

Flemish Standard Data Management Plan

Project: The crucial role of the sleep-wake system
in Alzheimer's Disease pathophysiology

Prof. Dr Maarten Van Den Bossche (Principal Investigator)
Anne-Marie Peeters (PhD Student)

1. General Project Information

Name Grant Holder & ORCID	Maarten Van Den Bossche 0000-0002-2989-6600 (Principal Investigator)
Contributor name(s) (+ ORCID) & roles	Anne-Marie Peeters 0000-0002-4837-4568 (PhD Candidate)
Project number ¹ & title	The crucial role of the sleep-wake system in Alzheimer's Disease pathophysiology (3M220475)
Funder(s) GrantID ²	Bijzonder Onderzoeksfonds, Program : KU Leuven Global PhD Partnerships
Affiliation(s)	x KU Leuven <input type="checkbox"/> Universiteit Antwerpen <input type="checkbox"/> Universiteit Gent <input type="checkbox"/> Universiteit Hasselt <input type="checkbox"/> Vrije Universiteit Brussel <input type="checkbox"/> Other: Provide ROR ³ identifier when possible:

¹ "Project number" refers to the institutional project number. This question is optional since not every institution has an internal project number different from the GrantID. Applicants can only provide one project number.

² Funder(s) GrantID refers to the number of the DMP at the funder(s), here one can specify multiple GrantIDs if multiple funding sources were used.

³ Research Organization Registry Community. <https://ror.org/>

Please provide a short project description	<p>There is accumulating evidence, both neurobiological and clinical, that dysregulation of the sleep-wake cycle could be fundamental in Alzheimer's Disease (AD). From a neurobiological perspective, clear links have been found between changes in sleep and changes in amyloid, tau and atrophy. Mouse model for tauopathies are characterized by marked sleep wake imbalance/hyperarousal, which is strikingly similar to the severe neuropsychiatric symptoms present in most AD patients. Indeed, sleeping problems and daytime agitation in are major causes for institutionalization of AD patients. The Locus coeruleus (LC) is a major regulator of wakefulness/arousal, cognition and stress, and the first brain region to be affected by tau pathology in AD. Orexins are neuropeptides crucial in the sleep-wake function. The orexine receptor type 1 is highly expressed in the LC. Recently, orexin receptor antagonists (ORAs) were developed to treat insomnia, and very interestingly produce physiological sleep. We hypothesize that changes in the sleep/wake system, are crucial in the pathophysiology of AD. We propose that dysregulation of the LC is a key cause of hyperarousal in AD, and that it can be treated to improve AD symptoms and progression. To investigate this, we set up a collaboration between the KU Leuven and the University of Melbourne, to study this system in detail in both mouse models for AD (in Melbourne) and in patients with AD (in Leuven). In a second step, we will look at the effect of ORAs on the sleep-wake system in a mouse model for tauopathy and in patients with AD.</p>
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2. Research Data Summary

WP1: Developing more insight in the underlying neurobiological mechanisms of agitation in people with Alzheimer's Disease (AD) and defining possible new biomarkers in peripheral blood.

Source: peripheral blood samples from patients with dementia, who are staying at the ward Cog K in Kortenberg.

Type: physical data (peripheral human blood), digital data from molecular biology experiments (high performance liquid chromatography of electrochemical detection, ELISA, ECLIA, immunoturbidimetry).

Format:

Blood samples from patients are stored in -80°C freezer, an excel list with the amount and origin of the samples is stored on REDCap (secured).

Experimental results are stored in secured databases in Microsoft Excel (.xlsx) and in text format (as overview list of samples, reports, papers in MS word).

Estimated volume: < 1Gb

Dataset Name	Description	New or Reused	Digital or Physical	Digital Data Type	Digital Data Format	Digital Data Volume (MB, GB, TB)	Physical Volume
Blood samples_AD	We will collect blood samples of patients with dementia who are staying at the ward Cog K in Kortenberg. We will also collect experimental data from biological experiments.	We will generate new data	We will collect physical data, namely human peripheral blood. Results from experimental data will be digital.	Experimental	.txt .xlsx	<1GB	1 to 2 samples per patient, 1 blood sample contains max 80ml, aim to include 48 patients

WP2: Investigating the role of the gut microbiome regarding agitation and sleep in people with Alzheimer's Disease.

