Designação do Projeto|	NEUROGENAI: Oxitocina intranasal para a psicopatologia social: mecanismos de acção e biomarcadores preditivos usando neuroimagiologia, genética e inteligência artificial
Código do Projeto|	LISBOA-01-0145-FEDER-030907
Objetivo Principal|	Reforçar a investigação, o desenvolvimento tecnológico e a inovação
Região de Intervenção|	Lisboa
Entidade Beneficiária|	FCiências.ID – Associação para a Investigação e Desenvolvimento de Ciências
Data de Aprovação|	13-03-2018
Data de Início|	12-06-2018
Data de Conclusão|	11-06-2022
Custo Total Elegível|	239.788,40€
Apoio Financeiro da União Europeia|	FEDER – 95.915,36€
Apoio Financeiro Público Nacional/ Regional|	OE – 143.873,04€

Objetivos

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 pupilometry 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.

Resultados Atingidos

The published articles are (all with pdf. readily available at https://dpratalab.wordpress.com/papers):

Castro Santos H; Rodrigues A, Ferreira S, Malhadas Martins M, Baptista T, Gama Marques J, Kirkpatrick B, **PRATA D.** The European Portuguese version of the Brief Negative Symptom Scale. ***Psychopathology***. In press.

Cosme G, Arriaga P, Rosa PJ, Mehta M, **PRATA D.** Temporal profile of intranasal oxytocin in the human autonomic nervous system at rest: an electrocardiography and pupillometry study. ***Journal of Psychopharmacology.*** *2023. 2698811231158233. doi:10.1177/02698811231158233*

Cogoni C, Fiuza A, Hassanein L, Antunes M, **PRATA D.** Computer anthropomorphisation in a socio-economic dilemma. ***Behavior Research Methods***. 2023. 10.3758/s13428-023-02071-y. doi:10.3758/s13428-023-02071-y

PRATA D, Silva M. Neuroimaging genetics of oxytocin: a transcriptomics-informed systematic review. ***Neuroscience and Biobehavioral Reviews*.** 2022. 142 – 104912

Vouga Ribeiro N, Tavares V, Bramon E, Toulopoulou T, Valli I, Shergill S, Murray R, **PRATA D.** Effects of psychosis-associated genetic markers on brain volumetry: A systematic review of replicated findings and an independent validation. ***Psychological Medicine.*** 2022. 1-16.

Zelenina M*, Kosilo M*, da Cruz J, Antunes M, Figueiredo P, Mehta M, **PRATA D.** Temporal dynamics of intranasal oxytocin in human brain electrophysiology. ***Cerebral Cortex.*** *2022.* 32(14):3110-3126*. *Equal contribution*

Kosilo M, Costa M, Nuttall H, Ferreira H, Scott S, Meneres S, Pestana J, Jerónimo R, **PRATA D**. The neural basis of authenticity recognition in laughter and crying. ***Scientific Reports (Nature Research).*** *2021. 11:23750.*

Tavares V, Monteiro J, Vassos E, Coleman J, **PRATA D.** Evaluation of genotype-based gene expression model performance: a cross-framework and cross-dataset study. ***Genes.*** 2021, 12(10), 1531.

Neto ML, Antunes M, Lopes M, Ferreira D, Rilling J, **PRATA D**. Oxytocin and vasopressin modulation of Prisoner's Dilemma strategies. ***Journal of Psychopharmacology.*** 2020. 34 (8): 891-900. IF: 4.2.

Simões B, Vassos E , Shergill S , McDonald C, Toulopoulou T , Kalidindi S, Kane K , Murray R, Bramon E, Ferreira H, **PRATA D.** Schizophrenia polygenic risk score influence on white matter microstructure. ***Journal of Psychiatric Research*.** 2020. 121:62-67. IF: 4.4.

PRATA D, Cosme G*, Costa-Neves B*, Vassos E**.** **Equal contribution.* Unravelling the genetic basis of schizophrenia and bipolar disorder with GWAS: a systematic review. ***Journal of Psychiatric Research***. 2019. 114:178-207. IF: 4.4.

Torres N*, Martins D*, Santos A, Veríssimo M**, **PRATA D**.** How do hypothalamic nonapeptides shape youth's sociality? A systematic review on oxytocin, vasopressin and human socio-emotional development. ***Neuroscience & Biobehavioral Reviews.*** 2018. *IF: 8.3. * ,**: Equal contribution.*

Tecelao D, Mendes A, Martins D, Bramon E, Toulopoulou T, Kravariti E, Murray R, **PRATA D**. The impact of psychosis genome-wide associated ZNF804A variation on verbal fluency connectivity. ***Journal of Psychiatric Research.*** *2018. 98:17-21. IF: 4.4*

The published MSc theses are:

Costa M. 2018. Authenticity Recognition in Laughter and Crying: An ERP Study. MSc Thesis.

Guerra L. 2018. Reinforcement Learning models of neuropeptide-modulated human brain function. MSc Thesis.

Zelenina M. 2018. Temporal Dynamics of Oxytocin: a Human Electroencephalography Study.MSc Thesis.

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

Monteiro J. 2020. Optimization and validation of a new gene-based eQTL score tool using brain transcriptome datasets. MSc Thesis.

Rafael Esteves. 2021. Effects of intranasal oxytocin administration on the salience of social stimuli: A pupillometry study. MSc Thesis.

Andreia Santiago. 2022. Effects of intranasal oxytocin administration on the salience of social stimuli: A ERP study. MSc Thesis.

Simoes J. 2022. Neural Response Effects of Oxytocin and Vasopressin on Human Learning for Social Cooperation. MSc Thesis.

Jensma A (VU University Amsterdam, The Netherlands). 2022. Absence of modulatory effect on the relative amplitude of neural frequencies after oxytocin administration during rest. MSc Thesis.

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