RACIAL DIFFERENCES IN THE ETIOLOGY OF DEMENTIA AND FREQUENCY OF ALZHEIMER LESIONS IN THE BRAIN

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Empirical observations suggest a preponderance of cases of sporadic Alzheimer's disease among whites relative to blacks. If true, this might indicate a genetic basis for nonfamilial Alzheimer's disease. Among 6,000 consecutive autopsies performed at The Johns Hopkins Hospital, 242 adults with dementia were identified. The 98 consultation cases were excluded from the data analysis because of potential selection bias. Among the remaining 144 cases, the proportions of whites and blacks were similar, yet the frequency of Alzheimer's disease was 2.6 times higher among whites ($P=0.001$), dementia due to Parkinson's disease was more frequent among whites ($P=0.05$), and the frequencies of multi-infarct dementia and dementia due to chronic ethanol abuse were higher among blacks ($P=0.004$ and $P=0.007$, respectively). Moreover, in brains from neurologically intact controls, incidental histologic lesions of Alzheimer's disease were observed more frequently in whites than blacks ($P=0.01$). These findings provide a strong argument in favor of genetic transmission of sporadic Alzheimer's disease.

Alzheimer's disease is a neurodegenerative disorder characterized by progressive dementia striking middle-aged and elderly individuals. It is the primary cause of dementia in the United States, accounting for 50% to 60% of cases.[1,2] The etiology is unknown, but epidemiologic risk factors include advanced age,[3] a positive family history of Alzheimer's disease,[3,4] prior head trauma,[5,6] and thyroid disease.[5] In addition, higher frequencies of chromosomal aberration with aneuploidy,[7] DNA breakage,[8] DNA repair defect,[9] or premature centromere division[10] (all presumably reflecting accelerated aging) have been reported in patients with Alzheimer's disease, but these findings are controversial.[11-13]

Familial or genetic factors are among the most intriguing pathogenetic mechanisms proposed for Alzheimer's disease. Only a small fraction of the cases is clearly familial with probable autosomal dominant inheritance,[14,15] whereas the majority appear to be sporadic. Nonethelesss, the following observations suggest that even sporadic cases may be transmitted vertically:

1. Among relatives of patients with nonfamilial Alzheimer's disease, there is an increased frequency of dementia, principally Alzheimer's disease[1,4,16] as well as Down's syndrome.[16,17]

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2. Virtually all adults with Down's syndrome develop classical histopathologic changes of Alzheimer's disease[18,19]; ie, cerebral atrophy with neuritic (senile) plaques in cerebral cortex and accumulations of neurofibrillary tangles in large pyramidal neurons.
3. In a study conducted in Israel, a significantly higher incidence of Alzheimer's disease of the presenile type was observed in European- or American-born compared with African- or Asian-born populations.[20]
4. In Japan, HLA-B16 was found to be significantly associated with senile dementia of the Alzheimer type.[21] The low frequency of this genotype among Japanese was thought to correlate with the lower incidence of Alzheimer's disease in Japan compared with Europe or the United States.[21] Other studies, however, have not found any definite correlations between HLA-A or HLA-B antigens and Alzheimer's disease.[22]

Our own observations of postmortem cases at The Johns Hopkins Hospital suggested a preponderance of whites with Alzheimer's disease. In this study, we sought to determine whether the frequency of various types of dementia differed for whites and blacks. In addition, we examined brains of neurologically normal adults, 60 years and older, to determine whether incidental histopathologic lesions of Alzheimer's disease occurred with different frequencies among elderly whites and elderly blacks.

