

ECNP Experimental Medicine Network

ECNP Congress, Milan

Sunday September 22 2024, 10:30 – 11:30

Meeting Minutes

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Chair: Dennis Hernaus

Introduction and summary of network activities

The meeting started with a round of introductions and an overview of recent initiatives that have come out of the Experimental Medicine Network.

As a first example, Gerry Dawson discussed the Psychiatric Ratings using Intermediate Stratified Markers ([PRISM](#)) project, which is coordinated by Martien Kas (University of Groningen) and lead by Hugh Marston (Boehringer Ingelheim). PRISM aims to find transdiagnostic illness markers (across schizophrenia and Alzheimer's Disease), with a special emphasis on social functioning/withdrawal. PRISM 1 and 2 data provided robust evidence for an association between default mode network connectivity and social functioning. Simon Braak explained how the effect sizes of these associations were similar across data waves.

As a second example, Dennis Hernaus presented on the Reward Task Optimisation Consortium ([RTOC](#)); an academic-industry collaboration that aims to develop standardized task-based paradigms for detecting motivational impairments (e.g., anhedonia, apathy). Critical aspects of reward and motivation paradigms (e.g., trial number, stimuli, money amounts) are usually not standardised, with each research group using their own approach. The RTOC developed standardised versions of these tasks (grip effort, doors tasks, reinforcement learning+working memory task) and administered them to people with depression and psychosis (results discussed further below).

The summary of on-going activities ended with a summary of the "Unmet Needs in Depression" Meetings; two Experimental Medicine stand-alone meeting organised in Frankfurt (February, June 2023). The consensus of these meetings was that the network is especially well-positioned to work on optimising the treatment pathway for novel antidepressants, developing new measurement tools/paradigms for motivational impairments, and patient outreach and dissemination.

On-going activities

Initial RTOC results have been submitted for publication and are under review. The first paper demonstrates that grip effort task performance differs between controls and people with depression (less willing to exert effort), but not between controls and people with schizophrenia (paper under



review). Some clinical participants exhibited a tendency to always exert effort, and these participants had different clinical (symptom) profiles. Ruth McKernan informed about the possibility of looking at medication effects, for which, unfortunately, there is too little data (n=40 per clinical group).

In addition to RTOC, the Experimental Medicine group has also put together a task force that is currently conducting a scoping exercise for translational considerations for drug development programmes targeting reward and motivation (lead by: Liz Tunbridge). Key topics have been identified and a primer paper is expected in the coming months.

Gerry Dawson and Daniel Umbricht discussed their recent "[*The role of biomarkers in clinical development of drugs for neuropsychiatric disorders - A pragmatic guide*](#)" paper (authors: Umbricht, Kas, Dawson). The paper highlights the role of biomarker in various stages of the drug development process. It was very well received by the journal, and one of the reviewers called it a "manifesto for the role of biomarkers in drug development". This emerged from the discussions at the "Unmet Needs in Depression" meetings (Frankfurt 2023, for minutes see <https://www.ecnp.eu/research-innovation/networks-thematic-working-groups/list-ecnp-networks/experimental-medicine/output>) and builds on work that Daniel Umbricht presented there.

New/Future activities

Some network members are currently exploring the possibility to conduct new initiatives.

The first initiative ("*Defining "pharmacotypes" of cognitive deficits in psychotic disorders*")/ **Umbricht Dawson, & Hernaus**) focussed on the use of task/neuroimaging (e.g., EEG) based measures to subtype people with psychosis into various cognitive deficit groups. The work is supposed to further build on other subtyping approach, like BSNIP.

The second initiative ("*Validating clinical endpoints for patient stratification and treatment response*")/ **Kas**) focusses on validating a new clinical endpoint for social functioning, which could also be used in clinical trials and meet regulatory standards. Data are expected to be collected via a digital (experience sampling) platform.

The third initiative ("*Validating biomarkers for patient stratification to improve clinical trial outcomes*")/ **Dawson**) focusses on systematically validation of biomarkers for screening for early compound failures and to stratify patients to enrich phase 2 trials.

The fourth initiative ("*Validating (dopamine-dependent) markers of reward and motivation*")/ **Hernaus**) proposed to use an available drug from ECNP's Medicine Chest (a selective D1 antagonist) to advance our understanding of the neuropharmacological basis of reward and motivation (impairments). As part of this initiative, members from the Prevention network (**Fusar-Poli**) and Experimental Medicine network (**Hernaus**) (other members forthcoming) will be teaming up to write a brief scoping review on currently available D1 and/or pro-cognitive treatments in early stages of mental illness.

Interested members are asked to contact the people leading the initiative (see above, or slides).



Indoc Research Platform

The meeting ended with a presentation from Stephane Pollentier and Dennis Doll of Indoc Research, a not-for-profit organization. Biomedical research generates increasingly larger and more complex datasets, and the results generated from these datasets often rely on custom algorithms or code. Indoc offers a Research Software Engineering service that targets these challenges, thus ensuring continuity and more impactful work. Indoc Research has experience with biomedical research and their not-for-profit model allows them to be partners in funding applications (which they also have experience with). Interested individuals can reach out to Dennis Doll and Stephane Pollentier of Indoc Research.

Final Notes

There will be another Experimental Medicine Stand-Alone meeting early in 2025. Should there be any interest in on-going or new initiatives, please reach out to [Dennis Hernaus](#) or [Gerry Dawson](#).