Exploring the science of how lifestyle impacts brain injury rehab

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Dynamic change in cortisol levels associated with severity, progression, and survival of patients with traumatic brain injury

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Conclusions

In the present study, we investigated serum cortisol levels in TBI cases, which is a form of stress that results in the secretion of increased serum cortisol levels immediately after trauma, that is, within 6 h of injury, decrease and trend to normal during overtime and recovery of patients. In this study, there was an increase in serum cortisol levels in severe TBI cases, whereas there was a gradual decrease in serum cortisol levels with the recovery of patients. In conclusion, we observed increased serum cortisol levels immediately after trauma. ….

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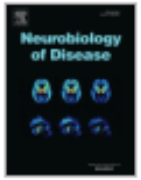

Review

Glucocorticoid impairs mitochondrial quality control in neurons

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Abstract

Neurons are particularly vulnerable to mitochondrial dysfunction due to high energy demand and an inability to proliferate. Therefore, dysfunctional mitochondria cause various neuropathologies. Mitochondrial damage induces maintenance pathways to repair or eliminate damaged organelles. This mitochondrial quality control (MQC) system maintains appropriate morphology, localization, and removal/replacement of mitochondria to sustain brain homeostasis and counter progression of neurological disorders. Glucocorticoid release is an essential response to stressors for adaptation; however, it often culminates in maladaptation if neurons are exposed to chronic and severe stress. Long-term exposure to high levels of glucocorticoids induces mitochondrial dysfunction via genomic and nongenomic mechanisms. Glucocorticoids induce abnormal mitochondrial morphology and dysregulate fusion and fission. Moreover, mitochondrial trafficking is arrested by glucocorticoids and dysfunctional mitochondria are subsequently accumulated around the soma. These alterations lead to energy deficiency, particularly for synaptic transmission that requires large amounts of energy. Glucocorticoids also impair mitochondrial clearance by preventing mitophagy of damaged organelle and suppress mitochondrial biogenesis, resulting in the reduced number of healthy mitochondria. Failure to maintain MQC degrades brain function and contributes to neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and Huntington's disease. However, mechanisms of glucocorticoid action on the regulation of MQC during chronic stress conditions are not well understood. The present review discusses pathways involved in the impairment of MQC and the clinical significance of high glucocorticoid blood levels for neurodegenerative diseases.

frontiers in Neuroscience

REVIEW
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Mitochondrial Dysfunction in Neural Injury

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Mitochondria are the double membrane organelles providing most of the energy for cells. In addition, mitochondria also play essential roles in various cellular biological processes such as calcium signaling, apoptosis, ROS generation, cell growth, and cell cycle. Mitochondrial dysfunction is observed in various neurological disorders which harbor acute and chronic neural injury such as neurodegenerative diseases and ischemia, hypoxia-induced brain injury. In this review, we describe how mitochondrial dysfunction contributes to the pathogenesis of neurological disorders which manifest chronic or acute neural injury.

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Psychological Stress and Mitochondria: A Systematic Review

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Conclusion - Overall, evidence supports the notion that acute and chronic stressors influence various aspects of mitochondrial biology, and that chronic stress exposure can lead to molecular and functional recalibrations among mitochondria. Limitations of current animal and human studies are discussed. Maladaptive mitochondrial changes that characterize this subcellular state of stress are termed mitochondrial allostatic load. Prospective studies with sensitive measures of specific mitochondrial outcomes will be needed to establish the link between psychosocial stressors, emotional states, the resulting neuroendocrine and immune processes, and mitochondrial energetics relevant to mind-body research in humans.

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Review Article

Traumatic Brain Injury and Mitochondrial Dysfunction

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Traumatic brain injury (TBI) is a major cause of death and disability in the United States and causes mitochondrial damage leading to impaired brain function. The purpose of this review is to (1) describe TBI processes and manifestations, (2) examine the mitochondrial alterations after TBI, specifically increased reactive oxygen species production, decreased bioenergetics and apoptosis and (3) current TBI treatments. There are various degrees of severity of TBI, yet all affect mitochondrial function. Currently, health care professionals use various methods to assess TBI severity—from brain imaging to serum biomarkers. The major cause of TBI-associated brain damage is secondary injury, which is mainly from mitochondrial injury dysfunction. Mitochondrial injury leads to oxidative stress and subsequent apoptosis and decreased cellular energy production. These brain cellular alterations impair neurologic functions, which are observed in individuals with TBI. The complex mitochondrial dysfunction after TBI requires treatment that specifically addresses the secondary injury. There are numerous therapies being used, including (1) hypothermia, (2) hyperbaric oxygen, (3) exercise and (4) antioxidants. Researchers are exploring novel approaches to prevent, diagnose and treat TBI focusing on maintaining mitochondrial function.