METHODS

Etiology of Dementia with Respect to Race

The anatomical diagnosis reports of The Johns Hopkins Medical Institutions autopsy service have been entered prospectively on computer since July 1980, and have been retyped retrospectively back to the first autopsy in May 1889. An on-line natural language index allows autopsies to be retrieved using any word or combination of words appearing in the anatomical diagnosis report; an on-line thesaurus assists the user in recalling synonymous terms that might be used to designate the same clinicopathologic entity.[23] The 6,000 autopsies performed at The Johns Hopkins Hospital between August 1973 and March 1986 were subjected to a computerized search to identify all patients with clinical evidence of dementia. The terms "dementia" and "Alzheimer's" were used to make the primary selection, but the final decisions were made on an individual basis after reviewing the clinical records. The only criterion for inclusion in this study was that dementia be documented clinically with a clear history of progressive cognitive impairment. For the purpose of this study, the information retrieved from the clinical records included age, race, sex, brain weight, and etiology of dementia. The etiology of dementia was confirmed by reviewing the radiographic, gross, and microscopic descriptions of the pathologic findings and, in complex or uncertain cases, the histologic sections of central nervous system tissue were also inspected. The data were analyzed to determine whether there were differences in the frequency of the various types of dementia between whites and blacks.

Detection of Incidental Alzheimer Lesions in Neurologically Normal Elderly Patients of Different Racial Origins

The normal patient groups consisted of 50 whites and 50 blacks, all 60 years or older, with no history of dementia or other underlying neurologic illness and less than 10% of the brain volume involved by a neuropathologic process at autopsy. All patients included in this part of the study had been regularly followed at The Johns Hopkins Hospital for non-neurologic illness; normal neuropsychiatric function was ascertained by the absence of evidence of cognitive impairment in the clinical histories or examinations. These patients were selected in order of their autopsy numbers, retrospectively from December 1985. All patients had been subjected to complete autopsy, and standard histologic sections from the frontal cortex, cingulate gyrus, hippocampus with temporal cortex (level of the lateral geniculate body), calcarine cortex, basal ganglia with insular cortex, substantia nigra, and locus ceruleus had been taken at the time of postmortem examination. Sections from the parietal lobe, amygdala, and nucleus basalis of Meynert were also available in some cases. Histologic sections stained with hematoxylin and eosin were examined to determine the frequency and extent of Alzheimer lesions; ie, neuritic plaques and neurofibrillary tangles as well as degenerative changes in the substantia nigra or locus ceruleus. In addition, one or two sections from frontal or temporal lobe cortex stained by the Bodian silver method and for immunoreactive neurofilament (SMI 31, 32, and 34) were surveyed to confirm the presence and extent of histopathologic lesions of Alzheimer's disease.

Alzheimer's and Parkinson's disease lesions were graded on a scale from 0 to 4. Grade 0 referred to the absence of histologic lesions. The following criteria were used to assess brains for the presence of Alzheimer lesions: grade 1, one or fewer neuritic plaques and neurofibrillary tangles per 200× microscopic field, with

TABLE 1. PATIENTS WITH DEMENTIA WHO UNDERWENT AUTOPSY AT THE JOHNS HOPKINS HOSPITAL: 1973-1986

	Hospitalized Subgroup			Consultation Cases
	Total	Whites	Blacks	Total
Number	144	78 (54%)	66 (46%)	98
Age* (yr)	71 ± 1	71 ± 1	72 ± 2	73 ± 1
Range	24-95	28-62	24-95	23-94
Sex				
Male	53%	59%	47%	54%
Female	47%	41%	53%	46%
Brain wt* (g)	1216 ± 12	1248 ± 17	1179 ± 15†	1155 ± 18†
Range	760-1700	760-1700	950-1500	900-1730

* Mean ± SE.
† $P<0.001$ compared with white patients in the hospitalized subgroup.

lesions confined to the hippocampus and medial temporal cortex; grade 2, one or fewer neuritic plaques and neurofibrillary tangles involving two or more different areas of the brain; grade 3, up to 5 neuritic plaques per 200× field in the hippocampus, amygdala, or two or more regions of neocortex; and grade 4, neuritic plaques and neurofibrillary tangles in densities exceeding grade 3 and indistinguishable from moderate or severe Alzheimer's disease. These criteria were based in part on the Khatchaturian diagnosis of Alzheimer's disease.[24] Criteria for assessing severity of Parkinson lesions included: grade 1, the presence of focal collections of extracellular pigment and pigment-laden macrophages; grade 2, changes similar to those found in grade 1 plus loss of neurons and gliosis; grade 3, changes seen in grade 2 plus occasional neurons with Lewy bodies or neurofibrillary tangles; and grade 4, changes indistinguishable from Parkinson's disease.

