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Commentary on "Perspective on race and ethnicity in Alzheimer's disease research"

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Abstract There are persistent disparities in Alzheimer's disease by race and ethnicity that are not well understood. The emphasis given to seeking a genetic basis for racial differences might be a distraction from the more relevant issue of identifying preventable causes of Alzheimer's disease. The majority of Alzheimer's disease cases are diagnosed as the late onset type and are unlikely to be inherited. Late onset Alzheimer's disease cases, therefore, more likely represent variations in gene expression than gene frequency. Although conceptual and methodologic problems have limited our understanding of this relationship, race-based studies provide important opportunities to understand the environmental factors associated with gene expression. Improving our understanding of the factors associated with race and ethnicity might help to clarify the epidemiology and course of Alzheimer's disease.

Keywords: Alzheimer's disease; Dementia; Blacks; Health disparities; Health inequities

Racial, ethnic, and national differences in the incidence, cumulative risk, and prevalence of Alzheimer's disease (AD) have been documented [1], but explanations for these differences have been elusive. Late onset AD accounts for the majority of AD cases and does not run in families but follows a racial and ethnic pattern [2]. Understanding how race and ethnicity are associated with AD risk can provide important information on the mechanisms and pathways that lead to the development of AD. Although there are conceptual and methodologic problems with using the terms *race* and *ethnicity*, these constructs might be markers for important environmental risk factors that affect gene expression potentially associated with AD.

Race is often confused with ethnicity [3], family history [4], genotype [5], human biologic variation [4], socioeconomic status (SES) [6], unmeasured social factors [7], and environmental context [7]. Some of the problems with the way race has been used in health research include lack of consensus on the definition of race (domestically or internationally), its poor measurement, and the changing definition on the basis of social and political considerations [8]. Race can be, however, a useful marker of one's exposure to environmental toxins and social disadvantage [8]. Ethnicity highlights cultural and behavioral factors associated with health [3] by providing "an appreciation of a range of cultural and behavioral attitudes, beliefs, lifestyle patterns, diets, environmental living conditions, and other factors" [9]. In the United States, race and ethnicity are determined by the U.S. Office of Management and Budget (OMB). The OMB has declared that "... race and ethnic categories, are neither anthropologically or scientifically based ... [but they] ... represent a social-political construction designed for collecting data on race and ethnicity of the broad population groups in this country" [3]. Therefore, U.S. racial and ethnic categories are socially not genetically based.

One of the consistent and most basic problems with genetic explanations for racial and ethnic differences in health is that these differences are often accompanied by an unacknowledged set of limitations. Socially and historically constructed racial categories do not correspond to biologic or genetic phenomena; they are non-genetic tools to organize populations within a sociopolitical paradigm. Very few genetic differences between races have been found that

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directly relate to health [10]. Most variants that are health-related represent random mutations in subpopulations or result from regional selection and are not related to continental race [10]. Although hair texture, skin color, and other phenotypic characteristics associated with race are influenced by genes, no one knows how these genes correspond to our social construction of race and ethnicity [10]. Demonstrated genetic differences concern variation in the percentages of people having particular gene types, but these categories are neither distinct nor fixed. Frank [11] argues that "Methodologically, the instability of ancestry estimates, the absence of established relationships between genetic variants and phenotype, strong correlations between ancestry estimates and unmeasured environmental exposures, as well as omitted variable bias, all threaten the validity of genetic analyses that use race/ethnic categories as valid units of analysis." Genetics affects nearly all aspects of health, but its contribution to health outcomes, and particularly our current pattern of racial and ethnic health disparities, suggests that genetics are secondary to social and environmental influences [12].