Source: feces samples of patients with dementia, who are staying at the ward Cog K in Kortenberg

Type: physical data (feces samples)), digital data from bacterial analysis of feces samples (16s rRNA gene sequencing, images related to the analysis of the feces samples).

Format:

Feces samples are stored in -80°C freezer, an excel list with the amount and origin of the samples is stored on REDCap (secured).

Experimental results are stored in secured databases in Microsoft Excel (.xlsx) and in text format (as overview list of samples, reports, papers in MS word). Images are stored as GIF or JPEG images.

Estimated size: 1-10 Gb

Dataset Name	Description	New or Reused	Digital or Physical	Digital Data Type	Digital Data Format	Digital Data Volume (MB, GB, TB)	Physical Volume
Faeces samples_AD	We will collect faeces samples of patients with dementia who are staying at the ward Cog K in Kortenberg. We will also collect experimental data from 16s rRNA gene sequencing.	We will generate new data	We will collect physical data (feces samples). Results from experimental data will be digital.	Experimental	.txt .xlsx .JPEG .GIF	<100GB	2 samples per patient, 1 stool sample contains 10 to 20g, aim to include 48 patients

<p>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.</p>	<p><i>We will reuse data of the following study: Prediction of Agitation in Dementia by Sensing (PAD, S62882). The 'PADS' dataset includes:</i></p> <ul style="list-style-type: none"> - <i>Digital raw data of the Chill+ wristband, with focus on actigraphy data</i> - <i>Digital raw data of non-contact sensing during nighttime including respiration rate, heartrate and activity.</i> - <i>Digital data of EMA (ecological momentary assessment) by proxy: Pittsburgh Agitation Scale (PAS) and the Richmond Agitation-Sedation Scale (RASS)).</i> - <i>Digital data of environmental/contextual parameters using sensors measuring room temperature, room humidity, light exposure of the patient, sound-related measurements, position of the patient on the ward or in the hospital.</i> - <i>Digital data of patient files including psychiatric and medical history, medication use, sociodemographic variables.</i>
<p>Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? If so, please describe these issues further and refer to specific datasets or data types when appropriate.</p>	<p><input checked="" type="checkbox"/> Yes, human subject data <input type="checkbox"/> Yes, animal data <input type="checkbox"/> Yes, dual use <input type="checkbox"/> No If yes, please describe:</p> <p>S62882 was approved by the EC UZ Leuven. We will file an amendment with the EC for WP1 and 2.</p>

<p>Will you process personal data⁴? If so, briefly describe the kind of personal data you will use. Please refer to specific datasets or data types when appropriate. If available, add the reference to your file in your host institution's privacy register.</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No If yes: We will use personal data (eg name of patients, date of birth) to identify patients in function of sample collection. All derivative data will be coded and thus pseudonymized. The file linking the code and personal identifiers age/dob will only be accessible to authorized individuals and stored in restricted access, secure environment managed by the KU Leuven/UZ Leuven ICT facility. The collection, processing and disclosure of personal data, such as patient health and medical information is subject to compliance with applicable personal data protection and the processing of personal data (Regulation (EU) 2016/679 also referred as the General Data Protection Regulation ("GDPR") and the Belgian Law of July 30 2018 on the protection of natural persons with regard to the processing of personal data).</p>
<p>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.</p>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No If yes, please comment:</p>

⁴ See Glossary Flemish Standard Data Management Plan

<p>Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material/Data transfer agreements, research collaboration agreements)?</p> <p>If so, please explain to what data they relate and what restrictions are in place.</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p>If yes, please explain:</p>
<p>Are there any other legal issues, such as intellectual property rights and ownership, to be managed related to the data you (re)use?</p> <p>If so, please explain to what data they relate and which restrictions will be asserted.</p>	<p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p>If yes, please explain:</p>

3. 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).

Protocols and details related to data collection and processing will be recorded and transcribed to Word or Excel files by the applicant (Anne-Marie Peeters). Data folders containing raw and processed data will be hierarchically organized and labelled based on the source of the data, the type of experiment, the date of data generation, and the different experimental conditions analysed.

We will include a README.txt document in the file with experimental data. This document will contain information on the study design, information on the context in which the data were gathered, the origin of the data and the context of the datasets and all necessary information for an independent analyst to use or reuse the data accurately and efficiently.

Data analysis methods and particularities (including metadata) will be described in text documents and Excel files included in these folders.

