

PROTOCOL N ° 2

Title: Quantitative assessment of the activation of brain areas with positive and negative emotional stimuli and its correlation with degrees of emotional disorder.

NCT number: not yet assigned

Document date: 06/01/2021

Updated: 10/11/2021

INCOR IMAGES - Bazan y Bustos 132. La Rioja (5300)

Main investigator: Ruben Novoa, MD Head of Magnetic Resonance Imaging at Incor Images.
rubennnovoa@gmail.com Tel: 3804509777

Collaborators: Graduates in production of Bioimages Maribel Oliva, Ivana Ceressa and Paolo Paez from the Magnetic Resonance Imaging Area of Incor Images.

REFERENTIAL FRAME

The technology applied in functional magnetic resonance imaging allows us to visualize on a color scale the changes in the blood flow of those sectors of the brain that increase their metabolic activity during a given action. This is achieved by mapping the volume of cerebral blood, known by its acronym in English as CBV (cerebral blood volume), which increases or decreases according to the metabolic activity in a certain region of the brain. This indirect method of measuring the metabolic activity of brain areas is very useful for anatomically identifying motor areas and critical functions in individual patients prior to neurosurgery, to allow better surgical planning. Currently this is its main application in healthcare practice. In the field of research it is applied in clinical neurology, psychiatry and psychology. Studies have been conducted on the activations of brain regions in basic emotions. There is less data on the quantitative differences of these activations in the Argentine population according to the degree of emotional disorder, this being the object of study of this project.

JUSTIFICATION

By comparing the findings of clinically of participants with different degrees of emotional disorder, treatment strategies can be developed based on the functional findings obtained.

PROBLEM STATEMENT

The diversity of feelings derived from basic emotions and the many possible combinations of their effects in emotional disorders, may mean that generic treatments for different clinical syndromes do not have the same efficacy in all patients. A more detailed study of the type and magnitude of brain activation related to the degree of emotional disorder will allow the development of personalized treatment strategies focused on obtaining better therapeutic results.

RESEARCH QUESTION

Are there differences in the activation of brain areas with positive and negative emotional stimuli that are related to the degree of emotional disorder that can be used in symptomatic patients to develop personalized treatment strategies?

GENERAL AND SPECIFIC OBJECTIVE

The general objective is to demonstrate the relationship between the activation of brain areas and its intensity with the degree of emotional disturbance. In turn, the recognized patterns will be compared with the different degrees of emotional disorder determined by a validated survey, to try to determine the weight of the emotional disorder on each type of activation according to the stimulus received as a specific objective on each one of them in particular.

HYPOTHESIS

The activation of specific brain areas follows common patterns for basic emotions and their derived feelings depending on whether they are positive or negative emotions, while in patients with emotional deficits the activation patterns are different and this difference can manifest itself in specific emotions.

METHODOLOGY TYPE OF STUDY

Initial exploratory, observational, cross-sectional study.

UNIVERSE

Population of the City of La Rioja.

SAMPLE

We estimate that 13 participants would give the study more than 80% power to detect a change between measures of 5% or more, using a linear mixed model for repeated measures, with a type I error of 5% (3).

INCLUSION, EXCLUSION AND ELIMINATION CRITERIA

Volunteers who express their informed consent to participate in the research protocol will be included. The exclusion criteria will be the impossibility of the patient to actively collaborate with the tests to be carried out for the measurement of emotional responses and / or the conditions that represent contraindications for carrying out MRI studies in general. The elimination criterion will be the appearance of any of the two exclusion criteria mentioned at any time during the development of the research.

OPERATIONALIZATION OF VARIABLES

Variable: increased metabolism of a brain area before the application of an emotional stimulus. The stimuli will be generated by paradigms designed to generate positive and negative emotional responses, using audiovisual material constituted by fragments of films validated for the local population (9), following in all cases the quality requirements of paradigms defined by the American Society of Functional Neuroradiology (ASFNR).

Type of variable: dependent, controlled.

Origin of the variable: attributive.

Operational definition: the increase in metabolism in a given brain area is indirectly quantified through mapping the brain blood volume in that area in relation to a stimulus. Indicator: The comparative mapping will be the input to determine the indicator in the comparative assessment of patients according to their score in the variable on emotional disorders. Measurement level: ratio or proportion.

Variable: The categorization of the volunteers by score for levels of emotional disturbance using the 37-question version of the CESIM, validated for the local population (10).

MEASUREMENT TOOLS

Philips Prodiva resonator, year of manufacture 2018, with 1.5 Tesla magnetic field, BOLD sequence, for the measurement of blood flow variations as an indirect parameter of the metabolic activation of specific brain areas, post-processing software incorporated in the resonator, sound circuit compatible with the resonance room for auditory stimuli and external projection of images with mirror system for visual stimuli.

