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Risk factors for incident Alzheimer's disease in African Americans and Yoruba

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Abstract

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Introduction—The incidence rate of Alzheimer's disease (AD) was found to be 2 times lower in Yoruba than in African Americans. This study was aimed at identifying the factors associated with increased risk of incident AD in the two communities.

Methodology—A two-stage design with initial screening using the CSI'D followed by neuropsychological test battery, relations' interview and physician assessment in a subsample.

NINCDS-ADRDA criteria were met for AD. The risk factor variables assessed included demographic, lifestyle, medical and family history items.

Results—In the Yoruba, AD was associated with age (OR = 1.07) and female gender (OR = 2.93). In African Americans, age (OR = 1.09) and rural living (OR = 2.08) were the significant risk factors, while alcohol was protective (OR = 0.49).

Discussion—Age was a significant risk factor for AD at both sites. The higher risk of incident AD in the Yoruba female, and in African Americans who resided in rural areas in childhood were similar with the prevalence cases. Alcohol emerged a protective factor in African Americans. More studies are required, including biological measurements, to adequately explain the differences in rates.

Keywords

Risk factors; Incidence; Alzheimer's disease; Cross-cultural study

Introduction

The dementias of the elderly constitute a growing public health problem worldwide. Alzheimer's disease (AD) is the most common type. The cost of care is enormous, and attention needs to be appropriately placed on intervening against the risk factors, where feasible. The cross-cultural approach has proved useful in identifying the putative risk factors for many diseases including AD. Such factors may either be environmentally determined or genetic, and possible interactions between them may also be detected. This is because of the wider diversity of environmental exposures when individuals living in developing countries are compared with those in western countries (Hendrie, 2001).

Since 1992, research teams from Indiana University (Indianapolis) and the University of Ibadan, (Ibadan, Nigeria) have been collaborating on longitudinal study of the prevalence and incidence of dementia and AD in community-dwelling elderly African Americans living in Indianapolis and Yoruba people living in Ibadan, Nigeria. Using identical methods, the age-standardized annual incidence rates of dementia and AD in African Americans were 3.24% and 2.52% respectively. These rates were significantly higher than the respective values of 1.35% and 1.15% obtained in the Yoruba (Hendrie *et al.*, 2001). We therefore investigated for the socio-demographic and self-reported medical as well as life-style risk factors in the cohorts as a way of explaining the site differences in AD incidence rates. Our findings are reported in this communication.

Materials and methods

A detailed description of the incidence study was previously reported (Hendrie *et al.*, 2001). Essentially, a two-stage designwas utilized comprising the administration of the Community-Screening Instrument for Dementia (CSI'D) to eligible participants. The incidence study was conducted in two waves – two and five years after the prevalence study. Sub-samples of the study participants were selected for clinical assessment according to established cut-off scores that were derived from discriminant function analysis. Details of these had been described (Hall *et al.*, 1996). The clinical assessment included a structured

interview with an informant, neuropsychological testing, and examination by a physician as well as laboratory and imaging studies. All the information obtained was utilized in the consensus diagnosis process within each site, and inter-site agreement was essential before the final diagnoses were recorded. The Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-IIIR) and International Classification of Diseases, 10th Revision (ICD-10) criteria were used to diagnose dementia (American Psychiatric Association, 1987; World Health Organization, 1992). For AD, the National Institute for Neurological and Communicative Diseases and Stroke – Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria were used (McKhann *et al.*, 1984).

Information on the risk factors of interest was obtained at the baseline screening interview. The socio-demographic variables documented included age, gender, marital status (interest was on whether widowed or not), and years of education. Rural residency was recorded as positive if the study participant reported growing up in a community with less than 2,500 inhabitants as previously used by Hall *et al.* (2000). For household composition, the study participants were asked whether they lived alone or with other individuals, who may either be the spouse or other persons in the same house. Regular alcohol consumption implied the individual had more than 10 drinks per week. Information on whether the individual ever smoked was also recorded. Self-reported medical history of hypertension, diabetes mellitus, ischaemic heart disease, cancer, stroke, head injury, depression and fractures were also noted. Information on current medications was also utilized in diagnosing the medical conditions the participants had. Lastly, family history of dementia and stroke were enquired about. Responses were reported as either positive or negative.

