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INVOLVEMENT OF NITRIC OXIDE IN INSULIN-INDUCED CHANGES IN MEMORY, OXIDATIVE STRESS AND BRAIN HISTOLOGY IN MICE

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ABSTRACT

Insulin has been reported to increase nitric oxide (NO) level in the brain but the biological significance of such effects is not well understood. The present study examined the involvement of NO on insulin-induced effects on brain oxidative stress, learning, memory and histology. Mice were grouped (n=6) and treated intraperitoneally, thus: Control group- distilled water; Insulin group- insulin (10 I.U./kg/day); Insulin+L-NAME group- insulin (10 I.U./kg/day) and L-NAME (50 mg/kg); L-NAME group- L-NAME (50 mg/kg). Learning and memory were assessed using novel object recognition test at the end of the experiment. Concentrations of NO, malondialdehyde (MDA), as well as glutathione peroxidase (GPx) activity, were determined in brain homogenates using assay kits. Histological examination of brain slides was also conducted. Insulin treatment resulted in higher levels of NO compared to controls ($p < 0.005$); and this effect was reversed by L-NAME treatment. With the increased NO level, there was concurrent increase in MDA concentration, decreased GPx activity (increased oxidative stress) and impaired memory in the treated animals. The increased oxidative stress was reversed by L-NAME treatment. Brain slides appeared normal and showed no indication of histopathological changes. These data led to the conclusion that sub-acute insulin treatment caused an NO-dependent increase in oxidative stress in the brain; insulin impaired non-spatial working memory but did not affect brain histology in the treated mice. Insulin treatment may have negative consequences on the brain through increased NO levels.

Key words: Nitric oxide, Oxidative stress, Learning and memory, Brain histology, Malondialdehyde, Glutathione peroxidase

INTRODUCTION

Insulin was discovered as a hypoglycaemic agent several decades ago, and has also been reported to increase NO level in the brain (Montagnani et al. 2001; Vincent et al. 2003), platelets (Trovati et al. 1997) and endothelium (Steinberg et al. 1994), but the biological significance of these effects are not well understood. There are conflicting reports on insulin effects on the brain: improvement in learning and memory (Choopani et al. 2008) and potential

harm due to induction of oxidative stress (Monnier et al. 2011); this calls for more studies to better understand these phenomena.

Based on the findings that insulin increases brain NO level (Montagnani et al. 2001; Vincent et al. 2003), and that NO (a free radical) is a known inducer of

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