INTERFEAR: Investigating the endogenous metabolite butyrate as an epigenetic modulator of fear memory

A Data Management Plan created using DMPonline.be

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Project abstract:

Maladaptive emotional memories contribute significantly to anxiety disorders. A novel strategy to treat anxiety disorders is utilizing agents that boost learning and memory mechanisms to promote long-term fear inhibition and support relapse prevention. Increasing histone acetylation, an epigenetic catalyzer of memory-enhancing gene transcription, is critical in (emotional) memory formation, and can be potentiated by histone deacetylase inhibitors (HDACis). However, human studies using HDACis are scarce and there is a pressing translational need for testing well-tolerated yet potent HDACis. Butyrate, an HDACi originating from microbial fermentation of dietary fiber in our large intestine, exerts potent effects on fear acquisition and extinction in rodent studies. In a sample of 146 healthy male participants, I found that blood levels of butyrate are positively associated with psychophysiological responses during fear memory acquisition. Building on these findings, my proposal addresses the translational gap in the role of HDACis in fear acquisition and (persistence of) extinction in humans by a) establishing a causal role of butyrate in fear acquisition and investigating HDAC inhibition as a mechanism of action, and b) examining the effects of butyrate on fear extinction and prevention of the return of fear. I hypothesize that butyrate will potentiate long-term fear acquisition/extinction memory retrieval as assessed using a Pavlovian fear conditioning paradigm.

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FWO DMP (Flemish Standard DMP)

1. Research Data Summary

List and describe all datasets or research materials that you plan to generate/collect or reuse during your research project. For each dataset or data type (observational, experimental etc.), provide a short name & description (sufficient for yourself to know what data it is about), indicate whether the data are newly generated/collected or reused, digital or physical, also indicate the type of the data (the kind of content), its technical format (file extension), and an estimate of the upper limit of the volume of the data.

				Only for digital data	Only for digital data	Only for digital data	Only for physical data
Dataset Name	Description	New or reused	Digital or Physical	Digital Data Type	Digital Data format	Digital data volume (MB/GB/TB)	Physical volume
Personal Data	Names, e-mail address, address, financial details, phone number, age, gender, height, weight, health data (diagnoses and symptoms, medication use, physiological data, data about mental health). This is created following: Signing informed consent, filling in forms in REDCAP, providing financial details for reimbursement	Generate new data	Digital	Observational	Text/numeric (coded, e.g., 1=Female); stored in RedCAP	50 MB max	
Evoked psychophysiological responses	Electrodermal activity; ratings of presented stimuli. This is created from Skin conductance responses from EDA data collected using AqKnowledge/Biopac (2000 Hz); subjective expectancy ratings called using Psychopy	Generate new data	Digital	Observational Experimental	Numeric; .acq file transferred to .xslx, .csv, .docx, .or .txt files.	max 1 TB	
Psychological and physical traits, states, symptoms	General anxiety; Depression; Personality dispositions (intolerance of uncertainty and distress tolerance); state and trait anxiety; gastrointestinal symptoms; generic assessment of side effects. To create this data, participants fill in the following questionnaires in REDCAP: Self-reported Questionnaires (GAD-7; PHQ-9; IUS-12; DTS-15; STAI; GASE; GSRS)	Generate new data	Digital	Observational Experimental	Numeric; stored in RedCAP	50 MB max	
Brain images	raw and processed structural MRI, fMRI, and PET images. To create this data, participants undergo PET/MR scanning. Processed images are generated using pipelines consisting of conversion to NIfTI, preprocessing (fMRIprep), and custom Matlab scripts	Generate new data	Digital	Observational Experimental	DICOM, stored in Brain Imaging Data Structure (BIDS) format, NIfTI (.nii), stored in BIDS format	max 1 TB	

If you reuse existing data, please specify the source, preferably by using a persistent identifier (e.g. DOI, Handle, URL etc.) per dataset or data type:

Not applicable.

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? Describe these issues in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes, human subject data

WP1:
Privacy Registry Reference: G-2023-7078-R2(AMD)
Medical Ethics Committee dossier S68430
Approval dates: 07/03/2024 and 12/03/2024 respectively.
WP2: Dossiers will be sent for approval prior to starting WP2.

