of the following topics: programming (e.g., Matlab, Python), machine-learning, fMRI-data analysis, neurofeedback. Strong interests for psychiatry and therapeutics as well as verbal communication skills in English are required. Apart from the formal entry requirements, the selection will be based on previous experience, relevance of educational training, experimental approach to problem solving, commitment and skills for team-working and ability to integrate local teams. Your application must be written in English and include a Curriculum Vitae, a cover-letter indicating the research area of interest and your motivation, a transcript of courses and results from the highest university-level course taken, a short description of your Master’s work and contact information for 2 referees.
Application procedure	The application procedure is detailed on the European programme PEARL website www.pearl-phd-lille.eu. The funding is managed by the I-SITE ULNE foundation which is a partnership foundation between the University of Lille, Engineering schools, research organisms, the Institut Pasteur de Lille and the University hospital. The application file will have to be submitted before April 15, 2020 (10h Paris Time) and emailed to the following address : international@isite-ulne.fr.
Net salary and Lump Sum	A net salary of about €1,600 + €530 per month to cover mobility, travel and family costs.