Robert D. Sanders, B.Sc., M.B.B.S., Ph.D., F.R.C.A., Recipient of the 2020 James E. Cottrell, M.D., Presidential Scholar Award

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THE 2020 recipient of the James E. Cottrell, M.D., Presidential Scholar Award is Robert D. Sanders, B.Sc., M.B.B.S., Ph.D., F.R.C.A. We served as his department chairs and mentors during his clinical and research training at Imperial College London (M.M.) and when he was assistant professor of anesthesiology at the University of Wisconsin-Madison (R.A.P.). We had the good fortune of watching, from front-row seats, a meteoric progression from his medical school in London to his recent appointment as Nuffield Chair of Anaesthetics at the University of Sydney, Australia. What follows are personal reflections of time spent observing and collaborating with a rising star in our discipline.

Rob was drawn to the field of anesthesia research in 2001, when he was in the latter half of his 6-yr training to become a doctor at Imperial College London. Although well into his clerkships, Rob had not yet found a clinical calling, but he had the bold idea of wanting to understand consciousness by exploiting the unconsciousness produced by anesthesia. In a trait that has become a hallmark of his career, Rob crafted a program of studies that had no precedent by convincing the chair of neurosciences, with whom he would do his coursework, and myself (M.M., as the chair of anaesthetics), with whom he would perform his practical studies, that this could be a route to an intercalated bachelor of science in neuroscience, which he later obtained with first-class honors. While Rob did not solve the consciousness conundrum as an undergraduate, he was well and truly launched on a career in anesthesiology and the neurosciences, and in the ensuing decade he completed his undergraduate medical degree (again with distinction), his registrar ("residency") training in anesthesiology, and then a Ph.D., all while publishing more than 40 articles.

During his time in London, and remotely thereafter, Rob led multiple projects involving anesthetics as diverse as xenon and dexmedetomidine, using them as probes to address mechanistic questions of neuroprotection and neurotoxicity. It is noteworthy that at a time when the unitary theory of anesthetic action held sway, Rob was able to show that this could not obtain, because the various behavioral elements of a single anesthetic agent had different mechanisms of action![1] Not satisfied with having to extrapolate, with all the usual caveats, from animal studies to patients, Rob then extended his training by undertaking a fellowship in clinical imaging and noninvasive techniques with which to probe neuroscientific questions in patients and volunteers; he used these as a springboard for his subsequent highly successful studies at the University of Wisconsin.

Fig. 1. Robert D. Sanders, B.Sc., M.B.B.S., Ph.D., F.R.C.A., recipient of the 2020 James E. Cottrell, M.D., Presidential Scholar Award.

Having rigorously trained in both basic science and clinical anesthetic practice, Rob straddled these seemingly disparate worlds, as exemplified by his next project. After

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reviewing data from the Randomized, Double-blind Trial in Ventilated ICU Patients Comparing Treatment with an Alpha2 Agonist *versus* a Gamma Aminobutyric Acid (GABA)–Agonist to Determine Delirium Rates, Efficacy of Sedation, Analgesia and Discharge Cognitive Status (MENDS I) trial (led by Pratik Pandharipande *et al.* at Vanderbilt), he was intrigued by the difference in mortality in the septic cohort between those sedated with midazolam *versus* dexmedetomidine.[2] Rob speculated that the reason for the difference lay in their divergent actions on the immune response, forming the basis for his Ph.D. Having established the adverse action of benzodiazepines on immunocytes in *in vitro* studies, he predicted that outcome of community-acquired pneumonia would be adversely affected in patients that chronically used these drugs for therapeutic purposes; that, in fact, turned out to be the case,[3] providing an important plank in the crusade against the use of benzodiazepines for sedation in critically ill patients who are prone to developing delirium and/or sepsis.

When Rob joined the faculty of the University of Wisconsin as assistant professor of anesthesiology in 2014, he refined his sights on two ambitious goals: (1) understanding the mechanisms of sensory disconnection and unconsciousness, and (2) establishing the pathophysiologic basis of perioperative delirium and cognitive decline. With the clear realization that making headway would require expertise beyond his own, he sought out and engaged with world-class investigators with related interests. These included Giulio Tononi, M.D., Ph.D. (Department of Psychiatry), who helped recruit Rob to Madison and with whom he collaborated on studies of consciousness and disconnection; Yuri Saalmann, Ph.D. (Department of Psychology), with whom Rob initiated studies of thalamocortical signaling under anesthesia in human volunteers and in nonhuman primates; Sterling Johnson, Ph.D. (Department of Geriatrics), who provided Rob with insight and access to the local Alzheimer disease research community; and Matt Banks, Ph.D. (Department of Anesthesiology), with whom Rob worked to develop an animal model of delirium. These connections proved to be productive; they led to more than 40 peer-reviewed articles during the past 5 yr, and a Mentored Patient-oriented Research Career Development Award and two Research Project Grants (R01) from the National Instititues of Health. In recognition of these academic achievements, Rob was awarded the 2018 Royal College of Anaesthetists Macintosh Professorship.

