UNIVERSITI TEKNOLOGI MARA

THE NEUROPROTECTIVE EFFECT OF HYPOTHERMIA BY DREAM IN ACUTE ISCHEMIC STROKE RATS

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MSc

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Ischemic stroke contributes to incapability and mortality in both developed and developing countries. Hypothermia has been used as the therapeutic avenue for ischemic stroke. Hypothermia for ischemic stroke has been focusing on the area of insult but limited on understanding the neuroprotection mechanism underlying it. Down regulatory antagonist modulator (DREAM) has been previously associated with neuroprotection by negative modulation of N-methyl-D-aspartic acid (NMDA) channel function and reducing NMDAR-mediated excitotoxic damage. The main objective of this study is to determine the neuroprotective effect of hypothermia via DREAM in acute ischemic stroke rats. A total of 48 male Sprague-Dawley rats (12 weeks old, the weight of 200g -280g) were divided into sham-operated (n=24) and ischemic stroke (n=24) groups. Each group was further subdivided into normothermia (37°C), mild hypothermia (35-33°C), moderate hypothermia (32-30°C), and severe hypothermia (29-27°C). The ischemic stroke was induced by middle cerebral artery occlusion (MCAO). The rats were assessed by simple tactile extinction test 1 hour post-MCAO followed by hypothermia. Hypothermia was induced by alcohol spraying, fanning and maintained for 3 hours. The temperatures of the rats were measured throughout the induction of hypothermia. The serum were collected by cardiac puncture. The levels of NSE and S100B were estimated by ELISA. The infarcted brain tissues were stained by 2,3,5-triphenyltetrazolium chloride (TTC) and the volumes were estimated. The cytoplasmic and nuclear proteins were extracted and estimated for DREAM by Western Blot. There were significant reductions in the infarct volumes of mild ($p \leq 0.001$) and moderate ($p \leq 0.05$) hypothermia treated ischemic stroke rats. There was a significant reduction of NSE level in mild hypothermia treated as compared to normothermia treated sham-operated groups ($p \leq 0.001$). There was a significant reduction in the NSE level by hypothermia ($p \leq 0.003$) and by an interaction between hypothermia and ischemic stroke ($p \leq 0.004$) among all groups. There were significant reductions of S100B level in mild ($p \leq 0.005$), moderate ($p \leq 0.005$) and severe ($p \leq 0.005$) hypothermia treated as compared to normothermia sham-operated groups. There was a significant reduction in the S100B level by hypothermia ($p \leq 0.003$) and by an interaction between hypothermia and ischemic stroke ($p \leq 0.004$) among all groups. There was a significant increment of nuclear DREAM level in mild hypothermia treated as compared to normothermia ischemic stroke groups ($p \leq 0.005$). Further analysis showed that there was a significant increment of nuclear DREAM level by ischemic stroke ($p \leq 0.006$) among all groups. Hypothermia evidenced to be neuroprotective by the reduction of infarct volume, NSE and S100B. The mechanism may involved DREAM as eflected by the changes in nuclear DREAM level.

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