Statistical Analysis of Data

The data were analyzed to determine whether whites and blacks differed with respect to the frequencies of the various types of dementia. In addition, we sought to ascertain whether the frequency of incidental histopathologic changes of Alzheimer's or Parkinson's disease differed for the two races. The data were analyzed with two-tailed Fisher's exact tests and student *t* tests using the SYSTAT programs written for the IBM personal computer. In addition, odds ratios were calculated to predict relative risk for each disease process among whites and blacks.

RESULTS

Population Basis

Statistics regarding the population served at The Johns Hopkins Hospital were available for the three-year period from July 1983 to June 1986. During that interval, 66,074 patients (68.4% white and 31.6% black) between ages 30 and 89 had been discharged from the hospital. Within this age range, the distributions of race and sex were uniform with respect to age subdivided by decade. Outside this range, the adult population was skewed; black females composed a large percentage (41%) of the 20- to 29-year-old group, and white females preponderated (87%) in the 90- to 99-year-old group.

Among those 30 to 89 years old, 3.1% had died, 44% of whom had undergone autopsy. With the deceased patients grouped by age in decades, there were no significant variations among the subgroups with respect to sex or race distribution. Overall, of the population that had undergone autopsy 69% were white and 31% were black; these proportions are identical to those of the inpatient (discharged) population served at The Johns Hopkins Hospital. Throughout the study period (1973 to 1986), adults (16 years and older) accounted for between 71% and 76% of the autopsy population. The profiles with respect to age, race, and sex distribution per 1,000 autopsy patients did not vary significantly over time and closely resembled the distribution observed during the three-year period when statistics were available for the entire hospital population.

Population Profile

Among 6,000 consecutive autopsies performed at The Johns Hopkins Hospital between 1973 and 1986, 242 patients with the clinical diagnosis of dementia or Alzheimer's disease were identified (Table 1). This group was comprised of 144 patients who had been cared for regularly at The Johns Hopkins Hospital (hospitalized

TABLE 2. ETIOLOGY OF DEMENTIA AMONG 6,000 CONSECUTIVE AUTOPSIES PERFORMED AT THE JOHNS HOPKINS HOSPITAL: 1973-1986

Etiology of Dementia	Hospitalized Subgroup N=144	Consultation Subgroup N=98
Alzheimer's disease	33.3%	75.5%
Multiple infarcts	13.2%	5.1%
Ethanol abuse	9.7%	1.0%
Parkinson's disease	4.2%	3.1%
Glioblastoma	3.5%	0
AIDS encephalitis	3.5%	0
Huntington's disease	3.5%	4.1%
Stroke	2.8%	0
Inherited metabolic	2.8%	0
Creutzfeldt-Jakob syndrome	2.8%	4.1%
Binswanger's disease	1.4%	0
Multiple sclerosis	1.4%	1.0%
Subcortical degeneration	1.4%	0
Subdural hematoma	0.7%	0
Hydrocephalus	0.7%	0
Dementia pugilistica	0.7%	0
Atherosclerosis	0.7%	0
Storage disease	0.7%	0
Multisystem degeneration	0.7%	0
Other	0.7%	4.1%
Unknown	11.1%	2.0%

subgroup) and 98 who had autopsies performed at Hopkins as part of an ongoing research interest in dementia (consultation subgroup). In the hospitalized subgroup, 54% were white and 46% were black, whereas all but one of the 98 patients in the consultation subgroup were white ($P<0.001$). Furthermore, the mean brain weight of white patients in the hospitalized subgroup was significantly higher than that of both the black patients and the consultation subgroup ($P<0.005$ for both groups). The age and sex distributions of all groups were similar.

