Joint Transnational Call on Neurodevelopmental disorders

I. General information

Acronym	DynAMoND
Project Title	Dynamics of affect modulation in neurodevelopmental disorders
Project website	https://dynamond.eu/
Start Date Consortium	January 2022
Date of the Report	01.05.2024

PARTNERS

Number	Principal Investigator	Organisation	Country
1 (Coordinator)	Prof. Dr. Andreas Reif	Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Goethe University Frankfurt (GUF)	Germany
2	Prof. Dr. J. Antoni Ramos-Quiroga (JARQ)	Vall d'Hebron Research Institute (VHIR), Group of Psychiatry, Addiction and Mental Health.	Spain
3	Prof. Dr. Giovanni de Girolamo	IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli (FBF), Unit of Epidemiological and Evaluation Psychiatry	Italy
4	Prof. Dr. Jan Haavik	University of Bergen (UiB), Department of Biomedicine	Norway
5	Prof. Dr. Nader Perroud	University Hospitals of Geneva (UNIGE-HUG), TRE Unit, Service of Psychiatric Specialties, Department of Psychiatry	Switzerland

1. Provide a short summary of the progress and major achievements of the joint collaboration to date. Briefly describe the progress achieved in each individual work package / task (please use your e.g. original Gantt chart for overview and indicate the involvement of each consortium partner):

eCRF Programming: The electronic Case Report Forms (eCRFs) have been effectively programmed for both secuTrial and REDCap systems. Currently, they are accessible across all five centers in the local languages, ensuring efficient and precise data collection as outlined in work package 1, objective 1.1, of our Gantt chart. The programming was chiefly executed by the German and Spanish consortium partners, with significant translation assistance provided by the remaining partners.

Use of Smartphone Apps: For data generation, we utilize electronic diaries captured through the smartphone apps movisense and m-Path, also as outlined in work package 1, objective 1.1 and milestone 1 and 2 of our Gantt chart. This was mainly done by the German consortium partner, also with significant translation assistance provided by the remaining partners.

These apps have been specifically acquired and programmed for our study requirements.
Participant Recruitment: Although participant recruitment has not yet met our target specifications, we have already secured a substantial number of participants. To date, 30 subjects have been successfully recruited at the German center, and over 90 participants were recruited in sum by all sites combined. Testing has commenced over the course of the one-year participation interval per participant. This is found in workpackage 1, task 1.4 and milestone 3. All partners were involved in this. A summary of the described progress and additional updates is provided below:

Work Packages Status:

- Complete list of all work packages as listed in the full proposal application form
- Indication of whether each has been fulfilled

Work package 1: Clinical study backbone and mobile assessment (Lead GUF)

- Objective 1.1 Setting up the eCRF and the EMA and phenotyping system ✓
- Objective 1.2 Recruitment, screening and inclusion of 120 ADHD, 120 BipD, 120 BPersD and 120 healthy probands
- Objective 1.3 Longitudinal phenotyping of the above probands over 12 months
- Objective 1.4 Studying the temporal dynamics of mood fluctuations according to the *Modified DynAffect Model*
- Task 1.1 Further development of the existing EMA and online systems (resp.: GUF) ✓
- Task 1.2 Development of the eCRF (resp.: GUF) ✓
- Task 1.3 Implementation of the recruitment pipeline (resp.: GUF, with VHIR, UiB, FBF, UNIGE-HUG) ✓
- Task 1.4 Maintaining and monitoring assessments (resp.: GUF) ✓
- Task 1.5 Statistical analyses of the EMA and online phenotyping data (resp.: GUF)
- Milestone 1 e/mHealth system is set up and ready to use (mo6) ✓
- Milestone 2 all preparatory steps taken and approvals in place (mo7) ✓
- Milestone 3 First patient in (mo7) ✓
- Milestone 4 First patient last visit (mo19)
- Milestone 5 Last patient last visit (mo31)
- Deliverable 1.1 Database freeze (mo32)
- Deliverable 1.2 Analyses on primary outcome finished (mo35)

Work package 2: Genetic determinants of emotional dysregulation (Lead VHIR):

Objective 2.1 Analysis of genome-wide data (resp.: VHIR)
Objective 2.2 Identifying genetic factors for parameters of the *Modified DynAffect Model* (resp.: VHIR)

- Task 2.1 Establishing a pipeline for genotyping and genetic analysis (resp.: VHIR, UiB, GUF)
- Task 2.2 Storing and analyzing genome-wide data (resp.: VHIR, GUF)
- Task 2.3 Correlating PRS to sub-phenotypes incl. *DynAffect* parameters (resp. VHIR, GUF)
- Milestone 6 All DNA extracted and genome-wide genotyping accomplished (mo24)
- Deliverable 4.1 PRS analyses for *DynAffect* parameters completed (mo36)

