

COLLABORATION AGREEMENT

1. PARTIES

Masaryk University
Žerotínovo nám. 617/9,
601 77 Brno
the Czech Republic
VAT no. CZ00216224

(“MU”)

and

Center of Functionally Integrative Neuroscience/MINDlab
Nørrebrogade 44
8000 Aarhus C

and

Aarhus University
Department of Clinical Medicine
Palle Juul-Jensens Boulevard 99
8200 Aarhus N,
Denmark
VAT no. 31 11 91 03

and

Aarhus University
Department of Biomedicine
Høegh-Guldbergsgade 10
8000 Aarhus C,
Denmark
VAT no: 31 11 91 03

(jointly “Institution”)

(the parties shall be referred to individually as a “Party” or jointly as the “Parties”)

2. BACKGROUND AND PURPOSE OF THE COLLABORATION

In the past, the vast majority of basic cognitive neuroscience studies have been conducted in isolation, examining the relationship between a single given neuroscientific measure and a single given cognitive phenomenon. This is problematic as single features rarely explain (in the statistical sense) more than 20% of the inter-individual variability. This is disappointingly low from a clinical perspective and casts doubt on the practical usefulness of much of basic cognitive neuroscience. It is the purpose of this project “Identification of sensory and cognitive characteristics from magnetic resonance (MR) data” (the “Study”/“Project”) to move beyond this limitation and use neural data in conjunction with genetic and other biological and behavioural measures to create models that are able to predict a wide range of cognitive characteristics with high accuracy at the individual subject level.

In this Project, we use a range of MRI sequences to gain broad knowledge on various neuroarchitectural characteristics of participants. These maps are then related to a wide range of behavioural/cognitive phenomena collected across around 20 hours of experiments per participant in order to examine how well these phenomena can be explained/predicted by neural characteristics. In addition, the explanatory/predictive power of MRI based maps, or the combination of MRI, genetics and blood biomarker profiles, are compared to maps using genetic information alone. Power analyses show that the most efficient and economical way of conducting the Project is to examine all behavioural and neural characteristics in a single, large sample of participants (500+). Given the large amount of tests, collaboration with international experts is ideal.

Hypothesis: We hypothesize that:

- A single MRI-based model of a wide range of neural characteristics statistically explains 70% or more of inter-individual differences for a wide range of sensory and cognitive characteristics.
- This model outperforms models based on genetics alone.
- A combined MRI, genetics and blood biomarker-based model will have high predictive power.
- Transcranial magnetic stimulation can be used to establish causal relationships for a subset of findings (specifically related to grey matter volume and cortical thickness).

3. SUBJECT OF THE COLLABORATION

The collaboration includes the design/implementation of behavioural experimental paradigms, sharing of genetic and biomarker information and MRI as well as analysis of the data collected in the Project at MU and at Institution.

4. THE ORGANISATION OF THE COLLABORATION

Participants in the collaboration are:

From Institution: xxxxxxxxxxxxxxxxxxxxxxxxxxxx

From MU: xxxxxxxxxxxxxxxxxxxxxxxx

The Study has attracted and may, in future, attract other collaborators (hereinafter "Other Collaborators"). So far the Other Collaborators are:

Members of the SkuldNet consortium (xxxxxxxxxxxxxxxxxxxxxxxxxxxx), COST Action CA18106 (<https://www.cost.eu/actions/CA18106/>) and Section for Clinical Mass Spectrometry, Danish Center for Neonatal Screening, Statens Serum Institut (SSI).

5. PERSONAL DATA

The Parties acknowledge that the Project/Study necessitates the processing of personal data (as defined in the General Data Protection Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation, further as "GDPR") and that each Party shall act as an independent data controller (as defined in the GDPR) in respect of the personal data pertaining to the Project that are in its possession.

In connection with the performance of the Study, Institution shall disclose personal data in the form of experimental behavioral data regarding individual sensory and cognitive characteristics, responses from psychological questionnaires, demographic data, data on physical and mental health, MRI data, genetic data (approximately 600.000 common SNP variants on the Infinium Global Screening Array (GSA), excluding 10.000 pathogenic markers), and blood biomarker data to MU for the sole purpose of the Project. MU shall disclose personal data in the form of experimental behavioral data regarding individual sensory

and cognitive characteristics, responses from psychological questionnaires, demographic data, data on physical and mental health, MRI data, EEG and electrophysiology data, and genetic biosamples and optionally blood biomarker data to Institution for the sole purpose of the Project.

The disclosure of personal data between Parties is based on art. 9 section 2 (j) and art. 6 section 1 (e) GDPR, and shall be undertaken in a secure manner as agreed upon by the Parties.