Adequately controlling for plausible alternative explanations makes the study of the relationship between AD and race and ethnicity even more complex but far more useful. In the U.S., Hispanics and African Americans have a higher incidence and prevalence of AD than whites, Asian Americans have rates comparable to whites, and Native Americans appear to have rates lower than whites [1,13]. Internationally, rates of dementia in South America, Europe, and the U.S. tend to be similar [1,14], rates of AD among Africans (Nigerians) were found to be significantly lower than for African Americans [15], and rates of dementia among Asian and European elders tend to be similar [1,14]. Racial differences have been found in most of the known risk factors for sporadic AD [1,2]: having a first-degree relative with AD [16], apolipoprotein 4 polymorphism [1,17,18], vascular risk factors (eg, stroke, hypertension) [1,15], chronic diseases (eg, diabetes mellitus) [1], serum cholesterol [1,15], behavior (eg, alcohol consumption, high-calorie and high-fat diets, sedentary lifestyles, and smoking) [2,15], SES [19], educational and cognitive factors [20], and environmental exposure to toxins (eg, air pollution, harmful metals, and pesticides) [2,21].

Race and ethnicity, however, are confounded by other variables associated with AD risk. Two examples of risk factors for AD that are confounded with race and ethnicity are cognitive activity and SES. Manly and Mayeux [1] indicated that cognitive activity is an important risk factor for AD that has been assessed by using educational attainment, literacy, income, occupational attainment, and SES. Although educational attainment is conceptually and empirically related to occupational attainment and SES, these constructs are fundamentally different from one another and from cognitive activity. The accelerated cognitive aging hypothesis of Whitfield [20] illustrates the complexity and confounding of several factors associated with cognitive aging and AD risk. He argues that differential exposure to chronic stressors, health problems (eg, vascular risk factors and diseases), and poor formative education (ie, under-resourced, segregated schools) all differentially affect African Americans, and each factor independently has been found to affect cognitive activity. Factors associated with formal education have been significant in several domestic studies, but studies in India and Africa did not find a relationship between AD and education or literacy [1].

SES is an important predictor of dementia [19] and AD [20]. SES also is accepted as the most robust and consistent factor affecting health outcomes [6,22]. Different measures of SES (income, education, and occupation [6]) are independently associated with rates of dementia and AD [1], and each measure is affected by one another. SES is a strong predictor of exposure to environmental toxins [22] and health status [6], but race is an independent predictor of SES [6,22] and AD.

There is no evidence that specific AD disease pathways vary by race and ethnicity alone, or that these socially defined groups are genetically homogeneous. The primary utility of race and ethnicity is their ability to capture the social and physical environmental factors that have been consistently shown to affect health. Race and ethnically based studies, therefore, are likely to yield valuable data on the mechanisms and pathways through which AD develops. Understanding these racial differences also matters because the populations developing AD are increasingly ones of color throughout the developing and developed world [14].

Hendrie [15] outlined the need to focus on gene-environment interactions for new hypotheses and theories to understand AD. This is likely a more useful strategy than exploring the genetic information of families with a high occurrence of sporadic AD. Research on AD needs the critical examination of environmental factors that influence gene expression because AD is more common in some racial or ethnic groups than others. Race and ethnicity should move from being control and descriptive variables to explanatory ones. Future research must help to explain the causal pathways through which race and ethnicity affect AD, distinguishing and clarifying plausible alternatives such as nationality and SES [8]. Expanding the study of the gene-environment interaction associated with AD risk to a more complex array of factors builds on the strength of the known risk factors for AD. This more complex examination of racial disparities in AD should be combined with more precise operational definitions of race and ethnicity as explanatory variables, parceling out vascular risk, behavior, and genetics. Examining populations with a high incidence of sporadic AD (eg, African Americans) and those with a low incidence of AD (eg, Yoruba [Nigerians]), for example, is useful because it allows for an examination of both the common and the unique factors associated with differences in risk based on the gene-environment interaction. Examin-

ing risk factors for AD by race and ethnicity is a way in which we can move from merely describing racial and ethnic differences in AD to explaining them.

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References

[1] Manly JJ, Mayeux R. Ethnic differences in dementia and Alzheimer's disease. In: Anderson NA, Bulatao RA, Cohen B, eds. Critical perspectives on racial and ethnic differences in health in late life. Washington, DC: National Academy Press; 2004. p. 95–142.

