WP 7 – Complete

End report for Project area: Synaptic Health
Start date: 1 January 2015 **Completion date: 30 September 2016**
Date of form completion: 1st December 2018

Team members
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Objectives
To develop synaptic health (SH) as a theme for experimental studies.
1. Facilitate the development of a synaptic plasticity research network
2. Identify key and innovative research questions
3. Use the expert network to shape and prosecute a coordinated programme of research on synaptic plasticity and neuro-regeneration.
4. To integrate the synaptic health network with other DPUK EM platforms and (inter-)national initiatives

To engage partners in new funding of Dementia research. The majority of research funds have come from supplementary Pharma input to DPUK (£570k, Janssen, AZ), with £130k from DPUK seed funding and £100k from ARUK. In addition, our workshops and UK meetings have been funded by Janssen and DPUK.

Lessons Learnt
We consider that this has been a very successful workpackage of DPUK and are proud that the initial investment of time in forming a network of individuals, with multi-disciplinary skills and interest in synaptic health, is bearing fruit. In particular, we were able to successfully obtain new direct research funds (total ~£800k) to set up EM7, in the form of the NTAD study (New therapeutics in Alzheimer's disease: MEG biomarker platform development). These funds came from Janssen (£450k), DPUK (£130k), AZ (£120k), ARUK (£100k).
In parallel, the team have made a major contribution to the EU-JPND initiative for standardisation and harmonisation of EMG biomarkers for dementia in 2017-18 (submitted Nov 18), and have prepared the multicentre neurophysiology component of the forthcoming Deep and Frequent Phenotyping study. We have also contributed to other initiatives including MRC MINDMAPS study, in piloting the relationship between synaptic ligand PET and neurophysiology. We have also progressed with data sharing, including a pilot study report due for submission Dec 18, and arrangements for M/EEG data sharing through the DPUK XNAT network which was previously used for MRI but can now support MEG data sharing.
The principal NTAD study in EM7 is progressing well, with further interest from industry, and interest from potential new partners. The group is currently (December 18) refining the details of a new project that will form part of the Experimental Medicine component of the DPUK renewal application.
A lesson learnt from this workpackage is that setting up experimental medicine studies at multi-sites in the UK is not straightforward when initiating research contracts, and University finance agreements, especially where the study has attracted an industrial partner that had previously been outside of DPUK. This led to delays in the start of the NTAD project. In the future a clearer up-front framework with university research offices will be required to avoid significant contracting and finance agreement delays.

Where all Milestones completed YES
This workpackage has successfully met all its objectives.

Deliverables	Milestones	Milestone deadline	Work package dependencies	Person(s) responsible
Objective 1: Facilitate the development of a synaptic plasticity research network				

D1.1 Core group with wider connections established	M1.1.1 Strategic lead identified and regular meetings taking place	M1.1.1 Complete	None	Rowe, Jones & Isaac
Objective 2: Identify key and innovative research questions				
D2.1 Establish a core set of research questions for future investigation	M2.1.1 Questions presented for discussion	M2.1.1 Complete	None	Rowe & Jones
	M2.1.1 Future phase planning	M2.2.2 Complete	None	Rowe & Isaac
Objective 3: Use the expert network to shape and prosecute a coordinated programme of research on synaptic plasticity and neuro-regeneration				
D3.1 Plan and implement a coordinated programme of research	M3.1.1 Applications prepared for internal / external grants	M3.1.1 Complete	None	James & Jones
	M3.1.2 Extended group, academic and pharma	M3.2.2 Complete	None	Rowe & Isaac
Objective 4. To integrate the synaptic health network with other DPUK EM platforms and (inter-)national initiatives				
D4.1 To reach out to Imaging and Stem cell platforms, and coordinate multi-level research integration	M4.1.1 Initiate group meetings and applications prepared	M4.1.1 Complete	Imaging and Stem cell	Rowe & Isaac
	M4.1.2 Complete group meetings and applications prepared	M.4.1.2 Complete		

Outcomes

Please include ALL outcomes that have been completed, including papers published, protocols created and any other form of Outcome achieved.

The workpackage did not expect research publication or protocol output by Dec 2018, but research outputs/publications are anticipated from 2019-2020 from work funded by DPUK. The primary aim was to build an active network of researchers with an interest in synaptic health who would succeed in conceiving, and undertaking, innovative experimental medicine studies. This has been achieved, through our series of workshops, monthly teleconferences and face-to-face meetings in planning and writing the protocols and applications.

Research protocols to study synaptic health have been established for (i) NTAD, (ii) Deep & Frequent phenotyping pilot study (iii) Deep & Frequent phenotyping main and (iv) MINDMAPS, although only NTAD has direct funding from DPUK. Protocols for standardisation and harmonisation of MEG for dementia research has been developed and submitted for publication with separate EU-JPND funding, but including many of the academic and industry partners from DPUK-EM7.

Synaptic Health Network researchers remain active and publications are expected in 2019-2020. The initial work of the group led to the award from DPUK for Experimental Medicine study number 7, NTAD, which is ongoing at Cambridge, Oxford and Cardiff. The total award was £800k with contributions from Janssen (£450k), AZ-MedImmune (£120k) and ARUK (£100k). Janssen have recently agreed to fund a supplementary PET study (~£400k) that will run alongside the current experimental protocol.

Therefore the investment of DPUK into this EM7 workpackage has already translated into leveraged funding for supplementary experimental medicine studies, and influenced national and international consortia for innovative Dementia research.

Executive Summary of Project

This workpackage aimed to increase knowledge and awareness of synaptic health, developing a multidisciplinary research network from across academia and industry. The network has initiated innovative experimental medicine studies in synaptic health, including the validation of a human neurophysiology longitudinal biomarker platform to support early-stage interventional studies and early-phase clinical trials; with increased sensitivity and mechanistic insights into human Alzheimer's disease pathogenesis.

It has identified, and facilitated, broader opportunities for understanding synaptic health in dementia as part of national and international research initiatives. It has proved to be an excellent example of a successful public-private partnership with academics, clinicians and industrial company staff contributing to meet the challenge experimental medicine studies and planning for new treatment studies. This work led directly to a successful application from the DPUK Experimental Medicine fund for the NTAD study (New therapeutics in Alzheimer's disease: MEG biomarker platform development) which is now recruiting patients and producing early promising results. This project benefits from additional industry investment to support a further PET study of synaptic health, connecting brain physiology and cognition.

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