Klotho-VS heterozygosity genotype linked to reduced alzheimer disease risk

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(HealthDay)—*Klotho*-VS heterozygosity (*KL*-VS^{HET+} status) is

associated with a reduced risk for Alzheimer disease (AD) and β-amyloid (Aβ) burden in cognitively normal individuals aged older than 60 years who carry apolipoprotein e4 (*APOE4*), according to research published online April 13 in *JAMA Neurology*.

Michael E. Belloy, Ph.D., from Stanford University in California, and colleagues combined 25 independent case-control, family-based, and longitudinal AD cohorts that recruited referred and volunteer participants to examine whether *KL*-VS^{HET+} status is associated with reduced AD risk and Aβ pathology. There were 36,530 eligible participants, of whom 13,782 were excluded; analyses were stratified by *APOE4* status.

The researchers found that in individuals carrying *APOE4* who were aged 60 years or older, the *KL*-VS^{HET+} genotype was associated with a reduced risk for AD (odds ratio, 0.75); this finding was more prominent at ages 60 to 80 years (odds ratio, 0.69). A reduced risk for converting to mild cognitive impairment or AD was seen for control participants carrying *APOE4* with *KL*-VS heterozygosity (hazard ratio, 0.64). In control participants with *APOE4* aged 60 to 80 years, *KL*-HS heterozygosity was associated with increased Aβ in cerebrospinal fluid and lower Aβ on positron emission tomography scans.

"Information on *KL*-VS status should also prove useful in further refinement of genetic risk profiles for both clinical trial enrichment and personalized genetic counseling," the authors write.

Several authors disclosed financial ties to the pharmaceutical industry.

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