Mental illness is by far the largest contributor to chronic illness in Europe, entailing half of all social welfare expenditure (WHO). However, neuropsychiatry lags behind other fields of medicine, both in the understanding of disease mechanisms and in the prediction of treatment response. This severely limits symptom recovery and people’s quality of life. With the present proposal, focused on the neuropeptide oxytocin (OT) and its promising pharmacological use, we aimed to improve both the pathophysiological and the therapeutic models of SCZ, with a focus on (the much neglected) social cognitive symptomatology.

This interdisciplinary project, was a double-blind and randomised-controlled pharmacological manipulation of OT, and a pharmacogenetics assessment of OT genetic influence, on brain function during a range of social tasks.
Team-wise, this project stemmed from a triangulation between: the host research institution (IBEB, FCUL/Fciencias.ID) and a novel academic-clinical collaboration with Psychiatric wards in 3 Lisbon hospitals/clinics.

Atividades

Several articles, and MSc theses, were published throughout the project by the project’s team, while fMRI data collection was being delayed (due to administrative delays, e.g. CAML’s Ethics Committee delayed response – which was aggravated by the COVID restrictions to clinical research). The team designed projects – from systematic reviews to original data studies using oxytocin pharmacological EEG and pupillometry, to existing data from collaborators. These projects, mostly all published, served to: 1) support the scouring of the state of the art in oxytocin and schizophrenia areas of research to improve the design of the study, 2) support the decisions regarding the analysis choices of the data collected during the project (for example, by comparing existing analytical tools and creating novel analytical tools), 3) support the interpretation of NEUROGENAI’s results, and 4) train the team in a range of skills from genetics, proteomics, machine learning and neuroimaging. Further publications, using pharmaco-fMRI and genetics with intranasal oxytocin randomized controlled administration involving schizophrenia patients, are being prepared and/or in submission to journals (as of May 2023).

In sum, the main activities were:

1) Literature systematization, skills training, methodological research and research on pre-existing databases, while ethics approval of NEUROGENAI was pending – which directly supported the current project’s research questions.
2) Oxytocin randomized controlled administration during EEG and pupillometry data collection with the same psychological paradigms later performed in the fMRI session – i.e. social reinforcement learning (salience) task, emotional video-clip task, emotion recognition task and resting state task - in healthy controls.
4) Exploration of recent statistical methodologies, a part from machine learning, such as the novel inter-subject-correlation analysis, for the analysis of the fMRI data.
5) For the fMRI session, schizophrenia patients were recruited at the Julio de Matos (CHPL) hospital and their data was collected (with healthy volunteers) in the CUF Infante Santo hospital. For the EEG and pupillometry session, data (only for healthy volunteers) was collected at ISCTE-IUL university with collaboration from SAMS.
The published articles are (all with pdf. readily available at https://dpratalab.wordpress.com/papers):


The published MSc theses are:


Simoes B. 2018. The influence of a schizophrenia polygenic risk score on white matter microstructure in schizophrenia, bipolar disorder and health. MSc Thesis.


Chesi D. (Maastricht University, The Netherlands). 2022. The influence of oxytocin on social cognition and symptom severity in schizophrenia. MSc Thesis.