An Examination into Select Causes, Diagnosis, and Treatment of Alzheimer’s Disease

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SELECT CAUSES, DIAGNOSIS, AND TREATMENT

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One of the most debilitating and frustrating diseases, Alzheimer’s disease (AD) still remains largely a mystery. Some of what is known, however, is the fact that there is general cognitive decline and memory impairment along with some behavioral changes. Many research studies have produced conflicting reports about Alzheimer’s, but there is a common ground among different findings. There is little opportunity to identify this commonality given the constraints of a limited analysis that is not conducive to research of all studies pertaining to a specific factor: a cause, diagnosis, or treatment. The purpose of this paper is to examine both mainstream as well as innovative approaches to the causes, diagnosis, and treatment of Alzheimer’s. The causes will be examined. The diagnoses looked at will be the serum copper levels and the P300 subcomponents. The treatments explored will be galantamine, a type of acetylcholinesterase inhibitor (AChEI), and drainage of cerebrospinal fluid (CSF).

Causes

The first possible cause is the genotypic factor of the APOE ε4 allele as an indicator of predisposition to Alzheimer’s. As mentioned by Hirono et al. (2002), previous research has indicated the APOE ε4 allele as “a well-known risk factor for developing AD” (p. 743). APOE ε4 allele has a substantial effect on the glucose metabolism in the brain. However, the exact reason why and to what extent remained largely unclear with mixed findings according to the various studies mentioned in the article. The authors suggested and based their hypothesis on the fact that it was because previous studies did not subdivide subjects into those with early onset and those with late onset AD. In doing this, Hirono et al. (2002) would be able to see why it has been shown in the past that the APOE ε4 allele “lowers[s] the age at onset of AD” (p. 744). In the early onset patients, who were homozygous for APOE ε4, Hirono et al. (2002) found lower
glucose metabolism in brain regions such as the right medial temporal lobe compared with APOE \( \varepsilon3 \) homozygote who had higher levels. In other areas such as the left posterior temporal cortex, however, there was a higher glucose metabolism in the \( \varepsilon4 \) and lower levels in the \( \varepsilon3 \). The fact that the levels ranged depending on the region of the brain does not rule out APOE \( \varepsilon4 \) allele as a potent factor in determining AD. It is simply indicative of the body’s overall difference in levels of any given substance. A deficiency in one region can be hazardous, while in another region it can be a necessity (Hirono et al., 2002). While the APOE \( \varepsilon4 \) allele has a causal factor in the early stages of AD, the late onset findings revealed no significant differences between APOE \( \varepsilon4 \) and \( \varepsilon3 \) homozygote, indicating that this is unique to early onset patients. From these findings, Hirono et al. (2002) were able to conclude that “APOE \( \varepsilon4 \) allele makes late-onset type AD occur earlier” (p. 748). Possessing this allele in the homozygous form can absolutely indicate the predictability of developing severe AD at an earlier age. This study was integral in proving the specific causes that lead homozygous carriers of APOE \( \varepsilon4 \) to develop AD, and where and how the brain is affected through glucose metabolism.

**Diagnoses**

There are several diagnostic measures for Alzheimer’s disease, including a wide range of written and oral indicators of cognitive impairment, which were often used to create a subject pool (Killiany et al., 2002; Silverberg et al., 2002). In addition, there are structural abnormalities present in AD which distinguish the disease. The abnormalities are further explained as the serum copper concentration levels and the events of the P300 subcomponents. Squitti et al. (2002) found “that copper is specifically linked to AD pathophysiology” (p. 1153). Specifically, the increase in the serum copper concentration levels affects the deterioration of the medial temporal lobe (Squitti et al., 2002), leading to progression of AD symptoms. Copper may also
have an effect on peroxide generation, which is correlated to several cognitively disabling diseases, including AD. Though the peroxide factor is not a sole determinant of AD specifically, it is useful to have multiple measures in order to accurately diagnose AD. Another factor contributing to AD deterioration was the brain’s antioxidant capacity, also known as, total radical-trapping antioxidant (TRAP). Squitti et al. (2002) found that lower TRAP levels indicated a patient suffering from AD. Interestingly, the lower TRAP finding also correlated with the AD patients carrying the APOE ε4 allele, the aforementioned cause and risk factor of AD. Squitti et al. (2002) noted that those with the APOE ε4 allele also had higher serum copper concentration than the healthy controls, providing a link with the research by Hirono et al. (2002). The research proved to be successful in establishing copper’s reliability as a determinant of the presence of AD and provided additional non-exclusive indicators helpful for precise diagnosis.

**Treatments**

The two treatments explored are relatively new and provide a fresh option to consider in the wake of treatments that have not been successful. Unfortunately, neither of these treatment options has the ability to stop AD altogether, though the slowdown of progression can provide an increased amount of normal or near normal cognitive and memory functioning for the patient.

**Shunting**

The first new treatment to consider involves surgically implanting a shunt in order to redirect CSF flow at a low level. Silverberg et al. (2002) based their study on the idea that many elderly develop AD possibly because of their age and the relationship to the decreased functioning of CSF. Low concentrations of Aβ proteins in the CSF are found in patients with
AD. Aβ proteins are important in the interstitial fluid for all regions of the brain, including memory related regions (Silverberg et al., 2002).

**Increased CSF Flow**

The researchers hypothesized that by improving CSF functioning, AD progression can be slowed. Comparing baseline and 12 month figures from the testing of the AD control group and the AD patients who received shunts, those without shunts declined at a much higher percentage than those patients who were treated with shunts. Thus, the improvement seen was thought to be attributed to the “increased blood flow to the cerebral hemispheres” (Silverberg et al., 2002, p. 1142).

**Regulation of flow.** The regulation of CSF flow influenced the vascular flow to the brain thereby, allowing better cognitive and memory functioning. Because of this, the researchers were able to confirm their hypothesis. From these findings, Silverberg et al. speculated that AD could be one of a type of diseases in which malfunction of CSF is a significant indicator of disease. This study was the first of its kind relating to CSF function and AD and as such had a limited subject pool receiving shunts (n= 15) and also had a large number of fallout. This, however, does not call for a dismissal or disregard of the findings. The researchers announced plans to perform a secondary related trial in order to allow these findings to become more generalized and make the treatment more attractive on a broader scale.

**Conclusion**

This paper examined the causes, diagnosis and treatments of Alzheimer’s disease. The APOE ε4 allele as a genotypic indicator, the P300 waves, and AChEIs all served as a commonly agreed upon cause, diagnosis, and treatment, respectively, among research previously discussed as well as research performed by the aforementioned authors. While brain region
volume level, serum copper levels, and CSF flow regulation provided new possibilities in
discovering more about Alzheimer’s, these causes, diagnoses, and treatments are a small
representation of the magnitude of information and research available. The selected studies were
chosen partly because in each case the researchers were successful in defining, isolating, or
caring for Alzheimer’s in some form. The success of the researchers was highlighted because it
shows what has been done to help those afflicted with the disease. It is imperative to continue
research into these factors as well as others because the more that is discovered, the more
possibility there is for a cure.


