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Data Descriptor

Microstructural and Metabolic Recovery of Anhedonic Rat Brains: An In Vivo Diffusion MRI and ^{1}H-MRS Approach

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Abstract: This article presents longitudinal ^{1}H-MR Spectroscopy (^{1}H-MRS) data from ventral hippocampus and in vivo diffusion MRI (dMRI) data of the brain from control and anhedonic rats. The ^{1}H-MRS and dMRI data were acquired using a 9.4 T preclinical imaging system. Before MRI experiments, animals were exposed to unpredictable chronic mild stress exposure for eight weeks and on the basis of a sucrose consumption test were identified as anhedonic and resilient. An age-matched group of animals, unexposed to the unpredictable chronic mild stress paradigm was considered as control. Data was acquired at the age of 18, 20 and 25 weeks in the anhedonic group and at the age of 18 and 22 weeks in the control group. This multimodal MRI data provides metabolic information of ventral hippocampus and dMRI based microstructural parameters of the brain.

Dataset: https://data.mendeley.com/datasets/jwyzdxxcbr/draft?a=1d82f079-e559-4a74-9764-fa2c9bed27df

Keywords: diffusion MRI; ^{1}H-MRS; chronic mild stress; kurtosis; hippocampus; amygdala

1. Summary

Chronic exposure to mild stressors (CMS) may lead to depression and other psychiatric disorders [1]. Unpredictable CMS exposure on rats is considered as a realistic model with demonstrated face, predictive, etiological and construct validity [2]. The animal model of depression can help to elucidate underlying metabolic and microstructural alterations in stress sensitive regions of the brain in comparison to controls. Stress sensitive brain regions, such as the hippocampus [3,4], prefrontal cortex [5,6], amygdala [7,8] and caudate putamen [9] have shown microstructural alterations in cadaver brains of patients with depressive disorder and in the brains of the animal model of depression. However, longitudinal assessment of recovery in metabolic and microstructural alterations are largely overlooked even though they can provide complementary information for treatment and management of depression. The article presented here utilized an in vivo diffusion MRI (dMRI) based approach to assess microstructural recovery of the stress sensitive brain regions and metabolic recovery of a ventral hippocampal region in CMS-induced anhedonic rats in comparison to age matched controls. Rats were identified as anhedonic on the basis of the sucrose consumption test during an eight-week long CMS paradigm [2]. Anhedonic rats were longitudinally scanned under in vivo MRI at the age

of 18, 20 and 25 weeks post- CMS paradigm. Control animals were also scanned at the age of 18 and 22 weeks. The findings of this study are published elsewhere [10], briefly, ^{1}H-MRS of ventral hippocampus showed enhanced NAA levels at week 3 post-CMS exposure, while the hippocampus and the amygdala showed microstructural alterations until 5 weeks post-stress exposure. Most of the metabolic and microstructural alterations at week 25 seem normalized in comparison to the controls. The data provided here could be useful for researchers planning a neuroimaging study of an animal model of depression or for doing follow-up analysis as it may provide insight into the neuroimaging of depression, which is useful for diagnosis or prognosis of patients with depressive disorder.

2. Data Description

The d-MRI parameter zip file contains formatted Excel sheets with values of the diffusion tensor metrics (axial diffusivity (AD), radial diffusivity (RD), fractional anisotropy (FA), and mean diffusivity (MD)) [11], and fast diffusion kurtosis metrics (mean of kurtosis tensor (MKT) [12] radial kurtosis tensor (W_T), and axial kurtosis tensor (W_L) [13]. Each column of the Excel sheets represents parametric values obtained from an animal and rows represents the number of voxels. The zip file contains a separate Excel file for each of the fitting parameters for each of the four regions of interest (ROIs): prefrontal cortex (PFC), hippocampus (HP), caudate putamen (CP) and the amygdala (AM). Consequently, each Excel file is named after the parameter and ROI (parameter_ROI). Each file provides data from different time points in separate Excel sheets. For the control group these sheets are labeled Ctr_Week18 and Ctr_Week22 and for the anhedonic group, Anh_week18, Anh_Week20, and Anh_week25.

