Effects of Insulin-Like Growth Factor-1 on Neurotransmitters of Memory

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Background: Alzheimer's dementia (AD) is characterized by profound memory loss. New models of treatment are needed since the prevailing amyloid hypothesis has not resulted in successful treatments. Changes in effectiveness of neurotransmission may alter learning and memory. Diabetes is an important risk factor for AD and insulin has previously been shown to affect neurotransmission. But little is known about a structurally similar protein that exists in the central nervous system: insulin-like growth factor-1 (IGF1). My goal was to find if IGF1 would positively or negatively affect the responses of neuronal cells to the neurotransmitter glutamate. Methods: Rat cortical neuron cell cultures were prepared and monitored for intracellular calcium levels under standardized conditions at regular intervals during application of glutamate receptor agonists in the presence or absence of insulin, IGF1, and inhibitors of specific glutamate receptors (e.g., CNQX). Results: In contrast to insulin, calcium influx in response to glutamate was significantly inhibited by IGF1. However, when NMDA receptors were isolated by the application of CNQX, the calcium influx through this class of receptor was elevated, consistent with the effects of insulin. Isolation of AMPA receptors by APV showed reduction in calcium influx, indicating that they were responsible for the main effect of IGF1 on responses to glutamate. Conclusion: IGF1 influences NMDA receptors similarly to insulin but has an opposite effect on the overall response to glutamate in cultures of rat cortical neurons. This indicates IGF1 has a unique role in processes related to neurotransmission and perhaps memory in AD.