Etiologies of Dementia

Twenty different primary etiologies of dementia were identified (Table 2). Within the hospitalized subgroup, the most frequent causes of dementia were Alzheimer's disease (33%), multiple infarcts (13%), chronic ethanol abuse (10%), and unknown (11%). Among the 16 patients (11%) without a known cause of dementia, a diagnosis could not be established in 12 because the brains had not been examined at autopsy. However, in the other four, an anatomic cause of dementia could not be identified, despite careful study. These four patients did not have any of the recognized neurodegenerative disorders. Whereas a single disease process was identified as the cause of dementia in 61% of the group (excluding the 11% with undiagnosed dementia), 28% had two or more conditions contributing to dementia. In every instance, however, it was possible to determine the primary or dominant neuropathologic process. Examples of secondary processes contributing to dementia included: marked dilatation of the ventricular system, ie, hydrocephalus (12%); severe occlusive atherosclerosis of the cerebral vasculature (5%); degeneration of the substantia nigra or locus ceruleus, not sufficiently severe to diagnose Parkinson's disease (3%); and chronic heavy ethanol abuse (3%).

In the consultation subgroup, Alzheimer's disease was present and the primary cause of dementia in 76%. Multi-infarct dementia was present in 5%, Huntington's disease in 4%, and Parkinson's disease in 3%. The primary neurodegenerative process was complicated by hydrocephalus in 23% and degeneration of the substantia nigra in 7%.

Racial Differences in the Etiology of Dementia

Because of potential selection bias in the subgroup of consultation patients, this group was excluded from the ensuing statistical analyses. However, one observation is

TABLE 3. RACIAL DIFFERENCES IN THE ETIOLOGY OF DEMENTIA AMONG 144 PATIENTS IN THE JOHNS HOPKINS GROUP

Etiology of Dementia	Frequency		Relative Risk		
	White (78)	Black (66)	White	Black	*P* value*
Alzheimer's disease	46.2%	18.2%	3.86	0.26	0.001
Multiple infarcts	5.1%	22.7%	0.18	5.56	0.004
Ethanol abuse	2.6%	18.2%	0.12	8.44	0.007
Parkinson's disease	6.4%	1.5%	4.45	0.22	$0.05<P<0.10$
Glioblastoma	5.1%	1.5%	3.51	0.28	NS
AIDS encephalitis	2.6%	4.5%	0.55	1.81	NT
Huntington's disease	5.1%	1.5%	3.51	0.28	NS
Stroke	1.3%	4.5%	0.27	3.67	NT
Inherited metabolic	1.3%	0	—	—	NT
Creutzfeldt-Jakob syndrome	5.1%	0	—	—	NT
Binswanger's disease	1.3%	1.5%	0.84	1.18	NT
Multiple sclerosis	1.3%	1.5%	0.84	1.18	NT
Subcortical degeneration	2.6%	0	—	—	NT
Subdural hematoma	0	1.5%	—	—	NT
Hydrocephalus	0	1.5%	—	—	NT
Dementia pugilistica	1.3%	0	—	—	NT
Atherosclerosis	0	1.5%	—	—	NT
Storage disease	2.6%	3.0%	0.84	1.18	NT
Multisystem degeneration	0	1.5%	—	—	NT
Other	0	1.5%	—	—	NT
Unknown†	7.7%	15.2%	0.47	2.14	NS
Complex‡	30.8%	25.8%	1.28	0.78	NS

* NS=Not significant; NT=Not tested.
† Diagnosis unknown for six whites and six blacks because brains were not examined at autopsy.
‡ Complex refers to the presence of superimposed conditions contributing to dementia, but not sufficiently severe to be the primary cause, eg, hydrocephalus.

worthy of reiteration: Alzheimer's disease accounted for 76% of the diagnoses, and 99% of these patients were white. The single black patient in this subgroup had multi-infarct dementia.

