Does Stroke Contribute to Racial Differences in Cognitive Decline?

Deborah A. Levine, MD, MPH; Mohammed Kabeto, MS; Kenneth M. Langa, MD, PhD; Lynda D. Lisabeth, PhD; Mary A.M. Rogers, PhD; Andrzej T. Galecki, MD, PhD

Background and Purpose—It is unknown whether blacks’ elevated risk of dementia is because of racial differences in acute stroke, the impact of stroke on cognitive health, or other factors. We investigated whether racial differences in cognitive decline are explained by differences in the frequency or impact of incident stroke between blacks and whites, controlling for baseline cognition.

Methods—Among 4908 black and white participants aged ≥65 years free of stroke and cognitive impairment in the nationally representative Health and Retirement Study with linked Medicare data (1998–2010), we examined longitudinal changes in global cognition (modified version of the Telephone Interview for Cognitive Status) by race, before and after adjusting for time-dependent incident stroke followed by a race-by-incident stroke interaction term, using linear mixed-effects models that included fixed effects of participant demographics, clinical factors, and cognition, and random effects for intercept and slope for time.

Results—We identified 34 of 453 (7.5%) blacks and 300 of 4455 (6.7%) whites with incident stroke over a mean (SD) of 4.1 (1.9) years of follow-up (P=0.53). Blacks had greater cognitive decline than whites (adjusted difference in modified version of the Telephone Interview for Cognitive Status score, 1.47 points; 95% confidence interval, 1.21 to 1.73 points). With further adjustment for cumulative incidence of stroke, the black–white difference in cognitive decline persisted. Incident stroke was associated with a decrease in global cognition (1.21 points; P<0.001) corresponding to ≈7.9 years of cognitive aging. The effect of incident stroke on cognition did not statistically differ by race (P=0.52).

Conclusions—In this population-based cohort of older adults, incident stroke did not explain black–white differences in cognitive decline or impact cognition differently by race. (Stroke. 2015;46:00-00. DOI: 10.1161/STROKEAHA.114.008156.)

Key Words: dementia ■ Medicare ■ stroke

Racial disparities in dementia exist in the United States. Older non-Hispanic blacks have greater risk (≈2-fold) of having cognitive decline (cognitive impairment or dementia), including Alzheimer disease and vascular dementia, than older non-Hispanic whites.1–5 Although much attention has focused on the role of differences in vascular risk factors, socioeconomic factors, and education in these racial disparities,6–9 less attention has focused on whether racial differences in exposure to acute health events might contribute to racial differences in cognitive decline.

The identification of potentially modifiable factors that contribute to demographic differences in cognition is critical to inform the study and development of strategies to reduce disparities and to prevent dementia. Acute stroke is preventable and may precipitate cognitive decline. Stroke is a potent risk factor for vascular dementia and can trigger the clinical expression of Alzheimer disease and incident dementia.3,10–12

Racial differences in stroke frequency and impact may contribute to the black–white disparity in cognitive decline. In the United States, blacks have markedly higher incidence and prevalence of stroke compared with whites, a disparity that continues until the age of 75 years.13 Moreover, acute stroke may have a greater detrimental impact on the cognitive health of blacks compared with whites. Blacks may be more likely to have poststroke cognitive decline (PSCD) than whites because blacks may have more severe strokes,14 less recovery after stroke,15 or less cognitive reserve.16 In addition, blacks may have a greater burden of cerebrovascular disease...
and pathology related to vascular risk factors and small-vessel disease, including white matter lesions. Some studies suggest that PSCD is more common in blacks, whereas others do not. Previous studies are limited by lack of adjustment for prestroke cognitive decline and depressive symptoms, important determinants of PSCD that may differ substantially by race. Indeed, most stroke studies cannot measure actual changes in cognition associated with stroke because they lack measures of participants’ prestroke cognitive trajectories or use proxy-reported measures. Currently, it is uncertain whether acute stroke has a greater detrimental impact on the cognitive health of blacks after controlling for prestroke cognitive decline and depressive symptoms.