Will you process personal data? If so, briefly describe the kind of personal data you will use in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes

Names, e-mail address, address, financial details (bank account number for reimbursement), phone number, age, gender, height, weight, health data (diagnoses and symptoms, medication use, physiological data, data about mental health), evoked psychophysiological responses (Electrodermal activity; ratings of presented stimuli during a task), brain images (PET and MR images). These data will be coded and thus pseudonymized, and stored on encrypted, password-protected KU Leuven restricted network, laptop, and/or backup hard-drives managed by the KU Leuven ICT facility.

Does your work have potential for commercial valorization (e.g. tech transfer, for example spin-offs, commercial exploitation, …)? If so, please comment per dataset or data type where appropriate.

- No

Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material/Data transfer agreements/ research collaboration agreements)? If so, please explain in the comment section to what data they relate and what restrictions are in place.

- No

The participants themselves are the only 3rd party. Agreements are thus part of the informed consent, mentioning the publication of results in scientific communications and the (re)use of data by other researchers.

Are there any other legal issues, such as intellectual property rights and ownership, to be managed related to the data you (re)use? If so, please explain in the comment section to what data they relate and which restrictions will be asserted.

- No

2. Documentation and Metadata

Clearly describe what approach will be followed to capture the accompanying information necessary to keep data understandable and usable, for yourself and others, now and in the future (e.g., in terms of documentation levels and types required, procedures used, Electronic Lab Notebooks, README.txt files, Codebook.tsv etc. where this information is recorded).

1. Data will be anonymized and uploaded onto the Open Science Framework (OSF) along with relevant code (see below for examples).
2. Raw data files will be kept in a common structure with individual data-files stored within participant sub-folders per experiment. Extracted data will be stored within separate participant sub-folders and aggregated data will be stored under the experiment parent- folder. A README.txt file will be present to explain this structure in the parent folder of each WP.
3. Evoked psychophysiological responses – raw psychophysiological data from AqKnowledge and Psychopy will be collected per participant and stored with a .txt file with a clear description of what the data are and how they were generated (e.g., the input, frequency, run time, setting, etc.). Data will be transcribed from its raw format to readable format will be stored and uploaded onto OSF.

4. Psychological and physical traits, states, symptoms – raw data will be collected and stored in RedCAP. It will be later extracted into .txt or .xlsx files and published on OSF.

5. Brain images - Processed images are generated using pipelines consisting of conversion to NIfTI, preprocessing (fMRIprep), and custom Matlab scripts. The scripts used to this end will be shared on OSF.

6. We will create and keep a Standard Operating Procedure (SOP) for the set up and analysis of the experiment and we will extensively document study design and research procedures, including the settings of data collection, participant selection, equipment details and settings, sampling methodology, specification of the raw data file names (which measures they refer to), information that describes the variable codes (referring to type and time of specific measurements) and used analyses methods, as well as any other information necessary for a secondary analyst to use the data accurately and effectively.

Will a metadata standard be used to make it easier to find and reuse the data? If so, please specify (where appropriate per dataset or data type) which metadata standard will be used. If not, please specify (where appropriate per dataset or data type) which metadata will be created to make the data easier to find and reuse.

- Yes

Where possible, metadata standards will be used, or if unavailable, the experimental and data analysis metadata will be stored in a structed manner alongside our research data in .csv, .docx, .xslx or .txt files (e.g. “README” files for each distinct dataset), based on commonly used terminology in the relevant fields.For the (f)MRI data, metadata are included in the BIDS file format. For the PET data, metadata will also be included in the BIDS file format if available by that time.

Metadata will be stored as Microsoft Word/pdf, .txt or .csv file under each experiment parent- folder. In addition, all code and anonymized data will be uploaded to the Open Science Framework with corresponding metadata to aid in re-use by other researchers.

3. Data storage & back-up during the research project

Where will the data be stored?

All digital data (questionnaire answers, subjective ratings, behavioral data, physiological recordings, and neural recordings) will be stored on the KU Leuven Onedrive server of the researcher and will only be accessible by the identified KU Leuven researchers. In addition, the full database will be stored on RedCAP.

Data in paper format (informed consent forms, payment information forms, inclusion/exclusion criteria forms) will be stored separately in a key-locked cabinet in a dedicated archive room of the research group).