Within the hospitalized subgroup of 144 patients, there were significant differences between whites and blacks with regard to the etiologies of dementia (Table 3, Figure). Alzheimer's disease accounted for 46% of dementia among whites, but only 18% among blacks. That is to say, the frequency of Alzheimer's disease was 2.6 times higher in whites than blacks ($P=0.001$), and the estimated probability (relative risk) for developing Alzheimer's disease was 3.86 times higher for whites than blacks. Although Parkinson's disease with dementia was observed more frequently in whites (6.4%) than in blacks (1.5%), and the risk of having Parkinson's disease was 4.45 times higher in whites, this difference did not reach statistical significance ($0.05<P<0.10$). The tabulation of Parkinson's disease both as a primary cause and contributing factor in the etiology of dementia, however, disclosed a trend toward a higher frequency of this neurodegenerative disease among whites ($P=0.05$). Blacks, on the other hand, had significantly higher frequencies of multi-infarct dementia ($P=0.004$) and dementia associated with chronic heavy ethanol abuse ($P=0.007$). The relative risks of these forms of dementia occurring in blacks were 5.56 and 8.44 times greater, respectively, than in whites. Except for Creutzfeldt-Jakob syndrome, which was observed only in white patients, the frequencies of all other causes of dementia were similar for the two races. Huntington's disease occurred in four white patients and in one black.

Frequency of Alzheimer Changes in Brains of Elderly Patients Without Neurologic Disease

The 50 white patients without neurologic disease ranged in age from 60 to 81 years, with a mean age of 69.0 ± 0.9 years and mean brain weight of 1347.8 ± 17.7 grams. The 50 neurologically normal black patients ranged in age from 60 to 90 years, with a mean age of 70.6 ± 1.0 and a mean brain weight of 1222.0 ± 21.9

grams. The brain weight of whites was significantly heavier than that of blacks ($P<0.001$), but the two groups did not differ in age or sex distribution.

Typical histopathologic changes of Alzheimer's disease were observed in 51% of the control patients. However, 67% of those patients (34% of the total) had mild focal lesions confined to the hippocampus and medial temporal cortex (grade 1). Thirteen percent had mild, but more widespread lesions of Alzheimer's disease, with involvement of the frontal, cingulate, insular, or calcarine cortex (grade 2). Three patients had moderate (grade 3) and one had severe (grade 4) histopathologic changes of Alzheimer's disease. None of the patients included in this part of the study had clinical evidence of dementia, and none had evidence of underlying neurologic disease manifested during their last admission. The frequency of histopathologic lesions of Alzheimer's disease was significantly higher among the white patients compared with black patients ($P=0.01$). For the most part, this difference was due to more widespread and more frequent moderate or severe lesions of Alzheimer's disease in whites. The frequency of focal neurofibrillary tangles and neuritic plaques confined to the hippocampus and medial temporal cortex was similar for the two races.

Degenerative changes in the substantia nigra or locus ceruleus were present in 38% of the patients. However, in 82% the degenerative changes were slight and consisted of focal accumulations of extracellular pigment and pigment-laden macrophages (grade 1). Grade 2 lesions were observed infrequently (7%), and grade 3 lesions with rare Lewy bodies were present in only one patient. No patients had frank histopathologic evidence of Parkinson's disease (grade 4). There were no significant differences in the frequency of degenerative histopathologic lesions in the substantia nigra or locus ceruleus with respect to race.

DISCUSSION

In this study, significant differences in the frequencies of various nosologic categories of dementia were observed between whites and blacks. White patients had higher frequencies of Alzheimer's disease and Parkinson's disease, whereas blacks had higher frequencies of multi-infarct dementia and dementia associated with chronic ethanol abuse. In addition, Creutzfeldt-Jakob syndrome was observed only in whites. Huntington's disease, which is transmitted genetically by autosomal dominant inheritance and occurs almost exclusively in whites,[25] was observed in four consultation cases and five hospitalized cases, all but one of whom were white.