Therefore, we determined whether acute stroke contributes to any observed racial differences in cognitive decline or whether the impact of acute stroke on cognition differs by race in a longitudinal, nationally representative cohort of older non-Hispanic white and black adults followed from 1998 to 2010. We hypothesized that black–white differences in cognitive decline is explained, at least partially, by blacks’ increased incidence of stroke and there is a greater detrimental effect of stroke on cognitive health in blacks.

Methods

Data Sources

Subjects were participants in the Health and Retirement Study (HRS). The HRS is a nationally representative longitudinal study of 37000 US residents aged ≥51 years. The HRS uses multistage area probability sampling from all 48 contiguous US states and the District of Columbia, with oversampling of blacks and Hispanics. The HRS has successfully recruited and retained minority participants. Every 2 years since 1992, HRS participants have been interviewed on cognitive functioning, physical health and functioning, disability, health insurance, and other factors. The HRS uses standardized instruments to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions. The HRS follows participants to collect data on valid, generalizable measures that are applicable to stroke and a range of health conditions.

Subjects

We identified black and white HRS participants aged ≥65 years who responded to the 1998 HRS interview and had linked Medicare data. We excluded participants who met any of the following criteria: (1) those with baseline severe cognitive impairment to eliminate floor effects that would limit our ability to detect cognitive decline with cognitive impairment defined as having a score on the modified version of the Telephone Interview for Cognitive Status (TICS-m) of ≤6, which is a valid measure of cognitive impairment in black and white community-dwelling adults; (2) those who were enrolled in Medicare fee-for-service for <80% of the study period; (3) those without ≥1 additional follow-up HRS interview; (4) those who required a proxy respondent at baseline; (5) those who had no follow-up information on the outcome; and (6) those who had evidence of recent incident stroke in Medicare claims (ie, during the 2-year period before the 1998 interview) to start with a study population without recent acute stroke.

Measurement of Cognition

Cognitive testing was performed at each biennial HRS interview. The HRS measures cognitive function using a modified version of the TICS-m, a global cognition test patterned after the Mini-Mental State Examination. The TICS-m assesses global cognition, learning, and memory—cognitive domains commonly affected by stroke. The 27-point TICS-m scale includes (1) an immediate and delayed 10-noun free recall test to measure memory (0–20 points possible); (2) a serial 7 subtraction test to measure working memory (0–5 points); and (3) a counting backward test to measure speed of mental processing (0–2 points). The TICS-m is validated as a cognitive screening instrument in blacks and whites and designed for the use in population-based studies. This approach is consistent with previous research of the effects of incident stroke explained the racial differences in cognitive decline during the study period from 1998 to 2010.

Incident Stroke

We identified incident strokes during the time interval between the 1998 and 2010 HRS interviews using the linked Medicare data and valid International Classification of Diseases—Ninth Revision-CM codes. Incident strokes were defined by a hospitalization or emergency department visit with a primary or secondary discharge diagnosis of ischemic (433.x1, 434.xx, and 436.xx) or hemorrhagic stroke (430.xx, 431.xx, and 432.xx). Incident stroke was treated as a time-dependent covariate that affects a participant’s cognitive test performance in all years after the stroke. Figure 1 in the online-only Data Supplement shows the conceptual model for the impact of incident stroke on cognitive function. We allowed participants to have ≥1 incident stroke because we investigated whether the cumulative incidence of acute stroke explained the racial differences in cognitive decline during the study period from 1998 to 2010.