[2] Mattson MP. Pathways towards and away from Alzheimer's disease. Nature 2004;430:631–9.

[3] Oppenheimer GM. Paradigm lost: race, ethnicity, and the search for a new population taxonomy. Am J Public Health 2001;91:1049–55.

[4] Foster MW, Sharp RR. Beyond race: towards a whole-genome perspective on human populations and genetic variation. Nat Rev Genet 2004;5:790–6.

[5] Cooper RS, Kaufman JS, Ward R. Race and genomics. N Engl J Med 2003;348:1166–70.

[6] LaVeist TA. Disentangling race and socioeconomic status: a key to understanding health inequalities. J Urban Health 2005;82(Suppl 3): iii26–34.

[7] Mays VM, Ponce NA, Washington DL, Cochran SD. Classification of race and ethnicity: Implications for public health. Annu Rev Public Health 2003;24:83–110.

[8] LaVeist TA. On the study of race, racism, and health: a shift from description to explanation. Int J Health Serv. 2000;30:217–9.

[9] Committee on Cancer Research Among Minorities and the Medically Underserved, Institute of Medicine. The unequal burden of cancer: an assessment of NIH research and programs for ethnic minorities and the medically underserved. Haynes MA, Smedley B D, eds. Washington, DC: National Academy Press; 1999.

[10] Pearce N, Foliaki S, Sporle A, Cunningham C. Genetics, race, ethnicity, and health. BMJ 2004;328:1070–2.

[11] Frank R. What to make of it? the (re)emergence of a biological conceptualization of race in health disparities research. Soc Sci Med 2007;64:1977–83.

[12] Kaufman JS, Cooper RS. Re: Hirsch C, Anderson ML, Newman A, Kop W, Jackson S, Gottdiener J, et al, for the Cardiovascular Health Study Research Group. The association of race with frailty: the Cardiovascular Health Study. Ann Epidemiol 2006;16:545–53. Ann Epidemiol 2007;17:157–8.

[13] Rosenberg RN, Richter RW, Risser RC, Taubman K, Prado-Farmer I, Ebalo E, et al. Genetic factors for the development of Alzheimer disease in the Cherokee Indian. Arch Neurol 1996;53:997–1000.

[14] Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M. Global prevalence of dementia: a Delphi consensus study. Lancet 2005;366:2112–7.

[15] Hendrie HC. Lessons learned from international comparative crosscultural studies on dementia. Am J Geriatr Psychiatry 2006;14:480–8.

[16] Green RC, Cupples LA, Go R, Benke KS, Edeki T, Griffith PA, et al. Risk of dementia among White and African American relatives of patients with Alzheimer disease. JAMA 2002;287:329–36.

[17] Hendrie HC, Ogunniyi A, Hall KS, Baiyewu O, Unverzagt FW, Gureje O, et al. Incidence of dementia and Alzheimer disease in 2 communities: Yoruba residing in Ibadan, Nigeria, and African Americans residing in Indianapolis, Indiana. JAMA 2001;285:739–47.

[18] Osuntokun BO, Sahota A, Ogunniyi AO, Gureje O, Baiyewu O, Adeyinka A, et al. Lack of an association between apolipoprotein E epsilon 4 and Alzheimer's disease in elderly Nigerians. Ann Neurol 1995;38:463–5.

[19] Goldbourt U, Schnaider-Beeri M, Davidson M. Socioeconomic status in relationship to death of vascular disease and late-life dementia. J Neurol Sci 2007;257:177–81.

[20] Whitfield KE. Challenges in cognitive assessment of African Americans in research on Alzheimer disease. Alzheimer Dis Assoc Disord 2002;16(Suppl 2):S80–1.

[21] Dosunmu R, Wu J, Basha MR, Zawia NH. Environmental and dietary risk factors in Alzheimer's disease. Expert Rev Neurother 2007;7: 887–900.

[22] Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. Public Health Rep 2001;116: 404–16.