INHIBITION OF ACETYLCHOLINESTERASE MODULATES NMDA RECEPTOR ANTAGONIST MEDIATED ALTERATIONS IN THE DEVELOPING BRAIN
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Background and aims: Exposure to N-Methyl-D-aspartate (NMDA) receptor antagonists has been demonstrated to induce neurodegeneration in newborn rats. However, in clinical practice the use of NMDA receptor antagonists as anesthetics and sedatives cannot always be avoided. This study investigated the effect of the acetylcholinesterase (AChE) inhibitor physostigmine on neurotransphin expression and the extracellular matrix during NMDA receptor antagonist-induced injury to the immature rat brain. Aims: The aim was to investigate matrix metalloproteinase (MMP)-2 activity, as well as expression of tissue inhibitor of metalloproteinase (TIMP)-2 and brain-derived neurotrophic factor (BDNF) after co-administration of the non-operative NMDA receptor antagonist MK801 (dizocilpine) and the AChE inhibitor physostigmine. Methods: Six-day-old Wistar rat pups received intraperitoneal injections of dizocilpine (+/-MK801; 0.5 mg/kg 0, 8, 16h) or vehicle in combination with physostigmine at 0 h and were sacrificed at defined timepoints (6, 12, 24h) following treatment. All procedures were approved by the local state authorities for animal welfare (G0182/09) and followed institutional guidelines. Results: Brains were processed for molecular analysis (real-time PCR, Western blotting and gelatin zymography) to measure BDNF, MMP-2 and TIMP-2. Results: The AChE inhibitor physostigmine ameliorated the MK801-induced reduction of BDNF mRNA and protein levels. MK801/MMP-2 activity and prevented increased TIMP-2 mRNA expression. Conclusions: The present study suggests that AChE may play a therapeutic role to target the toxicity resulting from NMDA receptor antagonist-induced injury in the developing brain. Our results show that a single application of the AChE inhibitor physostigmine modulates NMDA receptor blockade-induced changes in the levels of BDNF, MMP-2 and TIMP-2.

PREDICTING EXECUTIVE FUNCTION IN FIRST YEAR FOLLOWING PEDIATRIC TRAUMATIC BRAIN INJURY
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Background and aims: When parents are asked to describe their long-term concerns for their child with TBI, they often target executive dysfunction. Executive functions (EFs) are high-order cognitive abilities that mediate other cognitive processes. The mechanism of TBI-related EF changes is not well understood. Aims: We assessed the pattern of EF changes over the first year post-injury, including what EFs are affected, whether and how they recover, and potential predictors of these changes. Methods: 53 young, age 5 to 18 years, who had sustained uncomplicated mild to severe TBIs were recruited from five children's hospitals in Canada. Institutional Review Boards provided approval of the study. Parents completed rating of EF symptoms (Behaviour Rating Inventory of Executive Function) at time of injury (baseline) and at 3, 6, and 12 months post-injury. Serum protein and brain neuroimaging analysis provided potential biomarkers of TBI-related EF changes. Results: Parent reports of EF changes are heterogeneous following pediatric TBI with some abilities reportedly minimally affected (inhibition, planning, organization), while others exhibit decline in the first 3 months (working memory and initiation) or 6 months (emotional control, flexibility, and monitoring behaviour). Many EFs fail to fully recover one year following injury. Serum and brain biomarkers may predict persisting changes in EF. Conclusions: An acute brain MRI and serum biomarkers of brain injury may be important prognostic tools for predicting the course of EF changes following TBI, which is important for patients and their families because EFs are known to affect cognitive processes (memory and attention), academic achievement, and behaviour regulation.