Covariates

We combined self-reported race and ethnicity to create 2 racial/ethnic groups: non-Hispanic whites and non-Hispanic blacks. We selected covariates that were potential confounders of the relationships between race, stroke, and cognitive function based on the literature review. Covariates included baseline values of age, sex, and education (<12, 12, and >12 years), and cognitive function measured by the TICS-m. Baseline depression symptoms were measured with the Center for Epidemiological Studies Depression Scale. We included participants who reported a history of stroke in the 1998 HRS interview but had no evidence of a recent, incident stroke in Medicare claims (ie, during the 2-year period before the 1998 HRS interview). This approach is consistent with previous research of the effects of stroke on cognition and also acknowledges that the accuracy of self-reported stroke may be low in multiethnic populations (sensitivity of 32%; specificity of 79%), particularly in adults with older age, hypertension, vascular disease, or cognitive impairment.

Statistical Analysis

We compared descriptive characteristics and incident stroke by race using 2-sample t tests with equal variance or χ² tests as appropriate. Stroke incidence rates were calculated by race. Descriptive characteristics were compared between participants who did and did not have an incident stroke during follow-up. We calculated the...
unadjusted hazard ratios with 95% confidence intervals for time to incident stroke by baseline characteristics of participants using Cox proportional hazards regression.

We fit a series of linear mixed-effects models to determine changes in cognitive function over time. Time was expressed as the years from the date of the HRS interview in 1998. Model A included fixed effects associated with baseline values of participant demographics (age, sex, and education), clinical factors (history of stroke before 1996 and depressive symptoms [Center for Epidemiological Studies Depression Scale score]), cognitive function (TICS-m score), and random effects for intercept and slope for time. The models included random effects for intercept and slope to accommodate correlation of cognitive measures within participants over time and to allow participant-specific rates of cognitive change.

To answer the first research question of whether acute stroke frequency contributes to any observed racial differences in cognitive decline, model B added incident stroke as a time-varying incident stroke (binary) variable that indicated when and whether the participant experienced an incident stroke to model A. To answer the second research question of whether the impact of acute stroke on cognition differs by race, model C added a race-specific effect of incident stroke to model B to allow the level of cognitive function to change differently by race after an incident stroke. We related the decreases in mean cognitive scores associated with incident stroke to approximate equivalent changes in years of brain or cognitive aging by calculating the ratio of regression coefficients for incident stroke and age on cognition.

Sensitivity Analyses
We compared characteristics between included and excluded participants. We assessed potential attrition bias by repeating the linear mixed-effects models requiring participants to attend an increasing number of follow-up interviews (range, 2–5–6).

Results
The Figure shows the derivation of the study sample. There were 4908 participants available for analysis. Table I presents baseline characteristics of study participants by race. At baseline, blacks (n=453; mean age, 73.0±6.6 years) had younger age, fewer educational years, more depressive symptoms, and lower cognitive scores than whites (n=4455; mean age, 74.0±6.4 years).

We identified 34 of 453 (7.5%) blacks and 300 of 4455 (6.7%) whites with incident stroke over a mean (SD) of 4.1 (1.9) years of follow-up (P=0.53). The stroke incidence rate was 7.7 (95% confidence interval, 6.9–8.6) per 1000 person-years for whites and 8.5 (95% confidence interval, 6.1–11.9) per 1000 person-years for blacks. Participants with older age, lower cognitive scores, more depressive symptoms, and more frequent history of stroke at baseline were more likely to have an incident stroke during the study period (Table I in the online-only Data Supplement).

There were 224 deaths (49.5%) among the 453 blacks and 2170 deaths (48.7%) among the 4455 whites (P=0.76). There were 149 deaths (44.6%) among the 334 individuals with incident stroke and 2245 deaths (49.1%) among the 4574 without incident stroke (P=0.12). Stroke survivors had a mean (SD) of...
Table 1. Baseline Characteristics of Participants by Race: The Health and Retirement Study, 1998 to 2010