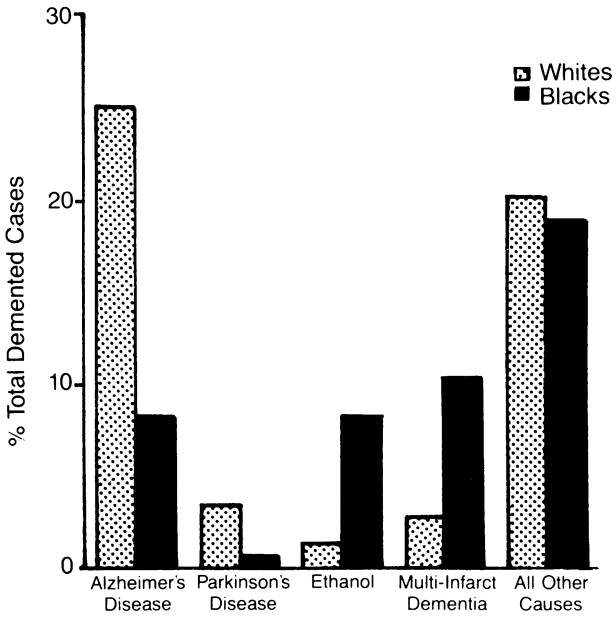

Figure. Racial differences in the etiology of dementia.

The black patient with Huntington's disease was in the hospitalized group, and his family history was proved positive by postmortem examination of relatives.

It is improbable that selection bias with respect to the distribution of patients autopsied at The Johns Hopkins Hospital accounts for the observed racial differences in the etiology of dementia because:

1. the demographic data available for each of the last three years of this study disclosed that the proportions of whites and blacks treated were 70% and 30%, and the proportions of each race who died were 70% and 30%;
2. the percentages of whites and blacks who underwent autopsy during each of the 16 years of this study were consistently about 70% and 30%; and
3. the age and sex distributions of the population served, those who died, and those who underwent autopsy were invariable during study period.

Although the population served at The Johns Hopkins Hospital may not be entirely representative of the general population in Baltimore, Maryland, the racial distribution of the patients on whom autopsies were performed was quite representative of the population served at Hopkins.

Although the frequency of multi-infarct dementia may have been higher among blacks because of the higher

incidence of systemic hypertension in this population, the significantly lower frequency of Alzheimer's disease in blacks cannot be explained on this basis. Differences in nutritional or socioeconomic status are also unlikely reasons for this lower frequency, unless an argument that affluence and education lead to Alzheimer's disease were accepted. Furthermore, if the incidence of Alzheimer's disease were the same for whites and blacks, a higher frequency of dementia in black patients would be expected due to the additional cases produced by hypertension and chronic ethanol abuse. Even if not diagnosed clinically, the frequency of histopathologically proven Alzheimer's disease should have been comparable for the two races. This was not the case. Instead, the frequency of clinical dementia in our population was the same for whites and blacks, the frequency of Alzheimer's disease was lower in blacks, there were no cases of histopathologically diagnosed Alzheimer's disease in blacks that had not been detected clinically, and the frequency of incidental Alzheimer's lesions in patients without evidence of neurologic impairment was lower among blacks.

The pathogenesis of ethanol-related dementia is unknown, and it is unclear why ethanol-related dementia occurred more frequently among blacks. The prevalence of alcoholism by race in Baltimore is unknown; however, the frequency of ethanol-related dementia observed in our autopsy population probably reflects the frequency of this disorder in the population served at The Johns Hopkins Hospital, as the demographic profiles of the two groups were similar. Racial differences in the frequency of ethanol-related dementia may reflect a genuine genetic predisposition, higher rates of exposure, or a complex interaction between the toxic effects of ethanol and poor nutritional status.