Work package 3: Environmental stress (Lead UiB):

- Objective 3.1 Measure the influence of stress on *DynAffect* parameters and sleep (resp.: UiB, GUF)
- Task 3.1 Bioinformatic analyses on stress, sleep and *DynAffect* parameters pe (resp: UiB)
- Deliverable 3.1 Mediation analysis of stressor exposure and sleep (mo36)

Work package 4: study management, project management implementation and dissemination (Lead GUF):

- Objective 4.1 Assuring completion of study goals w.r.t. attrition and compliance (resp. GUF)
- Objective 4.2 Enabling proper conduct of the study in terms of Ethical and Legal matters (resp. GUF) ✓
- Objective 4.3 Dissemination of the findings to all relevant stakeholders (resp. GUF, all)
- Task 4.1 Drafting and negotiation the CA (based on DESCA model) and the DMP (resp. GUF) ✓
- Task 4.2 Setting up SC and SED boards and organizing meeting, telcos, etc. (resp. GUF) ✓
- Task 4.3 Monitoring study progress (resp. GUF) ✓
- Task 4.4 Supervision of phenobank and biomaterial storage (resp. GUF, VHIR) ✓
- Task 4.5 Controlling and fostering dissemination activities (resp. GUF, all) ✓
- Milestone 7 Database cleared and ready to use (mo32) ✓
- Deliverable 4.1 CA Agreement (mo3) ✓
- Deliverable 4.2 All ethical approvals package (mo6) ✓

2. Has the original work plan been modified? If so, please explain the rationale (indicate which partners are involved)**:**
No

3. Have any problems occurred? If yes, please specify and describe the solutions implemented or envisaged. (indicate which partners are involved)**:**
Delays due to Ethics Approval and Data Protection: Some centers received their positive ethics approval later than planned, leading to a delay in the project's progress. Additionally, time-consuming disputes with data protection further slowed down progress.
Impact of Cyber Attack: A cyber attack on the University Hospital Frankfurt on October 6th, 2023, had significant consequences. The disconnection of all external server connections greatly hindered communication with already recruited participants and potential study candidates.
Issues with the eCRF secuTrial: The eCRF secuTrial was temporarily unavailable as a result of the cyber attack. This necessitated the implementation of interim solutions for data entry, causing additional delays. The implementation of the alternative eCRF REDCap was mainly done by the Spanish recruitment site but all partners had to find short term interim solutions for that.
Recruitment Status: To date, 30 of the planned 96 subjects have been recruited in Frankfurt. Overall we have recruited 93 participants in sum so far. This means that more time is needed for recruitment to meet the target objectives.

These factors have led to an overall delay compared to the original planning, and it will be necessary to adjust the timelines accordingly to meet the study goals.

4. Do you foresee work plan modifications? If yes, please describe the planned modifications and their rationale (indicate which partners are involved):
No

5. Have you required to implement amendments to the workplan/protocols/timeline of the project to follow recommendations of ethical committees during the last year?
We have submitted an amendment to our protocol to the ethical committee. This amendment reflects a minor change in the test plan, specifically an adjustment of the age limit for inclusion criteria from 40 to 50 years. This alteration aims to facilitate broader participant recruitment.

6. List the publications in which NEURON support has been acknowledged. For each publication highlight the name of the NEURON partners and indicate the partner number according to the numbering designation in section I (e.g. partner 1 or P1). Please provide a snapshot of the relevant acknowledgment section for each of the listed publications.

No.	Publication Type (Article, Book)	Publication (authors, title, journal, year, issue, pp.)	PMID	DOI	Partner(s)	Impact factor	Open access (Y/N)
1							
PASTE ACKNOWLEDGMENT SNAPSHOT HERE							
2							
PASTE ACKNOWLEDGMENT SNAPSHOT HERE							
3							
PASTE ACKNOWLEDGMENT SNAPSHOT HERE							
4							
SUBMITTED / IN PREPARATION							

Add lines as appropriate

7. Has the consortium produced databases, registries, or biobanks of potential use to other research projects? If so, provide a short description (please highlight the consortium partners involved)
No

8. Has the consortium been involved in patents, start-ups or other outcomes with impact to health? Short description (please highlight the consortium partners involved)
No

9. Did you use non-academic broad dissemination channels to communicate your project progress, i.e. social media, lay conferences? (Please indicate the dissemination channels and list references for project social media accounts if relevant)
No

Please submit by April 30th 2024 to: neuroncalls@agencerecherche.fr

NEURON JTC 2021 Secretariat