Apr 23rd, 9:00 AM - 4:00 PM

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TOWARD AN UNDERSTANDING OF ALZHEIMER'S DISEASE III: THE EFFECTS OF BETA-AMYLOID 1-42 ON THE RETENTION OF A SPATIAL TASK IN MALE RATS

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Alzheimer's disease is characterized neuropathologically by neurofibrillary tangles and neuritic plaques. One of the key components of the neuritic plaques is a 4 kd protein called ß-amyloid. In humans, ßA exists in varying lengths of amino acids, ranging from 39 to 43 amino acid residues in length. While recent studies have demonstrated that ßA(1-40) is toxic to cultured cells, with amino acids 25-35 apparently mediating the cell death, there remains somewhat of a controversy as to the effectiveness of the protein to cause cell death "in vivo" in rats. One issue that has been discussed at length is a methodological one. For example it has been proposed that ßA(1-40) protein aggregates very rapidly in most solvents thereby precluding reliable intracerebral injections. Recently, the 42 amino acid residue form of ßA has been purified and synthesized by Dr. Tony Giordano and his coworkers at Abbott Laboratories. Apparently this form has a much slower rate of sedimentation, thus increasing the probability of successful injections. In an attempt to further explore the effect of ßA on memory we bilaterally injected ßA(1-42), a scrambled form of the peptide, or DMSO, into the dorsal hippocampus of male rats. The effects of these injections were assessed on animals that had acquired a spatial learning task which consisted of entering arms on a radial arm maze in three consecutive trials. We injected .5 microliter of ßA(1-42), a scrambled version of the peptide, or the vehicle (DMSO) alone into the dorsal hippocampus. After surgery, the animals were allowed to recuperate and then were tested on the maze again. We recorded the session latency, the latency to first choice, the number of correct choices, the number reference memory error, the number of correct and incorrect errors, and the total number of choices. In addition, we calculated the percent of choices that were correct, the average choice latency, and the total number of errors. After two weeks of testing, we removed the bait from three of the arms and baited the three arms that were previously unbaited. After three days, all but two of the arms were left unbaited. This was done to try and delineate between those animals that were using procedural memory and those using declarative memory, which is presumably dependant on the hippocampus. The data were analyzed with an ANOVA. The rats were perfused after testing and histologies are currently being completed. Preliminary analysis revealed no significant difference between any of the three groups. This supports previous findings that ßA alone may not be enough to cause a significant behavioral deficit.