<table>
<thead>
<tr>
<th>Characteristics at Baseline</th>
<th>Non-Hispanic Whites</th>
<th>Blacks</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (SD)</td>
<td>74.0 (6.4)</td>
<td>73.0 (6.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>1845 (41)</td>
<td>157 (35)</td>
<td>0.005</td>
</tr>
<tr>
<td>Education, y</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>1113 (25)</td>
<td>248 (55)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>1641 (37)</td>
<td>98 (22)</td>
<td></td>
</tr>
<tr>
<td>&gt;12</td>
<td>1701 (38)</td>
<td>107 (24)</td>
<td></td>
</tr>
<tr>
<td>TICS-m score, mean (SD)</td>
<td>15.4 (4.0)</td>
<td>13.0 (4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CES-D score, mean (SD)</td>
<td>1.4 (1.7)</td>
<td>2.0 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of stroke, n (%)</td>
<td>211 (5)</td>
<td>31 (7)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

The 8-item CES-D score measures depressive symptoms on a scale from 0 to 8. CES-D indicates Center for Epidemiological Studies Depression Scale; CI, confidence interval; NA, not applicable; and TICS-m, modified version of the Telephone Interview for Cognitive Status.

3.4 (1.7) TICS-m tests before stroke and a mean of 2.2 (1.4) TICS-m tests after stroke. These did not differ by race.

Adjusted Changes in Global Cognition Over Time

During the study period, blacks had statistically greater cognitive decline than whites (adjusted difference in TICS-m score, 1.47 points; 95% confidence interval, 1.21–1.73) in linear-mixed models that adjusted for time and baseline values of age, sex, education, depressive symptoms, history of stroke, and cognitive score (Table 2, model A).

With further adjustment for cumulative incidence of stroke, the black–white difference in cognitive decline persisted (Table 2, model B). Incident stroke was associated with a statistically significant decrease in global cognition (adjusted decrease in TICS-m score, 1.21 points; P<0.001). This decrease corresponds to ≈7.9 years of cognitive aging based on the ratio of the regression coefficients for incident stroke and age on TICS-m score. The effect of incident stroke on cognition did not differ by race (P for race-specific effect of incident stroke=0.52; Table 2, model C). There was no evidence of accelerated PSCD after adjusting for the changes in cognition before and acutely after stroke (P for change in cognitive decline after stroke=0.42).

Sensitivity Analyses

Compared with included participants, excluded participants who were enrolled in Medicare fee-for-service for <80% of study months were more likely to have younger age, higher baseline cognitive scores, and no incident stroke during follow-up (all P<0.01). Individuals excluded because of baseline cognitive impairment were more likely to have older age, less education, and higher depressive symptom scores (all P<0.001) compared with included participants. Although whites comprised the majority of participants (64%) who were excluded because of baseline cognitive impairment, blacks were more likely to be excluded because of baseline cognitive impairment than whites (19% versus 4%; P<0.001). Results were similar in models requiring subjects to have 2, 3, or 4 follow-up interviews (data not shown).

Table 2. Adjusted Changes in Global Cognitive Function Over Time: Health and Retirement Study, 1998 to 2010