Research methods and practices (including the informed consent process) will be fully documented. Details on the setting of the data collection and the selection of participants will be documented. An overview of all steps taken to remove direct identifiers (e.g. name, date of birth) in the data will be added to the documentation.

The codebook will contain information about the study, files and variables. It will also provide instructions on how to read, analyse, interpret and verify the data.

All files will be stored on REDCap (secured).

<p>Will a metadata standard be used to make it easier to find and reuse the data?</p> <p>If so, please specify which metadata standard will be used. If not, please specify which metadata will be created to make the data easier to find and reuse.</p>	<p><input type="checkbox"/> Yes <input checked="" type="checkbox"/> No</p> <p>Text documents and Excel files stored within each experiment folder in REDCap will respectively contain guidelines describing data collection/analysis methods and all relevant metadata (including experimental conditions, sample keys, computational analysis pipelines and their parameters) to ensure the reusability of the data and the reproducibility of any further data generation.</p>
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4. Data Storage & Back-up during the Research Project

<p>Where will the data be stored?</p>	<p>Upon data collection/preprocessing, temporary copies of the digital data will primarily be stored in the UZ Leuven managed personal computer of the applicant (Anne-Marie Peeters). A copy of the data will be immediately uploaded to REDCap for long-term preservation and backup.</p> <p>Copies can be made and kept on personal devices in accordance with the level of authorisation of the user and the data security level of their device. Sensitive personal data concerning the study participants will be stored in a KUL/UZ secure environment. We will use KUL/UZ managed storage and file-sharing facilities as well as the REDCap platform for active use of the data during the project</p> <p>REDCap will be used to build the database of this project. We will ensure secure data storage at the start of the project and this for the full duration of the project and 5 years thereafter. A centralized network folder at KU Leuven servers will be used.</p> <p>Biological samples are stored in the laboratory in fridges, freezers (-80°C).</p>
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<p>How will the data be backed up?</p>	<p>Automatic backups for the disk capacity will consist of “snapshot” technology, where all incremental changes in respect of the previous version are kept online. It is standard procedure that 1 snapshot is made per day and that these snapshots are kept for 14 days. The end user can personally restore previously dated files from his or her Windows PC by using the “previous versions” function. Security groups can be set up to enable user management (by the local IT administrator). A mirror (an exact copy) of the data is provided in the second ICTS data center for “business continuity” or “disaster recovery” purposes. A file is copied to the second data center as soon as it is written to a drive. ICTS can put the copy online within an hour in case of disaster with the primary storage. The operating and maintaining of the storage solution is performed by ICTS.</p> <p>The data regarding results from biochemical analyses of blood and feces samples will be stored on the university's and UZ Leuven central servers with automatic daily back-up procedures.</p>
<p>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.</p>	<p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>If yes, please specify concisely: We expect REDCap to have enough back-up capacity to save all data and documents. If necessary, additional Gb can be obtained, for which we have budget available.</p> <p>For storage of samples we have currently sufficient storage space in fridges and freezers. If there would be a problem regarding the storage of samples, there is budget to buy an additional freezer.</p>

<p>How will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?</p>	<p>To access the original data (i.e., not the backed-up copies), one would need access to the systems. This can be either digitally, which would require knowledge of the IP addresses and login credentials, or physically. It is the candidate's responsibility to make sure these credentials are not only kept safe but of sufficient strength to deter any unwanted data manipulation. The identifiable biochemical data including results of blood and faeces samples from this study, will be managed, processed, and stored in a secure environment (KUL/UZ).</p> <p>Data-stored on UZ Leuven-managed personal computers are protected via password access to the computers, as set up by the UZ Leuven IT department. Off-site access to REDCap data is available from UZ Leuven personal computers and is password protected.</p> <p>Personal data will be pseudonymised by the investigator. All data will be treated confidentially and with due care during the project always in line with the guidelines of UZ Leuven regarding access to and use of patient data. The data from the medical file will be collected in a structured manner in a secured computer document. This file will be stored in a team-specific storage location on a server of KU Leuven or UZ Leuven. Data enabling patient identification will be pseudonymised. This means that the personal data will be processed in such a way that it can no longer be used attributed to a specific person without the use of additional information.</p> <p>For samples: the laboratory is locked every evening.</p>
<p>What are the expected costs for data storage and backup during the research project? How will these costs be covered?</p>	<p>For the storage of digital data using REDCap there will be a cost of 80euros/year. Since we have almost no large-volume files, we do not expect large costs for data storage.</p> <p>Regarding the storage of biological samples, we will work together with the UZ/KU Leuven Biobank. There will be a one-time administration cost of 300euro. We expect the costs of the intake of the samples to range from 384 to 576euros for 48 patients (4 to 6 samples per patient). The yearly cost of storage will range from 96 to 144 euros.</p> <p>The costs that are associated with storage will be covered by internal funding.</p>