The ^{1}H MRS_parameters zip file contains an Excel file with five Excel sheets. Each Excel sheet is named after a group (control (Ctr), anhedonic (Anh)) and the corresponding time point (Week 18, Week 20, Week 22 and Week 25). After the name of the group (Ctr/Anh), A1–A7 represent animal 1 to animal 7 of the corresponding group. The data contains the absolute concentration in the first column, Cramer-Rao lower bound (CRLB) in the second column, normalized metabolite concentration with total creatinine (Cr + PCr) in the third column and the name of the metabolites in the fourth column for each animal. The metabolites with >20% CRLB value were not included in the ^{1}H-MRS data. All raw ^{1}H-MRS and dMRI datasets are also available through the dataset link and may be used for alternative data analysis or comparison of the data.

3. Methods

Long Evans rats were exposed to a CMS paradigm for eight weeks and were identified as anhedonic (CMS responders) and resilient (CMS non-responders) based on a weekly sucrose consumption test [2]. After completion of the CMS paradigm, only anhedonic animals (n = 8) were scanned at the age of 18, 20 and 25 weeks, and an age matched control group (n = 8) was scanned at the age of 18 and 22 weeks using a preclinical MRI system (Bruker, Germany). The data of one animal in each group and at each time point had motion artifacts, therefore it not included in the data analysis. All experiments and animal handling were conducted in accordance with the national guidelines for animal research with permission from the Animal Experiments Inspectorate of the Danish Ministry of Food, Agriculture, and Fisheries, Denmark (2013-15-2934-00814)1H4.

3.1. ^{1}H Magnetic Resonance Spectroscopy (^{1}H-MRS) Acquisition and Analysis

In vivo ^{1}H-MRS data was acquired from the left ventral hippocampus of the rat brain using PRESS (Point resolved spectroscopy sequence) with TR/TE 5000/16 ms and 512 averages spanning 42 min of scan time. High-resolution anatomical images were used as reference images to place the voxel. Magnetic field homogeneity and water suppression pulses were optimized before spectrum acquisition. After data acquisition, zero and first-order phase corrections were applied to all in vivo spectra using the program LC model [14]. Subsequently, metabolite concentrations were estimated by referencing a "basis set" based on in vitro spectra. The LC model also outputs uncertainties of the metabolite concentration estimates in the form of Cramer-Rao lower bounds (CRLB).

3.2. d-MRI Acquisition and Analysis

In vivo d-MRI data was acquired with a fast kurtosis acquisition scheme described previously [10,15]. Briefly, data were acquired using a segmented EPI sequence (four segments) with parameters: diffusion times (δ/Δ) of 6ms/14ms, b-values 1.0 ms/μm^2 and 2.5 ms/μm^2 with three b0 images and nine directions (directions tabled in [13]). Other scan parameters were TR/TE = 2237/27 ms, number of slices = 38, isotropic resolution = 300 µm, matrix size = 128 × 64. Twenty averages were acquired, resulting in a total scan time of 1 h and 10 minutes. Saturation slices were placed in all the three orthogonal imaging planes to reduce motion artifacts during the MRI experiments. The d-MRI data were denoised [16] and corrected for Gibbs ringing artifact [17] in Matlab (The Mathworks, Natick, MA), before parameter estimation. The region of interest (ROIs) were manually delineated on b0 images of each dataset, according to the coordinates mentioned in the rat brain atlas [18] and literature [19,20] for each ROI. The statistical analysis of the data were also performed in Matlab using linear mixed model analysis, with animals as a random effect and group as fixed effect described elsewhere [7,10,21].

4. User Notes

The d-MRI data can be further analyzed to explore microstructural alterations and CMS recovery in any region of interest in the brain with other analysis methods. ^{1}H-MRS data from the ventral hippocampus can also be further analyzed with different post-processing methods to explore the consistency of the data or to compare with another dataset.

Supplementary Materials: 1: d-MRI_Parameters; 2. 1H_MRS_Paramteres are available at: http://www.mdpi.com/2306-5729/3/3/29/s1.

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