Each Party shall, in respect of the personal data pertaining to the Project that is in its possession, comply with all applicable data protection regulations (such as but not limited to the aforementioned GDPR) and any guidance or direction issued in this regard by the applicable supervisory authority, including in the exercise of its rights and obligations under or in terms of this Agreement. Each Party is as such and *inter alia* responsible for ensuring the confidentiality of such data and for implementing appropriate technical and organizational security measures to ensure an adequate level of security for its processing of such data.

The Parties undertake to notify each other in the event of a data security breach immediately upon becoming aware of such breach within 72 hours and to provide each other with reasonable assistance and/or information in such an event, in the event of any request made by a concerned data subject (as defined by the GDPR), in terms of the GDPR and/or in the event of any request made by the applicable supervisory authority.

6. OBLIGATIONS OF THE PARTIES

Institution's responsibilities:

Institution will provide: Experimental testing of participants recruited for the Study, local work on the implementation of MRI sequences and behavioral paradigms, DNA genotyping and quantitative blood metabolite measures on biosamples from participants, genetics and metabolite paradigms, input on analyses and manuscripts.

MU responsibilities:

MU will provide: Experimental testing of participants recruited for the Study, contributions to behavioural and/or MRI paradigms, assistance implementing these at Institution, biosamples for DNA genotyping and metabolomics, local work on the implementation of: MRI sequences, genetics and behavioural paradigms, work on analyses and manuscripts for contributed- and other paradigms (e.g. for manuscripts relating contributed behaviour to MRI data or methods manuscripts on the topic of contributed sequences/analysis methods). Optionally MU will provide quantitative blood metabolite measures from participants.

Both Parties undertake to:

- comply with the provisions in the Act on Processing of Personal Data in force at the time in question and regulations related hereto, including the regulation of 15 June 2000 No. 528 (the Personal Data Regulation),
- instruct its employees and consultants, who has access to and/or processes the personal data, about the requirements related to processing of personal data, especially about their obligation of confidentiality regarding the personal data which come to their knowledge in connection with their duties,
- implement and maintain technical and organisational security measures sufficient to protect data against accidental or unlawful destruction, loss or alteration and against unauthorized disclosure, abuse or other processing in violation of the provisions laid down in the Act on Processing of Personal Data,
- process personal information only for the purposes necessary for the Project,

- report any breaches of the personal data security to the supervisory authority, notifying the data subjects about breaches of personal data security, making analyses of the consequences regarding data protection and performing previous hearings,
- share only personal data that is pseudonymized,
- keep a key to link participants identities to the pseudonymised data at the facility where the data was originally collected,
- store the key according to the previous article for a maximum of 7 years from the data collection; after this period, the data collected will be anonymised (if the duration of the Study is longer than 7 years, the anonymisation will be carried out on an ongoing basis).

7. COLLABORATION MEETINGS

Before, during and after completion of the Study, the Parties shall discuss issues related to the Project, either at meetings, on e-mail or on the telephone together with the Other Collaborators in the Study. Part of these takes place in the context of the COST Action CA18106.

8. FINANCIAL SUPPORT

Expenses for analysis will be paid by the facility where they are performed at, either Institution or MU.

Expenses for data collection will be paid by the facility where they are performed, with the exception of blood metabolomics experiments and associated MRI measurements – they will be pre-paid by Institution in accordance with the terms under section (A-F) below.

- A. Payment for MU's data collection in connection with blood metabolomics experiments and associated MRI measurements ("Pre-paid Funds") will be paid as a fixed lumpsum payment in advance.
- B. The Parties agree that the total amount of the Pre-paid Funds is DKK 138,000 and this payment is considered payment in full with respect of section E - F below.
- C. Pre-paid Funds are solely targeted for the purpose of collecting data in connection with blood metabolomics and associated MRI measurements experiments and covers:
 - a. Compensation for study participants
 - b. Wages for nurse, research assistants and sampling coordinator
 - c. 50 standard MRI measurements
- D. MU must document all expenses related to blood metabolomics experiments and associated MRI measurements in writing to the Institution within reasonable time after defraying the expenses.
- E. MU must refund any excess Pre-paid Funds to the Institution if the documented expenses for the data collection is lower than the amount of Pre-paid Funds.
- F. MU is obliged to refund excess Pre-paid Funds upon written request from the Institution.