5. Data Preservation after the end of the Research Project

Which data will be retained for at least five years?	We expect all data to be kept.
Where will these data be archived (stored and curated for the long-term)?	<p>The digital data will be stored on the university's central servers (with automatic back-up procedures) for at least 10 years, conform the KU Leuven RDM policy.</p> <p>Biological and chemical samples will be stored at 4°C and/or as frozen samples in cryovials as appropriate via the UZ/KU Leuven Biobank.</p>
What are the expected costs for data preservation during the expected retention period? How will these costs be covered?	<p>Since we have no large-volume files, we do not expect large costs for data storage. The minor costs that may be associated with storage will be covered by internal funding.</p> <p>Regarding the storage of biological samples, we will work together with the UZ/KU Leuven Biobank. The yearly cost of storage will range from 96 to 144 euros for 4 to 6 samples per patient if we include 48 patients.</p> <p>The costs that are associated with storage will be covered by internal funding.</p>

6. Data Sharing and Reuse

Will the data (or part of the data) be made available for reuse after/during the project? Please explain per dataset or data type which data will be made available.	<p> <input type="checkbox"/> Yes, in an Open Access repository <input checked="" type="checkbox"/> Yes, in a restricted access repository (after approval, institutional access only, ...) <input type="checkbox"/> No (closed access) <input type="checkbox"/> Other, please specify: </p> <p>The type of data that will be made available will be determined on an ad hoc basis and in adherence with the informed consent of the participants and advice from the relevant ethics committees.</p>
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<p>If access is restricted, please specify who will be able to access the data and under what conditions.</p>	<p>Published data will be available to everyone. Experimental data and biological samples will be available only for people from the lab of the PIs. Access will be granted upon written request to the creators of the dataset. Commercial reuse is not allowed.</p>
<p>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 per dataset or data type where appropriate.</p>	<p> <input checked="" type="checkbox"/> Yes, privacy aspects <input type="checkbox"/> Yes, intellectual property rights <input type="checkbox"/> Yes, ethical aspects <input type="checkbox"/> Yes, aspects of dual use <input type="checkbox"/> Yes, other <input type="checkbox"/> No </p> <p>The project will make use of a set of analysed human blood and feces samples. Pseudonymized data can be made available for further analysis in line with the terms of the ICFs and following advice from the relevant local ethics committees and LRD (Leuven Research and Development).</p>
<p>Where will the data be made available? If already known, please provide a repository per dataset or data type.</p>	<ul style="list-style-type: none"> - In a restricted access repository - Upon request by mail - Other (specify): Different data types will be made available by different means according to the nature of the data and request. For example, pseudonymised pre-processed results from blood and faeces samples may be shared with collaborators for new analyses, spreadsheets with pseudonymised data can be made available on request. Publications relating to the study will be provided in open access via Lirias 2.0.
<p>When will the data be made available?</p>	<p>Upon publication of the research results</p>

Do you intend to add a PID/DOI/accession number to your dataset(s)? If already available, please provide it here.	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No If yes: We intend to add a PID/DOI/accession number to our datasets, this is not yet available.
What are the expected costs for data sharing? How will these costs be covered?	Expected costs associated with data sharing will mostly include publications costs. Publication costs will depend on the type of platform we will use. If we aim to publish in an open access journal, we expect a publication cost from around 3000 to 5000 euros per article.

7. Responsibilities

Who will manage data documentation and metadata during the research project?	The PhD candidate will be responsible for his/her own data.
Who will manage data storage and backup during the research project?	The PhD candidate will be responsible for his/her own data.
Who will manage data preservation and sharing?	This responsibility will lie with the supervisor, as this requires a long-term commitment most likely extending beyond the tenure of the PhD candidates.
Who will update and implement this DMP?	The end responsibility for updating and implementing the DMP is with the supervisor (promotor). To this end, the PhD candidates commit themselves to keeping the supervisor informed about the status of their respective data backup and preservation.