Does Vestibular Dysfunction Contribute to the Increased Prevalence of Alzheimer’s Disease in Females?

Dr. Fred H. Previc

ABSTRACT

Alzheimer’s disease (AD) is twice as likely to occur in females as males, and it is also linked to vestibular impairment, especially if spatial symptoms predominate. Given large-scale epidemiological data showing a two-fold greater prevalence in females for most vestibular disorders, the greater prevalence of AD in females could be linked to their greater prevalence of clinical vestibular dysfunction, although there are also sex differences in vestibularly mediated cognitive abilities in normals. Preliminary evidence suggests that the percentage of vestibular impairment in AD patients with predominant loss of topographical and other spatial abilities is similar in males and females. This and other evidence suggest that the overall greater prevalence of AD in females may be more due to their greater susceptibility to vestibular disorders rather than to normal differences in vestibular-mediated cognitive abilities associated with AD.

Keywords

Alzheimer’s, Vestibular, Sex, Prevalence.

One of the consistent findings concerning Alzheimer’s Disease (AD), is the nearly two-fold greater prevalence in females [1,2]. The pronounced female bias in AD which strikingly differs from other dementias that mostly show male biases [1], has been attributed to a variety of causes, including sex differences in longevity, inflammation, genetics, beta-amyloid production, sex hormones, and sociocultural factors [1].

None of these putative explanations seems by itself entirely satisfactory in accounting for the greater AD risk among females overall. For example, the female bias still exists in most studies when age-adjusted risk is considered [2], and the longevity as well as possibly the inflammation and sociocultural explanations should also apply to the other dementias, which show the opposite sex bias in most cases. Estrogen has been proposed as a protective agent against AD, but that would hardly account for the reduced male prevalence; furthermore, hormone (estrogen)-replacement therapy has produced equivocal results in preventing or delaying AD [2]. Finally, the most well-studied genetic difference between the sexes involves the ApoE4 gene variant [1,2], which affects beta-amyloid clearance even though beta-amyloid may not even be causal to AD [3].

One alternative explanation for the greater prevalence of AD among women is the role of sex differences in both normal and abnormal vestibular function. Based on a wide range of evidence, it has been proposed that vestibular loss contributes to the development of AD [4,5]. Vestibular inputs help drive a topographical/navigational system comprising the hippocampus and posterior cingulate and parietal-temporal cortices, all of which are involved in the signaling of the head in relation to extrapersonal space. One of the important functions of this system is to orient to, navigate in, and retain memories of, topographical space [4]. Vestibular loss causes deficits in navigation, path integration, and other topographical functions along with degeneration of key structures in the topographical neural network such as the hippocampus [4,5,7]. Loss of topographical functions such as way-finding and memory are among the earliest and most specific signs of impending AD [6], while the hippocampus, posterior cingulate, and parietal-temporal cortices are the first neural regions to degenerate in AD [4]. Vestibular and topographical functions are positively correlated in the normal population [8], and a dominant subtype of AD that presents with topographic spatial symptoms is almost always accompanied by vestibular impairment [5,9].
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References

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