9. CONFIDENTIALITY

All information disclosed or provided by a Party or produced during the Study, including but not limited to the Protocol annexed to this Agreement (which Protocol forms an integral part of this Agreement), and the results obtained during the course of the Study (hereafter the "Confidential Information"), is confidential. Each Party (hereinafter the "receiving Party") agrees to keep confidential and not to disclose the Confidential Information to any third party without the prior written approval of the other Party (hereinafter the "disclosing Party"). Each Party shall use the Confidential Information solely for the purposes of the Study. Provided that the receiving Party may disclose Confidential Information to those persons who need to know the same for the purposes of the Study or for the purposes of implementing this Agreement or for the purposes of enabling that Party to negotiate this Agreement or to bring forward a claim or to defend

itself in proceedings brought pursuant to this Agreement. Provided further that the receiving Party shall ensure that such persons respect the confidentiality obligations established by this Article.

Confidential Information shall not include information that: (1) is at the time of disclosure, or thereafter becomes, publicly available through no fault of the receiving Party; (2) is disclosed to the receiving Party by a third party entitled to disclose such information in a non-confidential manner; (3) is known to the receiving Party prior to disclosure under this Agreement, as shown by the receiving Party's prior written records; (4) can be documented to have been independently developed by the receiving Party without reliance on Confidential Information; (5) can be disclosed pursuant to articles 11 and/or 12 below (6) is required by applicable law and/or authority (including any court or tribunal) to be disclosed; or (7) constitutes personal data within the meaning of this Agreement and the General Data Protection Regulation 2016/679, the processing of which is governed solely in the manner stipulated by Article 5 above.

The obligations of confidentiality and restricted use contained herein are applicable during the term of the Agreement and shall, thereafter, survive for 5 (five) years from the date of the Agreement's expiration or termination.

10. OWNERSHIP OF DATA

Raw data provided and/or generated under this Agreement shall be owned by the Party at which Study participants are recruited to. For the avoidance of doubt, raw data constitutes personal data, unprocessed MRI data, raw genotyping data, raw blood metabolite data, responses of the raw questionnaire and unprocessed behavioural results, provided and/or generated by the Parties.

11. PUBLICATION POLICY

Authorships are defined according to the Vancouver guidelines for each publication before drafting. For each behavioural paradigm contributed, a principal article will be prepared, typically relating behaviour to neural and/or genetic and/or blood metabolite data. If consistent with Vancouver guidelines, the first author will be from the Party contributing the paradigm. In cases where xxxxxxxx has contributed substantially, he shares first or last authorship, or if no other obvious last author is involved, he will be the sole last author. In cases where xxxxxxxxxxxx has contributed substantially, he shares first or last authorship, or if no other obvious last author is involved, he will be the sole last author. In cases where xxxxxxxxxxxx has contributed substantially, he shares first or last authorship, or if no other obvious last author is involved, he will be the sole last author.

For each behavioural paradigm contributed by one of the Parties without involvement from the other Party in the idea, design or programming phase, that Party shall have the right to publish results concerning the behavioural data alone without involving other authors from the other Party. Without approval of both Parties, no such results may be published before the publication of a joint principal article or until 3 years after the primary data collection has finished. In any such publication, the general contribution of xxxxxxxxxxxx and the Other Collaborators shall be acknowledged. Any such individual publication shall be sent to the other Party for review thirty (30) calendar days before submitting the publication to the media concerned. During this review period, the other Party may ascertain the publication for any Confidential Information and request them removed from the publication. If one Party can document that such publication contains patentable rights belonging to that Party, this Party may request for up to additional sixty (60) calendar days' delay for submission of patent application.

After the publication of the principal article or 3 years after the primary data collection has finished, any Party and Other Collaborators related to the Study may use the data in publications, and authorship will be attributed according to contribution to each specific article. The contribution of the Party contributing to the paradigm shall be acknowledged. For any articles combining data from multiple behavioural paradigms and/or MRI/genetics and behaviour, xxxxxxxx shall be involved as a co-author. For any articles including

genetic and blood metabolite data xxxxx shall be involved as a co-author. For any articles involving data collected at MU xxxxxxxxx and xxxxxxxxx shall be involved as a co-authors.

Publications with methodological development using MRI, genetic, and/or behavioural data from this Project, need to obtain approval from both Parties ideally before the work commences, but at the latest thirty (30) calendar days before submitting the publication to the media concerned. Such publications are considered primary methods articles and acknowledge contributions of collaborators by co-authorships or mentions as appropriate. xxxxxxxxx will be credited as a co-author for his role in study design.

12. OWNERSHIP OF INTELLECTUAL PROPERTY RIGHTS

Ownership of the Parties' unpublished knowledge in the form of know-how, unpublished inventions or other specialised unpublished knowledge that the Parties have informed each other of or made available for the completion of the Study ("Background Knowledge") belongs to and shall remain with the Party who has so informed or made available.