Statistical analysis

We excluded subjects who were diagnosed as demented at baseline and those who were not clinically evaluated at either of the two follow-up waves. We compared individuals who developed incident AD to those who were diagnosed as non-demented. For both sites, subjects diagnosed as having other types of dementia were excluded from the risk factor analysis because of small numbers. Since the sampling scheme for selection of subjects for clinical assessment in our study resulted in unequal probabilities for selection, a specialized software, Survey Data Analysis (SUDAAN), for analyzing data from complex sampling was utilized. Frequency counts were used for all the variables of interest. The mean was used as summary statistics for ages, and compared using Student's *t*-test. Logistic regression model was used to calculate odds ratios between AD and each putative risk factor controlling for age and gender for each population. Multiple risk factors and interactions were not examined for because of small numbers of AD cases with respect to the Yoruba. Odds ratios and 95% confidence intervals were derived using the software SAS. Inter-site comparisons were made.

Results

A total of 1255 subjects completed the screening phase in Indianapolis. Their mean age was 77.4 years (s.d. = 6.4 years), 69.9% were females, and they had a mean of 10.0 years of education (s.d. = 3.0). Four hundred and ninety eight of them were clinically assessed, and 117 were diagnosed as having dementia with 89 (76.1%) AD cases. The mean ages, which ranged between 70 and 98 years, and the proportion of females in the non-demented and AD cases are shown in Table 1.

In Ibadan, 1225 study participants completed the screening. Their mean age was 75.6 years (s.d. = 6.7), and comprised 63.5% females with 0.9 year (s.d. = 2.5) as the mean number of years of education. Five hundred and thirty one study participants were clinically assessed with 70 diagnosed as having dementia and 62 (88.6%) AD cases. The means of their ages

which ranged between 70 and 101 years, and the proportion of females are shown in Table 2.

In African Americans resident in Indianapolis, the significant risk factors for incident AD were old age (OR = 1.09), rural living to age 19 years (OR = 2.08). Regular alcohol consumption was found to be protective (OR = 0.49) as shown in Table 1. Among the Yoruba, the significant risk factors for incident AD were old age (1.07) and female gender (OR = 2.93). Self-reported medical history of hypertension was found to be protective (OR = 0.33) as shown in Table 2. Education, marital status, living alone, past history of head injury, depression, ischaemic heart disease, strokes, fractures and family history of dementia were not associated with incident AD at either of the sites.

Discussion

Incidence studies are preferred when comparing populations at disparate sites because the prospective design obtains risk factor data prior to onset of disease, thus reducing possible biases due to retrospective attribution. In agreement with the findings in community-based studies, AD constituted the most common type of dementia at both sites (Rocca *et al.*, 1986; Henderson, 1986). In this study, it accounted for more than 75% of the demented cases. We found an association between age and incident AD at both sites which is in agreement with virtually all studies on the risk factor for the condition (Rocca *et al*., 1986; Henderson, 1986; van Duijn, 1996). The association between AD and increasing age in the Yoruba and African Americans suggests that AD is going to present a major public health problem worldwide with the ‘graying revolution’ already noted to be taking place.

Our results showed inter-site difference with respect to female gender and risk of incident AD. Whilst in the Yoruba, increased risk was found, as we had observed previously with our prevalence data (Hall *et al*., 1998), in African Americans, no association was found. Increased risk of AD in females has not been consistently reported in all studies (van Duijn, 1996). The association with female gender in the Yoruba may be related to their being older, since age is an established risk factor. On the other hand, it is possible that their lower educational attainment as compared with males because of cultural factors would affect their cognitive performance, and make them more likely to be selected for second stage assessment (Ogunniyi *et al.*, 2000). However, we found no association between education and risk of incident AD at either of the two sites, which may underscore the importance of low educational attainment.

Among African Americans, rural living up to the age of 19 years was found to be associated with increased risk of incident AD as we had earlier reported for prevalent cases (Hall *et al.*, 1998). The association with rural living probably served as a surrogate for other environmental exposures as a result of more extensive hours of farm labour (Hall *et al.*, 2000). We however could not ascertain what these environmental exposures might have been with the current study design to avoid recall bias. Rural residence has also been shown to be associated with low education which might suggest greater levels of poverty and resultant greater likelihood of deprivations (Hall *et al*., 2000).We did not find any significant association between education and increased risk of incident AD in African Americans hence could not test any interaction between rural residence and low education in this study.