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model A (n=4908)</th>
<th>Model B (n=4908)</th>
<th>Model C (n=4908)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black vs whites</td>
<td>−1.47 (−1.73 to −1.21)</td>
<td>&lt;0.001</td>
<td>−1.47 (−1.73 to −1.21)</td>
</tr>
<tr>
<td>Effect of incident stroke</td>
<td>NA</td>
<td>NA</td>
<td>−1.21 (−1.53 to −0.88)</td>
</tr>
<tr>
<td>Race-specific effect of incident stroke</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Baseline cognitive score (TICS-m, per point)</td>
<td>0.48 (0.45 to 0.50)</td>
<td>&lt;0.001</td>
<td>0.47 (0.46 to 0.49)</td>
</tr>
<tr>
<td>Baseline slope without incident stroke, per y</td>
<td>−0.31 (−0.33 to −0.30)</td>
<td>&lt;0.001</td>
<td>−0.30 (−0.32 to −0.29)</td>
</tr>
<tr>
<td>Age, per y</td>
<td>−0.15 (−0.17 to −0.14)</td>
<td>&lt;0.001</td>
<td>−0.15 (−0.16 to −0.14)</td>
</tr>
<tr>
<td>Women</td>
<td>0.24 (0.08 to 0.39)</td>
<td>0.002</td>
<td>0.22 (0.07 to 0.38)</td>
</tr>
<tr>
<td>Education, y</td>
<td>Referent</td>
<td>NA</td>
<td>Referent</td>
</tr>
<tr>
<td>&lt;12</td>
<td>1.10 (0.90 to 1.30)</td>
<td>&lt;0.001</td>
<td>1.11 (0.91 to 1.30)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>1.62 (1.42 to 1.83)</td>
<td>&lt;0.001</td>
<td>1.64 (1.43 to 1.84)</td>
</tr>
<tr>
<td>Self-reported history of stroke at baseline</td>
<td>−0.77 (−1.13 to −0.41)</td>
<td>&lt;0.001</td>
<td>−0.73 (−1.09 to −0.37)</td>
</tr>
<tr>
<td>Depressive symptom (CES-D) score, per point</td>
<td>−0.16 (−0.20 to −0.11)</td>
<td>&lt;0.001</td>
<td>−0.16 (−0.20 to −0.11)</td>
</tr>
<tr>
<td>Intercept</td>
<td>18.36 (17.31 to 19.41)</td>
<td>&lt;0.001</td>
<td>18.30 (17.25 to 19.35)</td>
</tr>
</tbody>
</table>

Linear mixed-effects models included fixed effects associated with baseline values of participant demographics, clinical factors, and cognition and random effects for intercept and slope for time. The cumulative incidence of acute stroke allowed participants to have >1 acute stroke between 1998 and 2010. Model A included time and baseline values of race, age, sex, education, history of stroke (before 1996), depressive symptoms (CES-D) score, and cognitive (TICS-m) score. Model B added incident stroke as a time-dependent covariate to model A. Model C added a race-specific effect of incident stroke to model B. CES-D indicates Center for Epidemiological Studies Depression Scale; CI, confidence interval; NA, not applicable; and TICS-m, modified version of the Telephone Interview for Cognitive Status.
Discussion

In this nationally representative cohort of older adults, we found no evidence that black–white differences in cognition are explained by blacks’ increased incidence of stroke or a greater detrimental effect of stroke on their cognitive health. Our data confirm that incident stroke is an important modifiable risk factor for cognitive decline. The effect of incident stroke on global cognition was equivalent to 7.9 years of cognitive aging.

We found that the stroke frequency did not explain blacks’ greater risk for cognitive decline compared with whites controlling for baseline cognition, consistent with other reports. In our study, blacks and whites had similar stroke incidence likely because the mean age of blacks and whites in our sample was 74 years, the age when the black–white disparity in stroke incidence attenuates. Although we excluded a greater percentage of blacks than whites with baseline cognitive impairment (19% versus 4%) consistent with previous research and cognitive impairment may be a more potent risk factor for incident stroke in blacks than in whites, stroke incidence was similar between blacks and whites with baseline cognitive impairment excluded from our sample (6.7% versus 5.3%; P = 0.49). It is also possible that the potential contributors to racial differences in cognitive decline (eg, neurodegenerative disease, socioeconomic factors, educational quality, genetic or biological factors, access and use of healthcare, vascular risk factors and their treatment, and early childhood exposures) have a larger effect and earlier onset of action than incident stroke occurring in older adulthood.

In addition, we found that the impact of acute stroke on cognition did not differ by race in older individuals. We may have had insufficient power because of sample size, but still our study sample is one of the largest to address this research question. Our cognitive measure may be insensitive to detect PSCD. The TICS-m is less sensitive to executive dysfunction after stroke. It is also plausible that the cognitive impact of stroke does not differ substantially by race after controlling for sociodemographics, depressive symptoms, and prestroke cognitive decline.