Stress-induced hyperglycemia is associated with higher mortality in severe traumatic brain injury

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RESULTS

During the study period, a total of 626 patients were included in the study group, having severe TBI defined by both GCS score of 3 to 8 and head AIS score being 3 or greater and also had available HbA1c and admission glucose levels. A total of 184 patients were admitted with hyperglycemia; 152 patients (82.6%) were diagnosed with SIH, and 32 patients (17.4%) were diagnosed with DH. When comparing patients with severe TBI adjusted for age, sex, injury mechanism, ISS, Revised Trauma Score (RTS), and lactic acid greater than 2.5 mmol/L, patients with SIH had a 50% increased mortality (HR, 1.49; 95% CI, 1.13–1.95) compared with the nondiabetic normoglycemia patients. DH patients did not have a significant increase in mortality (HR, 0.94; 95% CI, 0.56–1.58).

CONCLUSION

SIH is associated with higher mortality after severe TBI. This association was not observed among patients with DH, which suggests that hyperglycemia related to diabetes is of less importance compared with SIH in terms of mortality in the acute trauma and TBI patient. Further research is warranted to identify mechanisms causing SIH and subsequent worse outcomes after TBI.

Elevated Initial Blood Glucose Levels and Poor Outcome Following Severe Brain Injuries in Children

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The Journal of Trauma: Injury, Infection, and Critical Care 31(10):p 1356-1362, October 1991.

To determine whether elevations in blood glucose levels were related to neurologic outcomes following severe brain injuries in children, 54 patients 16 years of age or younger admitted to a regional trauma center with a Glasgow Coma Scale score of 8 or less over a 2-year period were retrospectively reviewed. The mean initial blood glucose level on hospital admission was significantly higher in the 16 patients with outcomes of death or vegetative state in comparison with that of the 38 patients with outcomes of good recovery, moderate disability, or severe disability (288 mg/100 mL vs. 194 mg/100 mL, t −2.74, p = 0.03). Blood glucose levels correlated significantly with indicators of the severity of the brain injury, which were also related to outcome. In contrast, blood glucose levels did not correlate with indicators of the severity of the extracranial injuries, although the latter were significantly related to outcome. Logistic regression analysis resulted in a model for prediction of outcome which included the Glasgow Coma Scale score on admission and the initial blood glucose level. The odds ratio of a poor outcome in this model in patients with blood glucose levels ≥ 250 mg/100 mL relative to those with lower levels was 8.3 (95% confidence interval 1.3–53.6). A simple prognostic score was derived from the logistic regression which improved upon the prediction of outcome using the Glasgow Coma Scale score alone in those patients with initial blood glucose levels ≥ 250 mg/100 mL. Our findings cannot address the questions of whether glucose administration after brain injury in children could be deleterious or of whether controlling hyperglycemia could be beneficial, but raise these issues for further study.

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The ketogenic diet as a therapeutic intervention strategy in mitochondrial disease

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Abstract

Classical mitochondrial disease (MD) represents a group of complex metabolic syndromes primarily linked to dysfunction of the mitochondrial ATP-generating oxidative phosphorylation (OXPHOS) system. To date, effective therapies for these diseases are lacking. Here we discuss the ketogenic diet (KD), being a high-fat, moderate protein, and low carbohydrate diet, as a potential intervention strategy. We concisely review the impact of the KD on bioenergetics, ROS/redox metabolism, mitochondrial dynamics and mitophagy. Next, the consequences of the KD in (models of) MD, as well as KD adverse effects, are described. It is concluded that the current experimental evidence suggests that the KD can positively impact on mitochondrial bioenergetics, mitochondrial ROS/redox metabolism and mitochondrial dynamics. However, more information is required on the bioenergetic consequences and mechanistic mode-of-action aspects of the KD at the cellular level and in MD patients.

