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Low Molecular Weight Dextran Sulfate (ILB®) Administration Restores Brain Energy Metabolism Following Severe Traumatic Brain Injury in the Rat

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Abstract: Traumatic brain injury (TBI) is the leading cause of death and disability in people less than 40 years of age in Western countries. Currently, there are no satisfying pharmacological treatments for TBI patients. In this study, we subjected rats to severe TBI (sTBI), testing the effects of a single subcutaneous administration, 30 min post-impact, of a new low molecular weight dextran sulfate, named ILB®, at three different dose levels (1, 5, and 15 mg/kg body weight). A group of control sham-operated animals and one of untreated sTBI rats were used for comparison (each group $n = 12$). On day 2 or 7 post-sTBI animals were sacrificed and the simultaneous HPLC analysis of energy metabolites, *N*-acetylaspartate (NAA), oxidized and reduced nicotinic coenzymes, water-soluble antioxidants, and biomarkers of oxidative/nitrosative stress was carried out on deproteinized cerebral homogenates. Compared to untreated sTBI rats, ILB® improved energy metabolism by increasing ATP, ATP/ adenosine diphosphate ratio (ATP/ADP ratio), and triphosphate nucleosides, dose-dependently increased NAA concentrations, protected nicotinic coenzyme levels and their oxidized over reduced ratios, prevented depletion of ascorbate and reduced glutathione (GSH), and decreased oxidative (malondialdehyde formation) and nitrosative stress (nitrite + nitrate production). Although needing further experiments, these data provide the first evidence that a single post-injury injection of a new low molecular weight dextran sulfate (ILB®) has beneficial effects on sTBI metabolic damages. Due to the absence of adverse effects in humans, ILB® represents a promising therapeutic agent for the treatment of sTBI patients.