A surprising finding was the apparent protective effect of hypertension for incident AD in the Yoruba. The diagnosis of hypertension was based on self reports and there could have been under-reporting because hypertension is a silent killer, and majority of the study participants may not have access to regular blood pressure measurements. Hence not much weight can be attached to this observation until objective blood pressure measurements are

utilized for that analysis. The observation could however sensitize one to what may be an important protective factor in the Yoruba, if proven in subsequent studies, since vascular factors are increasingly being shown to be important in the pathogenesis of AD. We had previously reported lower frequencies of vascular risk factors among the Yoruba as compared with the African Americans (Ogunniyi *et al.*, 2000; Hendrie *et al.*, 2004). In African Americans, on the other hand, two studies have shown the benefit of anti-hypertensive medications excluding the centrally-acting sympatholytic drugs in the preservation of cognitive functions (Richards *et al.*, 2000; Murray *et al.*, 2002).

A protective effect of regular alcohol consumption was observed in African Americans but not in the Yoruba. More African Americans (both non-demented and AD) drank alcohol regularly than their Yoruba counterparts from our data. The observed protective effect of regular alcohol consumption would be presumed to be due its enhancing the level of high density lipoprotein – the good lipid, and lowering triglycerides as well as the low and very low density lipoprotein fractions, and thus reducing the risk of vascular lesions. In a meta-analysis, Reynolds *et al.* (2003) showed that moderate alcohol consumption significantly lowered the risk of cerebrovascular diseases (CVD). The presence of CVD lesions has been shown in the Nun study to lower the threshold for the manifestation of cognitive impairment in AD (Snowdon *et al.*, 1997). Thus by lowering the risk of CVD, regular alcohol intake might perhaps be beneficial for cognitive performance.

In conclusion, our results showed significant age association with AD in both African Americans and the Yoruba. Inter-site differences in some of the risk factors were observed such as female gender among the Yoruba and rural living up to age 19 in African Americans. While alcohol consumption was protective in African Americans, self-reported hypertension was observed to be protective in the Yoruba. Further studies should be directed at the comparing blood pressure measurements and biochemical indices as well as genetic studies for the identification of possible gene-environmental interactions to explain the differences in AD incidence rates between the two communities.

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Table 1

Comparison of baseline demographic and medical conditions on the risk of Incident AD among African Americans

Variables	Incident AD *N* = 89	Non-Demented *N* = 381	OR (95% CI)
Age at diagnosis Mean (SD)	82.9 (7.1)	78.3 (7.0)	1.09 (1.06–1.13)*
Rural to age 19	43.8	32.0	2.08 (1.24–3.51)*
Alcohol consumption	18.0	34.6	0.49 (0.25–0.90)*
Female (%)	69.7	68.8	0.81 (0.47–1.41)
Years of education	8.7 (3.3)	9.4 (3.2)	0.95 (0.89–1.03)
Being widowed	59.6	45.1	1.27 (0.68–2.41)
Living alone	48.3	47.4	1.29 (0.65–2.66)
Hypertension	50.6	61.2	0.97 (0.59–1.63)
Smoking history	18.0	22.2	1.08 (0.48–1.39)
Past head injury	5.6	9.7	0.75 (0.24–1.98)
Depression	6.8	8.4	0.90 (0.29–2.40)
Past Stroke	7.9	12.4	0.68 (0.26–1.52)

*Statistically significant risk factor.

Table 2

Comparison of baseline demographic and medical conditions on the risk of Incident AD among the Yoruba

Variables	Incident AD *N* = 62	Non-Demented *N* = 461	OR (95% CI)
Age at diagnosis Mean (SD)	82.2 (10.0)	77.3 (7.5)	1.07 (1.04–1.11)*
Female (%)	83.9	66.8	2.93 (1.48–6.38)*
Hypertension	6.6	19.4	0.33 (0.10–0.85)*
Years of education	0.1 (0.8)	0.6 (1.7)	0.81 (0.53–1.07)
Being widowed	58.1	40.2	1.16 (0.61–2.27)
Living alone	9.8	10.8	1.16 (0.43–4.17)
Rural living to 19	29.0	25.4	1.25 (0.66–2.26)
Regular alcohol	15.0	24.1	0.82 (0.35–1.78)
Smoking history	18.0	22.2	1.08 (0.48–2.28)
Past head injury	3.2	2.4	1.15 (0.17–4.74)
Depression	14.5	12.4	1.40 (0.60–2.98)
Past Stroke	1.6	1.5	1.35 (0.07–8.34)

*Statistically significant.