Results cannot be generalized to younger individuals or those with severe cognitive impairment. Cognitive performance tests may overestimate or misdiagnose cognitive dysfunction in blacks. Selective attrition may lead to underestimation of cognitive decline because participants with worse cognition at baseline or after stroke die, drop out, or require a proxy. Reassuringly, analyses that accounted for attrition did not change our results, consistent with Salthouse’s work. Although black stroke participants have lower mortality rates than their white counterparts early during follow-up, this mortality benefit attenuates and reverses over time. We lacked information on stroke severity, subtype, or location and did not measure interim incidence of periventricular ischemia, microbleeds, or asymmetric strokes, which can affect cognition and possibly differ by race.

Conclusions

We found no evidence that racial differences in cognitive decline are explained by differences in the frequency or impact of incident stroke between blacks and whites, controlling for baseline cognition, in this nationally representative cohort of older adults.

Sources of Funding

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Disclosures

Research support included the National Institutes of Health (Drs Levine, Langa, and Rogers).

References


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Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2015/05/26/STROKEAHA.114.008156.DC1

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SUPPLEMENTAL MATERIAL

Does Stroke Contribute to Racial Differences in Cognitive Decline?

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The figure shows the longitudinal study design and conceptual model for the impact of incident stroke on cognitive function. We hypothesized that stroke is associated with an acute drop in cognitive function at the time of the event and also faster cognitive decline over the years following the event. Incident stroke was treated as a time-dependent covariate that permanently affects a participant’s subsequent cognitive test performance (i.e., we assumed that an incident stroke effects cognition in all years after the stroke).
Supplemental Table I: Unadjusted Hazard Ratios (95% Confidence Intervals) for Time to Incident Stroke by Baseline Characteristics of Participants: The Health and Retirement Study, 1998-2010

<table>
<thead>
<tr>
<th>Characteristics at Baseline</th>
<th>n (%)</th>
<th>Unadjusted Hazard Ratio (95% CI) for Time to Incident Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blacks, n, % (n=453)</td>
<td>35 (7.7)</td>
<td>1.11 (0.79-1.58)</td>
</tr>
<tr>
<td>Whites, n, % (n=4,455)</td>
<td>306 (6.9)</td>
<td>Referent</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women, n, % (n=2,906)</td>
<td>193 (6.6)</td>
<td>0.82 (0.66-1.02)</td>
</tr>
<tr>
<td>Men, n, % (n=2,002)</td>
<td>148 (7.4)</td>
<td>Referent</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12 years, n, % (n=1,361)</td>
<td>102 (7.5)</td>
<td>Referent</td>
</tr>
<tr>
<td>12 years, n, % (n=1,739)</td>
<td>116 (6.7)</td>
<td>0.82 (0.62-1.06)</td>
</tr>
<tr>
<td>&gt;12 years, n, % (n=1,808)</td>
<td>123 (6.8)</td>
<td>0.80 (0.62-1.04)</td>
</tr>
<tr>
<td><strong>Age per one year increase</strong></td>
<td></td>
<td>1.05 (1.03-1.07)</td>
</tr>
<tr>
<td><strong>TICS-m score per one unit increase</strong></td>
<td></td>
<td>0.93 (0.91-0.96)</td>
</tr>
<tr>
<td><strong>CES-D score per one unit increase</strong></td>
<td></td>
<td>1.08 (1.02-1.14)</td>
</tr>
<tr>
<td><strong>Self-reported history of stroke before 1996</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of stroke, n, % (n=243)</td>
<td>32 (13.2)</td>
<td>3.07 (2.13-4.43)</td>
</tr>
<tr>
<td>No history of stroke, n, % (n=4,665)</td>
<td>309 (6.6)</td>
<td>Referent</td>
</tr>
</tbody>
</table>

TICS-m is the modified version of the Telephone Interview for Cognitive Status. The 8-item CES-D score measures depressive symptoms on a scale from 0 to 8.