INFORMATION ACQUISITION

The training of Graduates in Production of Bioimages for the application of the fMRI paradigms will be in charge of the principal investigator. The design of the paradigms will be carried out by the principal investigator. At the time of the study, the acquisitions during the implementation of the paradigms will be made by the Graduates in Bioimagenes Production under the supervision of the researchers. The CESIM 37 questionnaires will be filled out by the participants prior to obtaining the fMRI images.

The technical parameters in the acquisition of the fMRI images will be the following: Volumetric acquisition in T1 will be made with a 1.2 mm slice thickness without gap, with TR 7000.0 and TE 154.9.

Two BOLD acquisitions will be made, the first with a positive stimulus and the second with a negative stimulus, obtaining in each one the slices with a 4 mm slice thickness without gap, TR 3000.0 and TE 50.0

The positive and negative paradigms have duration of 250 seconds each, with an initial rest period of 80 seconds, a validated video projection for 140 seconds and a final rest period of 30 seconds for the positive stimulus and 80-130-40 seconds for the negative stimulus.

STATISTICAL ANALYSIS PROGRAM

The final data processing will be carried out with statistical tools to quantitatively compare the activation areas in the different clinical scenarios according to the type of stimulus administered. The activation areas before the positive and negative stimulus will be quantified in cm³ and fMRI Z-score and correlated with the score of the emotional questionnaire. Pierson's correlation coefficient will be used for data of normal distribution or Spearman in case of not having normal distribution.

PLAN FOR THE PRESENTATION OF THE INFORMATION

Starting on July 1, 2021, it is planned to provide the Committee with information on the progress of the project every 30 days, namely on 8/1, 9/1, 10/1 and 11/1, 2021 to later present the final report.

SCHEDULE OF ACTIVITIES

Calibration and fine-tuning of the enabled software and tests in healthy volunteers of the auditory and visual paradigms developed by the researchers. From 7/1/21 to 7/25/21. fMRI sessions for the quantification of emotions in different parameters with healthy volunteers. From 7/28/21 to 10/30/21.

Statistical post-processing of results from 11/01/21 to 11/22/21. Presentation of the final report on 11/30/21 and subsequent submission to a scientific journal for consideration of its publication.

BUDGET

The use of the BOLD sequence to perform fMRI is provided free of charge by Philips for a limited period of time for the purposes of carrying out this research protocol. No disposables or medications are used. The necessary elements for the construction of paradigms, stationery, etc. they will be contributed by the researchers. No expenses are generated for

Incor, except for the use of the room, light, etc., during the MRI acquisitions that will be carried out at specific times without interfering with the healthcare task.

ETHICAL CONSIDERATIONS

The informed consent of each volunteer participant will be requested, including a personal interview to clarify any doubts that may arise and explain in detail and clearly the characteristics of the study. Attached is a letter of adherence to the 2013 Declaration of Helsinki. The researcher's Certificate of Ethics issued by the La Rioja Council of Physicians is attached. The protocol is presented for evaluation by INCOR's Ethics Committee.

BIBLIOGRAPHY

1-Ríos, M. Neurosychology and Functional Magnetic Resonance. Radiology. Volume 50, Issue 5, October 2008 , , pages 351-365. doi: 10.1016 / S0033-8338 (08) 76050-8

2-Posner, J. The neurophysiological bases of emotion: An fMRI study of the affective circumplex using emotion-denoting words. Hum Brain Mapp. 2009 Mar; 30 (3): 883–895.

3-Gur RE, Gur RC. Functional magnetic resonance imaging in schizophrenia. Dialogues Clin Neurosci. 2010; 12 (3): 333-343. doi: 10.31887 / DCNS.2010.12.3 / rgur

4-Kassam, K. Identifying Emotions on the Basis of Neural Activation. PLOS ONE

Published: June 19, 2013 <https://doi.org/10.1371/journal.pone.0066032>

5-Kevin S. LaBar: Multivariate neural biomarkers of emotional states are categorically distinct. Social Cognitive and Affective Neuroscience (2015). DOI: 10.1093 / scan / nsv032

6-Kragel PA, Knott AR, Hariri AR, LaBar KS (2016) Decoding Spontaneous Emotional States in the Human Brain. PLOS Biology 14 (9): e2000106.

<https://doi.org/10.1371/journal.pbio.2000106>

7-Gu, S. An Integrative Way for Studying Neural Basis of Basic Emotions With fMRI. Front. Neurosci., June 19, 2019 | <https://doi.org/10.3389/fnins.2019.00628>

8-Shunta - Cocha, F. Validation of an abstract reasoning paradigm for Functional Magnetic Resonance (fMRI). Ecuadorian Journal Neurology Vol. 29, No 2, 2020.

9-Michelini, Y. Characteristics of the emotional experience induced by film fragments in a sample of young Argentines. Interdisciplinary, 2015, 32, 2, 367-382.

10-Muñoz Rodriguez M, Korzeniowski C (2019) Validation of the epidemiological questionnaire in mental symptoms -CESIM- in the Argentine population. Journal of Public Health, (XXIII) 2: 8-24 June 2019