Rob's research is notable for its innovation, its breadth, and the unusual translational capacity that it offers. An example of his extremely innovative thinking is the concept of "connectivity" as a dimension of cognitive function that can be impacted by anesthesia or disease. In 2012, Rob published a provocative concept article[4] that explored the various dimensions of cognitive function. Previously, responsiveness to behavioral command had been considered as an accepted surrogate for consciousness. In that publication, Rob advanced the concept that "unresponsiveness is not equal to unconsciousness," and he argued that events in the external world might influence the internal mental state only when there is adequate connectivity between sensory input and thalamocortical function, even if "internal consciousness" was present. Moreover, he argued that this new dimension of cognitive function could be modulated by anesthetic drugs, as well as by physiologic and pathophysiologic conditions. In his research at the University of Wisconsin, Rob confirmed that "connectedness" can indeed vary independently of consciousness and responsiveness, both under anesthesia and during sleep.[5] He also found that unresponsiveness is associated with changes in feed-forward cortical connectivity[6]—an intuitive contrast to the changes in feedback cortical connectivity that other investigators have associated with unconsciousness. This work adds substantially to our understanding of the brain, and how it can be impacted by drugs and disease.

The diversity of research to which Rob has contributed is also remarkable. He has conducted detailed investigations of cognitive function in the perioperative period in patients who are at risk for cognitive decline.[7–9] He has conducted electroencephalographic (EEG) and magnetoencephalographic measurements of human volunteers to understand what types of EEG signatures accompany changes in connectedness and consciousness.[5,6,10–13] He has studied how novel treatments such as xenon can impact recovery from central nervous sytem injury and anesthesia.[14–16] He has studied the EEG correlates of amyloid, tau, and neurodegenerative pathologies in aging and dementia.[17] He has examined age-related changes in magnetic resonance imaging measurements of cortical thickness as a possible contributor to delirium and dementia[18] and collaborated with the Detection and Neurological Impact of Cerebrovascular Events In Noncardiac Surgery Patients: A Cohort Evaluation (NeuroVISION) group in identifying associations of perioperative covert stroke and longer term cognitive decline.[19] Perhaps of most significance to date, he has investigated the impact of surgery on the longitudinal cognitive trajectory through collaboration with the Whitehall study.[9]

It is hard to overstate the potential impact of the type of translational research that Rob is conducting. Postoperative delirium is a major challenge faced by elderly patients, who represent an increasing fraction of the surgical cohort. It has been recognized by the American Society of Anesthesiologists as one of the high impact areas that must be addressed for improvement in perioperative care. Delirium is associated with substantial costs in terms of human disease burden and financial implications. Rob is addressing this issue head-on, identifying factors that can be used to identify patients at high risk who can receive additional attention in the perioperative period in hopes of reducing their morbidity and mortality.[7,8,20] Even more importantly, by studying the underlying pathology that leads to delirium, novel strategies for prevention and

treatment can be identified. This type of research is difficult but exceedingly important.

While this all describes Rob's hard-driving academic life, these efforts have not detracted from his dedication to the clinical side of the specialty, where he has worked tirelessly on development of clinical guidelines for anesthetic practice[21] based on associations of preoperative blood pressure and medications with postoperative mortality.[22–26] He has also inspired numerous residents and other clinical colleagues to join him in these academic pursuits.[11,27–29] Likewise, Rob's dedication has not kept him from making a strong commitment to family life. Rob and his spouse, Dr. Helen Manning, a fellow physician, are devoted to their three children, Kate (10), Henry (8), and Heidi (5), who have not just tolerated, but thrived as their parents now embark on their second intercontinental voyage.

What these vignettes demonstrate are the many characteristics that have enabled Rob to be selected for this prestigious American Society of Anesthesiologists Presidential Scholar award. Rob is a self-starter who has (1) the intellectual capacity to frame bodacious questions in a tractable manner, (2) the initiative to acquire the resources needed to conduct the necessary studies, (3) the fortitude to cajole busy scientists and clinicians to join him in these worthy pursuits, (4) the persistence to overcome the perpetual obstacles, (5) the self-effacement with which to deflect praise, and (6) the willingness to help others in both vocational and extravocational activities. Rob's academic journeys have taken him from his Geordie heritage in the north east of England, to London (both Imperial College and University College), and to Madison, Wisconsin; each of these sojourns have resulted in scientific successes. The same will no doubt be true in his new location in Sydney, Australia, because the necessary ingredients are hard-baked into his being.

Competing Interests

The authors declare no competing interests.

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