Published in final edited form as:

J Am Geriatr Soc. 2009 July ; 57(7): 1308–1309. doi:10.1111/j.1532-5415.2009.02292.x.

APOE Genotype and Risk of Developing Physical Limitations in the Elderly

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To the Editor: Apolipoprotein E (APOE) gene is one of the genes with a huge impact on longevity and successful aging. The APOE polymorphism has been associated with lipid or cognitive disorders, which may result in cardiovascular disease or Alzheimer's disease.¹ In older adults, stroke and cognitive impairment are all risk factors for physical disability. Thus more researches have been conducted to examine whether the APOE genotype is independently associated with physical limitations in the older population. While these studies^{2–5} do improve our knowledge on the relationship between APOE gene and physical function in older adults, no attention has been paid to investigating the role of this gene in the development of functional decline at different stages. The progressive decline of physical function in older adults usually begins with the limitation of mobility function, continues to deteriorate into difficulty in coping with complex household works, and finally results in inability to complete self-care tasks.⁶ We conducted a prospective nested case-control study of genetic variation in the APOE gene and risk of deterioration in physical functioning in Taiwan, with a particular interest in the transitions of mobility, Instrumental Activities of Daily Living (IADL), and Activities of Daily Living (ADL) decline.

Samples were from 924 study participants of the Social Environment and Biomarkers of Aging Study (SEBAS) in 2000.⁷ SEBAS included an in-home interview and a physical examination at the hospital. The in-home interview collected information on self-reports of physical limitations, demographic and social variables, and cognitive measures. Mobility includes 9 tasks involving general mobility function of upper and lower extremities. IADL covers six tasks involving living environment. ADL incorporates six personal care tasks. Mobility decline was defined as having no difficulty in all 21 tasks in 2000 but experiencing difficulty in at least one of the 9 mobility tasks in 2003. IADL decline was defined as having

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions

Conception and design: T-Y Lan. Acquisition of data, analysis and interpretation of data: T-Y Lan and W-C Chang. Manuscript drafting: T-Y Lan and T-H Lan. Manuscript revision for important intellectual content: B-S Hurng.

Sponsor's Role: The sponsors plays no role in the design, methods, subject recruitment, data collections, analysis, or preparation of the manuscript.

difficulty in at least one mobility task but no difficulty in all ADL and IADL tasks in 2000, but experiencing difficulty in at least one mobility and one IADL task but no difficulty in all ADL tasks in 2003. ADL decline was defined as having difficulty in at least one mobility and one IADL task but no difficulty in all ADL tasks in 2000, and experiencing difficulty in at least one mobility, one IADL, and one ADL task in 2003. The APOE genotyping was conducted using DNA extract obtained from whole blood. During the three years of follow-up, there were 91, 79, and 35 participants identified as having mobility, IADL, and ADL decline, respectively. For each subject with mobility, IADL, or ADL decline, one control subject without the specific decline was matched for age and sex. For example, one subject with only mobility difficulty in both the 2000 and the 2003 interviews was age- and sex-matched to the subject with IADL decline. Odds ratios (ORs) for subjects carrying $\epsilon 2$ or $\epsilon 4$ allele were estimated using conditional logistic regression adjusting for risk factors relevant to functional decline,^{8,9} including body mass index (BMI), heart disease, stroke, arthritis, cognitive impairment, and physical activity. Updated information of these covariates obtained from the 2003 interview was used in the adjusted models.

Because physical function of cases at baseline had not deteriorated, the prevalence of disability-related diseases and factors including BMI, cognitive impairment, and physical activity was similar and tested without statistically significant differences between cases and controls. The distribution of all six APOE genotypes ($\epsilon 2/\epsilon 2$, $\epsilon 2/\epsilon 3$, $\epsilon 2/\epsilon 4$, $\epsilon 3/\epsilon 3$, $\epsilon 3/\epsilon 4$, and $\epsilon 4/\epsilon 4$) and frequencies of the three APOE alleles ($\epsilon 2$, $\epsilon 3$, and $\epsilon 4$) were statistically insignificant between cases with controls for all three groups. Table 1 shows the risks of developing mobility, IADL, or ADL limitations for older adults with the $\epsilon 2$ or $\epsilon 4$ allele. The presence of APOE $\epsilon 2$ or $\epsilon 4$ allele was not related to the declines of physical functioning.