All non-patentable findings, information, data or results originating from the Study shall be the property of Institution regardless whether this knowledge was created by Institution or MU. Provided that analysis methods generated under or by virtue of this Agreement shall not be considered a finding, information, data or a result within the meaning of this paragraph.

All analysis methods generated under or by virtue of this Agreement shall be owned by the Party that generated them. In the event that such analysis methods were generated by the Parties jointly, they shall be owned by the Parties jointly. The Parties shall discuss protection and/or possible licensing of joint analysis methods in a separate agreement if necessary.

During the term of the Project, the Parties shall grant each other a free, irrevocable and non-exclusive right to access and use their respective Background Knowledge for the purpose of completing the Study. This right shall only apply to work in connection with the Study.

The Parties shall grant each other a free, irrevocable, worldwide, and non-exclusive right to access and use all findings, information, data, results and analysis methods generated under or by virtue of this Agreement for internal non-commercial research and educational purposes as well as for publication subject to the Publication Policy in article 11.

13. LIABILITY & INDEMNITY

The purpose of a non-interventional study is to study standard clinical practice, and requests for any additional insurance of indemnity are not expected. Should however the need for indemnification be required, the provisions contained in this article 13 shall apply taking into account local law and practice.

Each Party (the 'indemnitor') undertakes to fully indemnify and hold harmless the other Party (the 'indemnitee') in respect of any and all damages, losses, costs (including the costs of enforcement), demands, claims (including judicial claims), liabilities, expenses, legal expenses and judgements of any nature whatsoever incurred or suffered by the indemnitee arising as a consequence of negligence or wilful misconduct or breach of this Agreement by the indemnitor.

Neither Party is liable to the other for any incidental, special, punitive, exemplary, consequential or statutory damages, or any damages resulting from lost profits, interruption of business or loss of goodwill, howsoever arising, even if they have been advised of the possibility of such damages.

No Party shall be liable for any delay or failure to perform its obligations under this Agreement if such delay is due to Force Majeure. "Force Majeure" shall mean any cause beyond such Party's control, including,

but not limited to, terrorist acts, fire, explosion, war, civil strife, riots, strike, lockout or major/regional power or utility supply failure.

This is provided that the Party affected by Force Majeure must without delay inform the other Party. Provided further that Force Majeure shall not include the acts or omissions of Other Collaborators unless these acts or omissions are too a result of Force Majeure.

14. REPRESENTATION & WARRANTIES

Each Party confirms to the other Party that (a) it shall comply with all applicable international, national, state, provincial, regional and local laws and regulations in exercising its rights or fulfilling its obligations hereunder (b) the research to be undertaken pursuant to the Project as well as the Project itself have been approved, including from an ethical perspective, in accordance with its internal rules and procedures; & (c) that to the best of its knowledge, it owns or has the necessary authorisation to use the Background Knowledge provided by it pursuant to article 12 for the purposes stipulated in the same article, provided that any Background Knowledge provided as aforesaid is provided on an "AS IS" basis. To the extent permitted by applicable law, each Party specifically disclaims any implied warranties of merchantability and/or fitness for a particular purpose with respect to such Background Knowledge.

Provided that the Parties shall enter into agreements with the Other Collaborators that legally bind them to abide by terms and conditions which are equivalent, both in substance and in effect, to the terms and conditions of this Agreement and which ensure that the other Party's rights and obligations hereunder are not hampered by their added participation in the Study. Such agreements must, moreover, ensure that all collaborators in the Study, including the other Party, work together efficiently and effectively in the interests of the Study.

Provided further that the Parties also represent and warrant that they will conduct the experiments outlined in the Protocol in accordance with applicable law and the procedures outlined therein, that they will prioritize participant safety and that they shall take all precautions necessary, in accordance with applicable law, to ensure said safety. The Parties confirm that, where it is required for the purposes of the Project to process personal data (as defined in Regulation (EU) 2016/679, the 'GDPR'), including but not limited to where it shall collect data and where it shall share data with the other Party pursuant to this Agreement, such processing shall conform to all applicable data protection laws and ethical principles, including the afore-mentioned GDPR, and shall be undertaken only following the requisite approval from its Research Ethics Committee/s, which approval shall be annexed to this Agreement.

The Parties understand and agree that the research undertaken pursuant to this Agreement shall be undertaken by each of them on a best effort basis without any warranty or representation relating to a certain defined outcome.

15. AMENDMENT & ASSIGNMENT

Any amendments, including additions and deletions, to this Agreement must be in writing and signed by the authorised representatives of each Party.

No Party may assign, subcontract or otherwise transfer its rights or obligations under this Agreement without the prior written consent of the other Party.

