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Characterization and Quantification of Multimodal Cerebral Monitoring Events and their Relationship to Spreading Depolarizations in Brain-Injured Patients

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The common denominator among the various types of brain injury is the fact that the primary injury is essentially irreversible; one can only attempt to prevent so-called secondary insult in order to protect the still-intact neurons surrounding the injury. The focus of the present study was on the hemodynamic, metabolic and electrocorticographical events resulting from this secondary ischemia with the goal of quantifying pathological changes in these parameters as well as charting their effects on outcome. Specifically, the bedside neuromonitoring technology that has been developed over the past 20 years was utilized to quantify and characterize transient pathological tissue changes for the very first time and to explore their causes as well as their effects on outcome. Electrocorticographical data was examined with respect to spreading depolarizations (SD), a relatively newly discovered phenomenon in man found to be linked to secondary insult and infarct deterioration.
A total of 24 brain-injured patients requiring craniotomy with a mean age of 52±11 years took part in this prospective observational study at the University of Heidelberg between September of 2004 and September of 2006. In addition to the "standard" neurointensive care unit monitoring measures (heart rate, temperature, blood pressure, etc.), patients received the following additional probes: an invasive intracranial pressure probe, a linear strip electrode (6 or 8 platinum contacts; Wyler, 5/10 mm; Ad-Tech Medical Instrument Corp., Racine, WI) for EcoG data, a cerebral microdialysis probe (CMA70/71, CMA, Solna, Sweden) and a regional cerebral blood flow probe via thermodiffusion (QFlow500, Hemedex Inc., Cambridge, MA).
A total 3,628 hours of monitoring time from 24 brain-injured patients were analyzed and a total of 1,398 transient metabolic and hemodynamic events were identified and scrutinized for their causality.
Hemodynamic events accounted for up to 27% of monitoring time and microdialysis events accounted for up to 74% of monitoring time, on average, respectively, which are surprisingly high numbers. Primary injury was found to be the cause of 0% of these events in some parameters (e.g. cerebral hyperglycemia), and up to 76% of others (e.g. lactate/pyruvate ratio). Up to 1/3 of these events had unknown causes after extensive analysis. Causes found included many expected factors such as arterial hypotension for CPP and vasospasm for CBF, but also many unexpected factors such as nursing maneuvers. The majority of causes found are factors within the control of the NICU team such as hypocapnia, systemic hypo- and hyperglycemia, arterial hypotension and hyperthermia and are thus avoidable.
In addition, 397 spreading depolarizations were identified in 13 of the 24 patients, which confirms their presence in brain-injured patients. Further, their causality was explored with respect to the hemodynamic and metabolic parameters in order to better understand their pathophysiology and function. CBF was found to be especially affected by the occurrence of SD as well as cerebral glucose and lactate levels and the more global parameters systemic hyperglycemia, hypoglycemia and hypotension.

Lastly, patient outcome as determined by GOSe and SF-36 scores at the time of the 6-month follow-up exam were used in a correlation analysis to explore the impact of these hemodynamic, metabolic and electrocorticographical changes in brain-injured patients on their outcome. The only factors found to positively influence outcome as measured by the GOSe was the number of SD after 7 days and the number of events caused by hypocapnia. Events caused by systemic hypotension had a negative correlation with GOSe. SF-36 outcome was also positively correlated with SD after 7 days as well as the number of L/P events. Events caused by seizure and unclear events were found to be positively related to outcome as well. A negative correlation could be identified with systemic hypotension and SF-36 outcome.

In summary, although a direct causal relationship between transient hemodynamic and metabolic events could not be appreciated, important information about their causes could be made, which not only influences future studies, but more importantly influences current clinical management strategies. Similarly, though our SD analyses were inconclusive with respect to outcome, we have both affirmed the existence of SD in brain-injured patients and described important hemodynamic and metabolic characteristics, which will aid future studies in this exciting area of research.