This lack of association is in agreement with findings from three similar studies using ADL tasks, 3 a mobility task only, 10 or a combination of mobility, IADL, and ADL as the measures of physical limitations.⁴ The $\epsilon 4$ allele has been linked with decreased longevity through developing cognitive impairment and cardiovascular disease, whereas the $\epsilon 2$ allele increases longevity and promotes successful aging.¹ Although APOE plays an important role in aging process, both $\epsilon 2$ and $\epsilon 4$ alleles, based on our study results, do not have a direct link with the decline of physical function at different stages. It is possible that APOE may affect physical function indirectly through cognitive impairment and cardiovascular disease, and the association disappears when cardiovascular disease and cognitive function are all considered.

Acknowledgments

The SEBAS was supported by the Demography and Epidemiology Unit of the Behavioral and Social Research Program of the National Institute on Aging, US. This study was based on data from the SEBAS provided by the Population and Health Research Center, Bureau of Health Promotion in Taiwan. The interpretation and reporting of these data are the sole responsibility of the authors.

References

1. Smith JD. Apolipoproteins and aging: emerging mechanisms. *Ageing Res Rev.* 2002; 1:345–365. [PubMed: 12067591]
2. Albert SM, Gurland B, Maestre G, Jacobs DM, Stern Y, Mayeux R. APOE genotype influences functional status among elderly without dementia. *Am J Med Genet.* 1995; 60:583–587. [PubMed: 8825902]
3. Bader G, Zuliani G, Kostner GM, Fellin R. Apolipoprotein E polymorphism is not associated with longevity or disability in a sample of Italian octo- and nonagenarians. *Gerontology.* 1998; 44:293–299. [PubMed: 9693262]

4. Blazer DG, Fillenbaum G, Burchett B. The APOE-E4 allele and the risk of functional decline in a community sample of African American and white older adults. *J Gerontol A Biol Sci Med Sci*. 2001; 56:M785–M789. [PubMed: 11723155]
5. Carmelli D, DeCarli C, Swan GE, et al. The joint effect of apolipoprotein E epsilon4 and MRI findings on lower-extremity function and decline in cognitive function. *J Gerontol A Biol Sci Med Sci*. 2000; 55:M103–M109. [PubMed: 10737693]
6. Fried LP, Ettinger WH, Lind B, Newman AB, Gardin J. Physical disability in older adults: a physiological approach. Cardiovascular Health Study Research Group. *J Clin Epidemiol*. 1994; 47:747–760. [PubMed: 7722588]
7. Goldman N, Turra CM, Gleib DA, Seplaki CL, Lin YH, Weinstein M. Predicting mortality from clinical and nonclinical biomarkers. *J Gerontol A Biol Sci Med Sci*. 2006; 61:1070–1074. [PubMed: 17077201]
8. Fried LP, Guralnik JM. Disability in older adults: Evidence regarding significance, etiology, and risk. *J Am Geriatr Soc*. 1997; 45:92–100. [PubMed: 8994496]
9. Stuck AE, Walthert JM, Nikolaus T, et al. Risk Factors for Functional Status Decline in Community-living Elderly People: A Systematic Literature Review. *Soc Sci Med*. 1999; 48:445–469. [PubMed: 10075171]
10. Melzer D, Dik MG, van Kamp GJ, et al. The apolipoprotein E e4 polymorphism is strongly associated with poor mobility performance test results but not self-reported limitation in older people. *J Gerontol A Biol Sci Med Sci*. 2005; 60:1319–1323. [PubMed: 16282567]

Table 1

Associations between APOE alleles and risk of mobility, IADL, or ADL decline

APOE allele	Cases	Controls	OR (95% confidence interval)	
	n	n	Unadjusted	Adjusted*
Mobility decline group				
ε2				
Absent	77	77	1.00	1.00
Present	14	14	1.00(0.43–2.31)	1.03(0.42–2.49)
ε4				
Absent	79	79	1.00	1.00
Present	12	12	1.00(0.43–2.31)	1.18(0.48–2.94)
IADL decline group				
ε2				
Absent	65	70	1.00	1.00
Present	14	9	1.56(0.67–3.59)	1.57(0.62–3.97)
ε4				
Absent	64	67	1.00	1.00
Present	15	12	1.33(0.56–3.16)	1.46(0.54–3.90)
ADL decline group				
ε2				
Absent	29	28	1.00	1.00
Present	6	7	0.83(0.25–2.73)	0.44(0.03–6.18)
ε4				
Absent	33	28	1.00	1.00
Present	2	7	0.29(0.06–1.38)	0.36(0.02–6.03)

* Adjusted for BMI and the following factors updated until the 2003 interview: heart disease, stroke, arthritis, cognitive impairment, and physical activity.