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Preface

Special Issue on Cerebral Autoregulation: Measurement and modelling

The purpose of the current Special Issue on Cerebral Autoregulation is to highlight recent advances in the assessment of cerebral autoregulation, with contributions from many of the leading interdisciplinary research groups in the field. Autoregulation usually refers to the ability of the cerebrovascular bed to maintain a relatively constant blood flow in response to arterial blood pressure changes and is considered a key mechanism in protecting the brain from damage due to under- or over-perfusion. Closely related mechanisms maintain an adequate blood supply when other physiological conditions change, such as those resulting from fluctuations in arterial CO_2 levels, metabolic demand or intracranial pressure. The clinical implications of autoregulation span from neonates to the elderly population and include vascular disease, stroke, head trauma, neurodegenerative diseases and anaesthesia. Research interest in this field has grown over recent years, and in 2011 led to the founding of an international, interdisciplinary research group on the topic – the cerebral autoregulation network (CARNet – http://www.car-net.org/). The collaboration of this network has made this Special Issue possible – and we are very grateful for all contributors for submitting and reviewing the papers.

Modern physiological measurement techniques have made it possible to accurately and noninvasively measure arterial blood pressure (especially non-invasive techniques using finger plethysmography) and cerebral blood flow (by transcranial Doppler ultrasound or NIRS) at high temporal resolution, allowing the dynamic nature of autoregulation to be assessed and monitored over extended periods. The assessment of dynamic rather than the static responses in flow to changing blood pressure has become the dominant method, primarily due to the much simpler experimental procedures required. The assessment of autoregulation however continues to present major challenges in terms of measurement methods and experimental protocols, as well as data analysis, with respect to robustly detecting and grading autoregulation from the recorded data. This has resulted in new interdisciplinary research avenues and to the application of a wide range of mathematical and engineering tools in order to quantify autoregulation in health and disease, with the ultimate aim of enhanced understanding of the relevant physiology and clinical exploitation and improved, personalized care. To date, no gold-standard method for assessing autoregulation has become established and the benefits of this research to patients have remained relatively limited. A growing awareness of the potential importance of this brain-protective mechanism motivates the increasing research effort focused on methods to quantify autoregulation. There is also an increasing realization of the complexity of the underlying physiology, pathophysiology and the challenges in relevant physiological measurements, which must be included in the search for sensitive biomarkers of impaired autoregulation. The present Special Issue brings together a number of recent advances in that direction.

A number of papers in the Special Issue deal with the assessment of autoregulation using spontaneous physiological variability, an increasingly popular experimental protocol that minimizes interventions on the subjects and is therefore readily applicable in repeated recordings even in vulnerable patients. A land-mark multi-center study is presented by van den Abeleen et al., led primarily by J. Claassen on behalf of CARNet, and examines the between-center variability of one of the most popular methods to assess dynamic autoregulation: transfer function analysis. A closely related study also authored by van den Abeleen provides a much needed review of transfer function analysis methods reported in the literature. Both these papers are working towards standardizing methods to improve our ability to compare results across studies. Transfer function analysis is only one of many methods employed. The paper by Zweifel et al. provides a very useful review of a very large body of work originating from the group in Cambridge on using correlation measures to assess cerebral haemodynamic control. The article by Angarita Jaimes et al. evaluates an array of different measures to assess autoregulation by comparing their performance in detecting impaired autoregulation induced by hypercapnia. This work highlights the challenge of defining what is 'best' for measuring functioning or impaired autoregulation, when there is no gold-standard to work with. The complexity of autoregulation and its assessment are further brought out by the recently emerging approaches to assess its time-varying (nonstationary) characteristics. The review article by Panerai summarizes the physiological factors that give rise to this phenomenon, as well as the main approaches that have been used to date to obtain time-varying measures of autoregulation. The article by Kostoglou et al. illustrates a novel methodological approach to obtain time-varying, multivariate models of autoregulation, based on function expansions of data-driven models and its application to a hypercapnic experimental protocol. Non-linear, multivariate closed loop interactions between blood pressure, flow

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and CO_2 are explored in the paper by Marmarelis and co-workers. The two articles by Elting et al. address the important issue of the reproducibility and variability of autoregulation measures. The first article examines the variability of the autoregulation index by considering the effect of very low frequency fluctuations in the relevant physiological signals and suggests that reduced variability, as well as more pronounced differences between healthy subjects and stroke patients are observed when this effect is removed. The second article deals with the effect of a passive cyclic leg raising protocol on the reproducibility and variability of dynamic autoregulation indices. Both these papers and that of Kostoglou et al. suggest the benefit from reducing the confounding effects of CO_2. In a similar vein, the paper by Gommer et al. shows the benefit of correcting for changing blood pressure when assessing the blood flow response to visual stimulation.

The papers presented here demonstrate the challenges in measurement and the contributions of modelling in progressing towards robust biomarkers of impairment and a better understanding of autoregulation, and finally, as we all hope, benefit to large numbers of patients. We wish to extend our warm thanks to all contributors for submitting high quality articles to this Special Issue, which we hope will prove highly successful and help in driving further research on this important topic, as well as all the paper reviewers.

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