KALLIKREIN-1 AS A POTENTIAL BIOMARKER OF GLOBAL CEREBRAL ISCHEMIA AND NEUROPROTECTION IN JUVENILE MICE
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Background and aims: Neuroprotective therapies are needed to improve the outcomes following ischemic brain injury from cardiac arrest in children. Previously we showed a monoclonal antibody to CD18 (aCD18ab) injected following injury blocks cerebral and systemic inflammation and improves neuronal survival and spatial memory in a 2 vessel occlusion (2VO) model of forebrain ischemia in juvenile mice. Aims: To discover serum biomarkers of cerebral ischemia and neuroprotection. Methods: This study was conducted in strict accordance with the Hospital for Sick Children and the University of Ottawa Animal Care Committees, and Canadian Council of Animal Care guidelines. Mice were randomized to 3 groups: 1) 2VO injected with 2 mg/kg aCD18ab; 2) 2VO injected with control antibody and; 3) sham. We included 10 mice in each of the 3 groups. Serum samples were taken at 24 hours following injury or sham operation and low abundance proteins were identified using tandem mass spectrometry. Results: More than 400 serum peptides were identified by mass spectrometry. Serum kallikrein-1 was significantly differentially expressed in the three groups. There was a 7 to 56 fold increase in the mice subject to 2VO and treated with a control antibody compared to sham, and a 98 to 505 fold increase in the mice subject to 2VO and treated with aCD18ab compared to sham. Conclusions: Our results suggest kallikrein-1 may be an important biomarker of neuroprotection which could be used in pilot randomized controlled trials of this neuroprotective therapy in children with cardiac arrest.

THE IMPACT OF THE IMPLEMENTATION OF AN ADAPTIVE SEDATION ALGORITHM ON THE COMFORT OF CHILDREN VENTILATED MECHANICALLY
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Background and aims: Sedation-anaesthesia to critically ill children in pediatric intensive care unit should optimize their comfort and safety. It must be evaluated and adapted frequently. Aims: The objective of this study is to evaluate the effects of the implementation of an adaptive sedation algorithm on the comfort of children ventilated mechanically. Methods: Prospective Observational study was conducted from November 2010 to November 2012, in single center. Were included all children less than 15 years, ventilated and sedated through combination of Hypnovel / sufentanil and do not require deep sedation therapy, at least 24 hours in pediatric intensive care unit. The process of evaluation was guided by COMFORT Behavior sedation Scale (2) The time spent in optimal sedation area was (COMFORT B between 11 and 17) The time spent in over-sedation (COMFORT B <11) and the time spent in area under sedation was (COMFORT B > 17). Results: 71 children were evaluated by comfort B scale. Their age was between 3-6yrs and the main causes for sedation-analgesia were neurological and respiratory disease. The Hypnovel / sufentanil combination was used in 67%. The mean number of evaluation was 11.8 per patient. The Time spent in optimal zone was 71.8%, in under sedation was 16.9% and in over sedation area was 11.2%. Conclusions: Our study showed that the use of an evaluation by (B Scale) is useful to scale and proportion the algorithm sedation and can help to predict the optimal sedation and reduced the time spent in areas of over and under sedation.

COMPARISON THE EFFECT OF BREASTFEEDING AND WRAPPING NEONATES ON BCG VACCINATION PAIN
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Background and aims: Pain is an unpleasant subjective experience that leaves short- and long-term negative effects in children and adults. Unlike adults, neonates are more sensitive to the negative effects of pain. Aims: to investigate the effect of swaddling and breastfeeding and its combination effect on pain caused by BCG vaccine in healthy and term neonates. Methods: in this double blind study 131 full healthy neonates were placed in three interventions and a control group randomly. Heart rate and blood oxygen saturation were monitored at base time, injection time and 2 min after vaccination. Also neonates’ faces were filmed and then based on the films their pain intensity was measured by NFCS index. ANOVA, Kruskal-Wallis and Mann - Whitney were employed to analyze the data. Results: The primary outcomes showed that the mean rating of pain intensity and changes in heart rate at injection time compared to the baseline was significant in the groups. No significant differences in terms of blood oxygen saturation changes were observed between groups (sig>.005). Conclusions: This study innovates from earlier studies in 3 aspects: the different interventions were evaluated separately as well as the combination of both breastfeeding and wrapping before and after the vaccination until the end of recovery; breastfeeding applied before vaccination and facial expressions as well as physiological responses were assessed during the procedure.