Review: Traumatic brain injury and hyperglycemia, a potentially modifiable risk factor

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ABSTRACT

Hyperglycemia after severe traumatic brain injury (TBI) occurs frequently and is associated with poor clinical outcome and increased mortality. In this review, we highlight the mechanisms that lead to hyperglycemia and discuss how they may contribute to poor outcomes in patients with severe TBI. Moreover, we systematically review the proper management of hyperglycemia after TBI, covering topics such as nutritional support, glucose control, moderated hypothermia, naloxone, and mannitol treatment. However, to date, an optimal and safe glycemic target range has not been determined, and may not be safe to implement among TBI patients. Therefore, there is a mandate to explore a reasonable glycemic target range that can facilitate recovery after severe TBI.

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Original article

Phase I single center trial of ketogenic diet for adults with traumatic brain injury

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Conclusions

This pilot study shows that KD is feasible in the management of TBI patients. A randomized controlled trial (RCT) is justified to further understand the optimal serum BOB levels, dose and duration of KD in TBI and its effect on the outcome.

JOURNAL ARTICLE

Progress in research on the role of clinical nutrition in treating traumatic brain injury affecting the neurovascular unit

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https://doi.org/10.1093/nutrit/nuac099

Abstract

The neurovascular unit (NVU) is composed of neurons, glial cells, and blood vessels. NVU dysfunction involves the processes of neuroinflammation, and microcirculatory disturbances, as well as neuronal injury after traumatic brain injury (TBI). Traditional anti-inflammatory drugs have limited efficacy in improving the prognosis of TBI. Thus, treatments that target NVU dysfunction may provide a breakthrough. A large number of clinical studies have shown that the nutritional status of patients with TBI was closely related to their conditions and prognoses. Nutrient complexes and complementary therapies for the treatment of TBI are therefore being implemented in many preclinical studies. Importantly, the mechanism of action for this treatment may be related to repair of NVU dysfunction by ensuring adequate omega-3 fatty acids, curcumin, resveratrol, apigenin, vitamins, and minerals. These nutritional supplements hold promise for translation to clinical therapy. In addition, dietary habits also play an important role in the rehabilitation of TBI. Poor dietary habits may worsen the pathology and prognosis of TBI. Adjusting dietary habits, especially with a ketogenic diet, may improve outcomes in patients with TBI. This article discusses the impact of clinical nutrition on NVU dysfunction after TBI, focusing on nutritional complexes and dietary habits.

Chapter 10 - High-fat diets in traumatic brain injury: A ketogenic diet resolves what the Western diet messes up neuroinflammation and beyond

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Abstract

Traumatic brain injury (TBI) is a debilitating neurological condition which presents a major health burden. Neuronal and metabolic consequences of the trauma, be it single or multiple, mild or severe, extend beyond the acute, initial insult to a chronic, secondary injury which determines functional outcomes. Secondary injury processes comprise distorted cellular energy homeostasis, oxidative stress, neuroinflammation, and consequently apoptotic or necrotic cell death. In fact, the modifying effects of dietary components on neurobehavioral processes indicate a mediating role for metabolism in secondary injury. Indeed, neuronal markers, like brain-derived neurotrophic factor (BDNF), present a link between energy homeostasis and neuroplasticity. High-fat diets (HFD) were shown to differentially impact secondary injury by inducing distinct metabolic states. Particularly, a Western diet (WD), composed of high fat and sugar, aggravates secondary TBI worsening anxiety, as well as motor and cognitive function. Conversely, a high-fat, low-sugar ketogenic diet (KD) resolves these manifestations and suppresses TBI-induced excitotoxicity and epilepsy. Underlying mechanisms for the characteristic HFD-induced alterations of TBI include modulation of mitochondrial function demonstrated as changes in mitochondrial permeability transition pore (mPTP) expression and activity as well as variations in bioenergetics. Exaggerated oxidative stress and neuroinflammation are thought to contribute to such observations in a vicious cycle. Additionally, long-term epigenetic changes are also involved. This chapter highlights molecular mechanisms associated with WD and KD feeding in different experimental models of TBI and provides insight into potential therapeutic targets for the management of TBI consequences.