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## **Defining Cerebral Autoregulation-Guided Therapeutic Targets in Sepsis**

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Changes in cerebral autoregulation during sepsis may play a critical role in the high morbidity and mortality among patients with sepsis-associated encephalopathy (SAE). Sepsis guidelines recommend mean arterial pressure (MAP) of greater than 65 mmHg for adequate organ perfusion. Bedside assessment of cerebral autoregulation may help to individualize hemodynamic targets that optimize brain perfusion. We have shown that near-infrared spectroscopy (NIRS) monitoring can distinguish optimal MAP for autoregulation in patients with SAE. The overall goal of this proposal is to determine whether hypoperfusion defined by individualized autoregulation-guided targets is associated with increased incidence and severity of SAE as compared to that defined by standard thresholds. First, we will use data-driven approaches to identify risk factors for differences between empiric targets and therapeutic targets tailored to autoregulation. We will monitor sepsis patients with NIRS for 3 days and explore high frequency variables that affect optimal MAP and autoregulatory limits. Next, we will test the hypothesis that patients with SAE and poor neurocognitive outcome are managed at MAPs differing more from their autoregulation-based targets than are patients without SAE. Neurocognitive evaluations will be performed at set intervals up to one year. Our findings could greatly influence sepsis management. Trends in how specific variables affect optimal MAP could help individualize targets and will provide the necessary data to design and power a future randomized trial to evaluate the effect of individualizing therapy. Personalized goals based on cerebral autoregulation monitoring may decrease the impact of SAE and improve outcome from sepsis.