16. TERM AND TERMINATION

Once signed by all the Parties, this Agreement will become effective if and when complete and unconditional approval of the research to be undertaken pursuant to the Project as well as the Project itself is given by the Parties' relevant Research Ethics Committee/s and will remain in effect until the Study is completed unless terminated earlier by either Party as provided below.

The Agreement may be terminated by either Party with a written notice of 2 months to the other Party.

The expiration or termination of this Agreement shall be without prejudice to the rights and obligations of the Parties accrued prior to expiration or termination. Moreover, without prejudice to article 9 that shall survive the expiration or termination of the Agreement as stipulated therein, the rights and obligations arising from Articles 5, 10, 11, 12, 13 and 14 (where reasonably applicable) shall indefinitely survive the expiration or termination of this Agreement.

Timeframe:

The Study commenced on August 1 2019. Expectancy of the Study is 7 (seven) years from its commencement.

17. VENUE AND APPLICABLE LAW

This Agreement shall be exclusively governed by, and construed in all respects in accordance with the laws of Denmark, without regard to its conflicts of laws rules. Provided that MU will not be required to breach any mandatory statutory laws to which it is subject.

Any disputes arising in connection with this Agreement shall be settled by negotiation between the Parties. Any claims, controversies or disputes arising out of or in connection with this Agreement which cannot be settled amicably between the Parties shall be subject to the exclusive jurisdiction of the competent court of Aarhus, Denmark

18. GENERAL

This Agreement constitutes the entire agreement and understanding of the Parties in relation to the matters dealt within it and supersedes any previous agreement, writing or other communication (including verbal) between the Parties relating to the subject matter of this Agreement.

Nothing in this Agreement creates or has the effect of creating an agency, joint venture, partnership or other similar relationship between the Parties. No Party has authority or power to bind the other in any respect.

If a provision of this Agreement is adjudged to be invalid or unenforceable, the said provision shall be severed without affecting the validity and enforceability of the remainder of this Agreement.

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Masaryk University

Director of the Central European Institute of Technologies
Mgr. xxxxxxxx, LL.M.

Center of Functionally Integrative Neuroscience/MINDlab:

Clinical Professor, Head of Centre
XXXXXXXXXXXXXXXXXX

**Aarhus University,
Department of Clinical Medicine:**

Head of Department
XXXXXXXXXX

**Aarhus University,
Department of Biomedicine:**

Head of Department
XXXXXXXXXX

Agreed and accepted:

XXXXXXXXXXXX

XXXXXXXXXXXX

XXXXXXXXXXXX

APPENDIX 1: PROTOCOL

- 1) MRI sequences:
 - a. Quantitative multi-parameter mapping (MPM)
 - b. Diffusion tensor imaging (DTI)
 - c. Resting state fMRI
- 2) EEG
- 3) Behavioural test battery indexing basic perceptual, cognitive, and meta-cognitive function
- 4) Buccal swabs and blood samples for DNA analyses
- 5) Demographics
- 6) Metadata
- 7) WAIS – Wechsler Adult Intelligence Scale
- 8) Questionnaires:
 - a. NEO-PI-R – Revised NEO Personality Inventory
 - b. ARSQ2 – Amsterdam Resting State Questionnaire 2
 - c. MAIA2 – Multidimensional Assessment of Interoceptive Awareness 2
 - d. VVIQ2 – Vividness of Visual Imagery Questionnaire 2
 - e. CFQ – Cognitive Failures Questionnaire
 - f. CES-D – Center for Epidemiologic Studies Depression Scale
 - g. OSS – Olfaction Sensitivity Scale
 - h. NSS – Noise Sensitivity Scale
 - i. Dream Recall Questionnaire
 - j. Freiburg Mindfulness Inventory
 - k. MMQ – Multifactorial Memory Questionnaire (Ability subscale)
 - l. MMQ – satisfaction subscale
 - m. IDEA – Inventory for Déjà vu Experiences Assessment
 - n. GSS – Glasgow Sensory Sensitivity Scale
 - o. PSS – Perceived Stress Scale
 - p. AQ-Short – Autism-Spectrum Quotient, abridged version
 - q. NEO-FFI – NEO Five Factor Inventory
 - r. VDS – Visual Discomfort Scale
 - s. SGI – Sensory gating inventory
 - t. CAPS – Cardiff Anomalous Perception Scale
 - u. MACE – Maltreatment and Abuse Chronology of Exposure
 - v. STAI – State Trait Anxiety Inventory
 - w. ASI – Aberrant salience questionnaire
 - x. CHi-II – Cortical hyperexcitability index II