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Editorial

EDITORIAL

International Delirium Pathophysiology & Electrophysiology Network for Data sharing (iDEPEND)

Robert D. Sanders[1,*], Leiv Watne[2], Shawniqua Williams Roberson[3], Eyal Y. Kimchi[4], Arjen J. C. Slooter[5], Colm Cunningham[6], Kirill V. Nourski[7], Ben J. A. Palanca[8], Richard Lennertz[9] and Matthew I. Banks[9]

[1]University of Sydney & Royal Prince Alfred Hospital, Camperdown, NSW, Australia, [2]Oslo Delirium Research Group, Akershus University Hospital, & Institute of Clinical Medicine, Campus Ahus, University of Oslo, Oslo, Norway, [3]Critical Illness, Brain Dysfunction and Survivorship (CIBS) Center, and Departments of Neurology and Biomedical Engineering, Vanderbilt University Medical Center, Nashville, TN, USA, [4]Department of Neurology, Northwestern University, Chicago, IL, USA, [5]Departments of Psychiatry and Intensive Care Medicine, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, [6]Trinity Institute of Neurosciences, Trinity College Dublin, Dublin, Ireland, [7]Department of Neurosurgery & Iowa Neurosciences Institute, University of Iowa, Iowa City, IA, USA, [8]Departments of Anesthesiology and Psychiatry, Washington University School of Medicine in St. Louis, St. Louis, MO, USA and [9]Department of Anesthesiology, University of Wisconsin, Madison, WI, USA

*Corresponding author. E-mail: robert.sanders@sydney.edu.au

Summary

In an era of 'big data', we propose that a collaborative network approach will drive a better understanding of the mechanisms of delirium, and more rapid development of therapies. We have formed the International Delirium Pathophysiology & Electrophysiology Network for Data sharing (iDEPEND) group with a key aim to 'facilitate the study of delirium pathogenesis with electrophysiology, imaging, and biomarkers including data acquisition, analysis, and interpretation'. Our initial focus is on studies of electrophysiology as we anticipate this methodology has great potential to enhance our understanding of delirium. Our article describes this principle and is used to highlight the endeavour to the wider community as we establish key stakeholders and partnerships.

Keywords: biomarker; collaboration; delirium; electrocorticography; electroencephalography; surgery

In an era of 'big data', collaborative networks facilitate rapid answers to complex questions. We propose that understanding the mechanisms of delirium, and hence the development of therapies for this condition, is a formidable task that requires such a collaborative approach. In depth, multi-modal phenotyping of patients is a critical step to defining the neural correlates of delirium. Once these correlates are firmly established, causal relationships can be established through preclinical animal models and clinical trials in patients.

Although delirium science advances on many fronts, we argue that EEG and invasive electrophysiology (i.e. intracranial EEG [iEEG]) has much to offer in the study of delirium. Particular strengths of the EEG include the direct sampling of neurophysiological data on a rapid time scale and fine precision that can be achieved at the patient's bedside. The feasibility of EEG to inform the study of delirium has been established over several decades (dating back to work by Engel and Romano[1]). More recent advances involve sophisticated analytical and modelling approaches to gain key insights into brain network connectivity and metrics of information content of the brain.[2–5] Correlates between patient symptoms and other biomarkers (e.g. systemic inflammation) provide

additional support for the utility of EEG to provide insights into delirium pathophysiology.[2–4,6,7] Lastly, EEG-based measures of delirium are associated with important clinical outcomes including mortality.[8,9]

The primary limitation of EEG is the poor spatial resolution that is somewhat mitigated by modelling approaches or directly mitigated by studying iEEG in neurosurgical patients. The latter approach also has the potential of characterising delirium arising from multiple triggers (e.g. surgery, seizure) in the same patients. As imaging techniques advance, we hope EEG may be complemented by concurrent positron emission tomography, magnetic resonance imaging, and optical imaging approaches that are currently logistically difficult in patients with delirium. Another limitation in the study of EEG data, in the setting of delirium, is the lack of collaborative expertise to advise on the collection and analysis of these data. Presently, these electrophysiology 'skills' are held by a small group of experts.

To address this limitation, we have formed the International Delirium Pathophysiology & Electrophysiology Network for Data sharing (iDEPEND) group with a key aim to 'facilitate the study of delirium pathogenesis with electrophysiology, imaging, and biomarkers including data acquisition, analysis, and interpretation'. To bridge knowledge gaps, iDEPEND will facilitate harmonised data collection protocols, data sharing, and advice on analysis and interpretation. Our aim is to disseminate these skills to a broader population of researchers through advice, hands-on demonstration, and collaborative data analysis and interpretation. In addition, experts with experience in EEG studies of delirium will convene to establish guidelines to inform study design and provide harmonised data protocols. These guidelines will be published in peer-reviewed journals and curated on a dedicated website to facilitate broad access.

We propose that data will be shared in a deidentified manner with unblinding conducted after standardised preprocessing of data where possible. Metrics derived from data analysis will be shared back with the primary site with advice on the appropriateness of further analysis. Scientific decisions for protocolised analysis will be discussed by a steering committee comprising study principal investigators providing data and experts in the field. A principal investigator will be the person in charge of a biomarker, electrophysiology study of delirium, or both, with an ethics-approved protocol for data collection shared with the steering committee. Electrophysiology experts will be recruited with suggestions from the steering committee.

Discussions will be held to address and guide how preclinical electrophysiology can be harmonised across models with maximum relevance to the human state of delirium.[10,11] Much of the recent EEG work has been conducted in the perioperative space, hence our submission to *BJA Open*, but a key ambition of the network is to facilitate electrophysiology research in medically ill and critically ill patients, leveraging perioperative discoveries.

Currently, funding for the network is from departmental resources, but we anticipate the submission of grants to support the acquisition, analysis, and interpretation of the data. Individuals interested in being part of the network should reach out directly to the first author, RDS. Our goal is to be as inclusive as possible though we acknowledge that, at this stage, our proposal has grown organically; as the network develops, it will be important to develop network structure, governance, and encourage diversity. Although the purpose of iDEPEND is to facilitate analysis of electrophysiology data in the first instance, we are optimistic this framework may be extended to biomarker analyses across human and animal cohorts to aid a better fundamental understanding of delirium pathogenesis.

Authors' contributions

Proposed the article: RDS
Identified the co-authors: RDS
Wrote the first draft: RDS
Commented on the draft: all authors

Declarations of interest

RDS is an editor of the *BJA*. The other authors declare that they have no conflicts of interest.

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