The significantly higher frequency of so-called sporadic Alzheimer's disease among whites provides a strong argument for vertical transmission of or genetic susceptibility to this disorder. This argument is strengthened by our observation that "incidental" histopathologic lesions of Alzheimer's disease in neurologically normal elderly individuals occurred more frequently and were more widespread in whites than blacks. Presumably these incidental lesions represent an early phase in evolution of Alzheimer's disease. The findings of this study corroborate epidemiologic studies that demonstrate racial differences in the incidence of Alzheimer's disease with a preponderance of cases among whites and disproportionately fewer cases among Orientals and blacks.[3,20,21] Moreover, the results suggest that so-called sporadic Alzheimer's disease has a genetic basis, although the transmission and penetrance are probably more complex than in familial Alzheimer's disease. The localization of amyloid β protein on chromosome 21[26] and mapping of the genetic defect causing familial Alzheimer's disease on chromosome 21[27] support the argument that sporadic Alzheimer's disease is genetically transmitted because the clinical features of dementia and the neuropathologic findings are identical in the familial and sporadic forms of the disease.[28]

The results of epidemiologic studies regarding the incidence and prevalence of Parkinson's disease are not conclusive with respect to genetic transmission or racial predilection. One study suggests that within the United States both the incidence and prevalence of Parkinson's disease may be higher among whites than blacks.[29] However, another study showed no difference in the prevalence of Parkinson's disease with respect to race.[30] In Japan, the incidence and prevalence rates of Parkinson's disease are similar to those observed in whites in the US.[31] In China, Parkinson's disease is probably equally as prevalent as it is in US whites.[32]

Despite these equivocal or negative findings with respect to race and Parkinson's disease, there is concrete evidence in favor of genetic transmission of or susceptibility to Parkinson's disease. First, familial cases of Parkinson's disease have been observed.[33,34] Second, the frequency of Parkinson's disease among relatives of probands with early-onset idiopathic Parkinson's disease is about three times higher than in the general population.[33] Third, Parkinson's disease has been associated with lower frequencies of the HLA haplotypes A1B8 and A2B5.[35] Among findings that negate evidence for a genetic basis of this disease, studies have shown virtually no concordance for Parkinson's disease between pairs of monozygotic twins.[36-38] These conflicting observations may stem from the case definitions employed. Parkinson's disease has protean manifestations and may be associated with tremor or akineto-rigidity, with or without dementia. No attempts have been made to target research toward understanding the epidemiology of Parkinson's disease with dementia versus Parkinson's disease without dementia. In the present study, comparison of the groups of 50 white and 50 black neurologically normal patients showed no significant racial differences in the frequency of Parkinson lesions. However, a significantly higher frequency of dementia caused wholly or in part by Parkinson's disease was observed in whites with dementia compared with blacks. One question raised by these findings is whether Parkinson's disease with dementia has a genetic basis with a greater degree of penetrance than Parkinson's disease without dementia.

The neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and Pick's disease also occur along familial lines[39,40] and have, as a major neuropathologic feature intraneuronal accumulations of immunoreactive neurofilament, as are evident in Alzheimer's and Parkinson's diseases.[41-44] The incidence and prevalence of ALS are also significantly greater in whites than blacks.[45] Moreover, Down's syndrome occurs predominantly among people of European ancestry and is relatively uncommon in people of Asian[46] or African[47] descent. Virtually all patients with Down's syndrome who survive beyond 35 years of age develop Alzheimer's disease, at least histopathologically.[48,49] Together, these findings suggest that neurodegenerative diseases associated with abnormalities or accumulations of neurofilaments are transmitted vertically and probably have a genetic basis. The racial differences in the frequencies of these diseases would also imply that the transmitted factor or genetic variant originated in Europe, as is the case for Huntington's disease. The observations that Creutzfeldt-Jakob syndrome, a transmissible spongiform encephalopathy,[50] may be familial and occurs more frequently in families with Alzheimer's disease[51] together with the finding of racial or genetic differences in the frequencies of neurodegenerative diseases associated with disorders of neurofilaments, such as Alzheimer's disease or Parkinson's disease, bolsters the argument that such diseases may be caused by vertically transmitted virus-like pathogens.

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