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Invited review

Utility of transcranial Doppler ultrasound for the integrative assessment of cerebrovascular function

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ABSTRACT

There is considerable utility in the use of transcranial Doppler ultrasound (TCD) to assess cerebrovascular function. The brain is unique in its high energy and oxygen demand but limited capacity for energy storage that necessitates an effective means of regional blood delivery. The relative low cost, ease-of-use, non-invasiveness, and excellent temporal resolution of TCD make it an ideal tool for the examination of cerebrovascular function in both research and clinical settings. TCD is an efficient tool to access blood velocities within the cerebral vessels, cerebral autoregulation, cerebrovascular reactivity to CO_2, and neurovascular coupling, in both physiological states and in pathological conditions such as stroke and head trauma. In this review, we provide: (1) an overview of TCD methodology with respect to other techniques; (2) a methodological synopsis of the cerebrovascular exam using TCD; (3) an overview of the physiological mechanisms involved in regulation of the cerebral blood flow; (4) the utility of TCD for assessment of cerebrovascular pathology; and (5) recommendations for the assessment of four critical and complimentary aspects of cerebrovascular function: intra-cranial blood flow velocity, cerebral autoregulation, cerebral reactivity, and neurovascular coupling. The integration of these regulatory mechanisms from an integrated systems perspective is discussed, and future research directions are explored.

Contents

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1. Introduction

Maintenance of adequate cerebral blood flow (CBF) is necessary for normal brain function and survival. That the brain receives ~15% of total cardiac output and is responsible for ~20% of the body's oxygen consumption, despite being 2–3% of total body weight, is testament to its high energetic cost. This, combined with a very limited ability to store energy (the brain's total energy pool would theoretically allow it to function for ~12 min were energy substrate supply abolished) requires effective regulation of blood supply. Numerous pathologies such as head trauma, carotid artery disease, subarachnoid hemorrhage and stroke result in disturbances to the regulatory mechanisms controlling CBF (Hossmann, 1994; Panerai, 2009). However, the skull makes it difficult to measure parameters such as blood flow and blood velocity. Many approaches such as radio-opaque tracers, radioactive markers and similar methods are inadequate because of poor temporal resolution (see Table 1 for a summary of the advantages and disadvantages of other methods). Key factors that determine adequate CBF for maintenance of cerebral oxygen delivery are: (1) sensitivity to changes in arterial PO_2 and PCO_2 (cerebrovascular reactivity) and the unique ability to extract a large amount of available oxygen; (2) effective cerebral autoregulation (CA) that assists maintenance of CBF over a wide range of perfusion pressures, helping to prevent over/under perfusion and consequent risk of hemorrhage or ischemia, and (3) matching of local flow to localized metabolic needs (neurovascular coupling; NVC). The high temporal resolution and non-invasive nature of transcranial Doppler ultrasound (TCD) make it a useful tool in the assessment of integrative cerebrovascular function in terms of cerebral reactivity, autoregulation and NVC. New technologies are further increasing the utility of TCD. For example, combining TCD with microbubble contrasting agents allow for quantification of local changes in perfusion for measuring absolute volumetric flow (Powers et al., 2009). However, the interaction of ultrasound with microbubble contrast agents is complex and beyond the scope of this review; the reader is referred to Powers et al. (2009) for a detailed review of the current state of contrast TCD technology. With or without contrast, a TCD machine is relatively inexpensive ($20,000–$50,000 USD); moreover, TCD is easy to use and it is safe in healthy and disease states alike. For these reasons TCD is practical in the clinical setting, where it is used to assess a variety of different cerebrovascular pathologies.

The principal aim of this review is to summarize the utilities of TCD in the assessment of cerebrovascular function with respect to other common measurement tools. Specifically, we aim to: (1) examine the advantages and disadvantages of TCD in the context of other imaging metrics; (2) highlight the optimum approaches for insonation of the basal intra-cerebral arteries; (3) provide a detailed summary of the utility of TCD for assessing cerebrovascular reactivity, autoregulation and neurovascular coupling and the clinical application of these measures, and (4) provide recommendations on the integrative assessment of cerebrovascular function and avenues for future research.

2. Techniques for the measurement of cerebral blood flow and velocity

Kety and Schmidt (1945) were the first to quantify CBF using an inert tracer (e.g., nitrous oxide, N_2O). The reference method for the measurement of global CBF, the Kety-Schmidt method is based on the Fick principle, whereby the arterio-venous difference of an inert tracer is proportional to the volume of blood flow through the brain (Kety and Schmidt, 1948). The tracer is infused until tension equilibrium is attained (the saturation phase) and then terminated, after which the concentration falls towards zero (the desaturation phase). Simultaneous arterio-jugular venous samples