How will the data be backed up?

The data will be stored on OneDrive and RedCAP which both have automatic daily back-up procedures.

Is there currently sufficient storage & backup capacity during the project? If yes, specify concisely.
If no or insufficient storage or backup capacities are available, then explain how this will be taken care of.

- Yes

KU Leuven Onedrive allows 2 TB of data storage on personal drives. RedCAP also allows at least 10 MB of storage. These will be used to store all data except brain imaging data.

The network drive at the level of the research group has 4 TB of storage space, which can be extended flexibly if needed and will be used for storage of brain imaging data.

How will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

All data will be managed, processed and stored on secure, password-protected and encrypted network drives managed by the KU Leuven ICT facility and in restricted-access, key-locked rooms (for the paper informed consent forms). Access to the network drives is only possible for registered KUL personnel and the PI will determine access rights to dedicated project folders. All personal laptops and external drives will be

password-protected and encrypted. The information that links individual to the unique number will be stored separately on the KU Leuven Onedrive server of the researcher and will only be accessible by the identified KU Leuven researchers.
All screens will be locked when not in use.

What are the expected costs for data storage and backup during the research project? How will these costs be covered?

There is no cost associated with data storage and backing up. However, if unexpected costs arise, they will be covered via the bench fee. Storage on the central KU Leuven servers is 156,60 EUR/TB/year, with an estimated total data size of 2,5 TB. This will be paid from the FWO working budget. RedCAP also requires annual payment of 80 EUR, which is covered from the bench fee.

4. Data preservation after the end of the research project

Which data will be retained for at least five years (or longer, in agreement with other retention policies that are applicable) after the end of the project? In case some data cannot be preserved, clearly state the reasons for this (e.g. legal or contractual restrictions, storage/budget issues, institutional policies...).

The payment information form will be destroyed following data collection. All other data will be retained for at least 5 years after the end of the project.

Where will these data be archived (stored and curated for the long-term)?

After completion of data collection, and until 25 years after the end of the project, all digital data will be stored on a secure archival KU Leuven-based server. The log file linking participants' identity to their participant ID and the payment information form will be destroyed following data collection. Paper data (informed consent forms) will remain stored in key-locked cabinets for that duration.
Anonymized data will also be uploaded onto the Open Science Framework (OSF) where it can be accessed publicly.

What are the expected costs for data preservation during the expected retention period? How will these costs be covered?

The costs to archive the digital data are estimated at 156,60 EUR/TB/year and will be paid from the current project.

5. Data sharing and reuse

Will the data (or part of the data) be made available for reuse after/during the project? In the comment section please explain per dataset or data type which data will be made available.

- Yes, in an Open Access repository
- Yes, in a restricted access repository (after approval, institutional access only, …)

All data used in publications will be made available online. We will aim to share both the raw data and extracted data. Pseudonymized data can be shared within the research unit, uploaded in open access repositories or shared upon request.

If access is restricted, please specify who will be able to access the data and under what conditions.

Not applicable.

Are there any factors that restrict or prevent the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)? Please explain in the comment section per dataset or data type where appropriate.

- No

All data used in publications will be made available online. We will aim to share both the raw data and extracted data. The dataset will be pseudonymized and uploaded to the Open Science Framework.

Where will the data be made available? If already known, please provide a repository per dataset or data type.

Open Science Framework

When will the data be made available?

Upon publication of the research results

Which data usage licenses are you going to provide? If none, please explain why.

CC-BY-NC-SA-4.0

Do you intend to add a PID/DOI/accession number to your dataset(s)? If already available, you have the option to provide it in the comment section.

- Yes

It's not yet available

What are the expected costs for data sharing? How will these costs be covered?

There are no expected costs for data sharing. The Open Science Framework is free of charge.

6. Responsibilities

Who will manage data documentation and metadata during the research project?

The postdoctoral fellow (B.D.), administrative/technical staff and PI working on this project.

Who will manage data storage and backup during the research project?

The postdoctoral fellow (B.D.), administrative/technical staff and PI working on this project.

Who will manage data preservation and sharing?

The PI of this project.

Who will update and implement this DMP?

The PI bears the end responsibility of updating & implementing this DMP. The postdoc (B.D.) shares this responsibility during her appointment at KUL.