An Approach for Defining Cognitive Decline in Epidemiologic Studies

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Abstract:
Introduction: Prospective studies of cognitive decline are vital for the identification of risk factors and preventative strategies, but there is no established definition of cognitive decline in epidemiologic studies. To plan a case-cohort biomarker study, a panel of experts sought to identify 500 participants with significant cognitive decline in the REasons for Geographical and Racial Differences in Stroke (REGARDS) cohort.
Methods: REGARDS is a population-based cohort of 30,239 black and white Americans enrolled from 2003-7 in their homes and followed by telephone. Global cognitive function was measured serially using the Six Item Screener (SIS), and learning, memory, and executive function using Word List Learning (WLL), Word List Recall (WLR), and Animal Fluency (AF) tests. In an initially cognitively intact cohort (SIS > 4 at baseline), cognitive decline was defined as performance 1.5 SD below the age-, race-, sex-, and education-based norms on 2 of 3 cognitive domain scores (AF, WLL, WLR).
Results: Median follow up time was 3.6 years for the WLL/WLR and 3.0 years for AF. A score of >1.5 SD from predicted on at least 2 of the 3 cognitive domains at the most recently administered test identified 543 cases. Further restriction to >1.6 SD identified 497 cases. Most (85.5%) cases were impaired on WLL and WLR only; 14.5% of cases had impairment on AF (Figure 1). By design, age, sex, race, and education did not differ between cases and non-cases. Residence in the stroke belt region, lower income, diabetes, heart disease, current smoking, alcohol abstinence, lack of weekly exercise, higher body mass index, and higher C-reactive protein were associated with case status.
Conclusion: Defining cognitive decline based on deviation from age-, race-, sex-, and education- predicted scores on at least 2 cognitive domains identified a case phenotype that was associated with other demographic and adverse vascular risk factors.

Figure 1. Venn diagram of cognitive decline (score >1.6 SD lower than age-, sex-, race-, and education-predicted on WLL, WLR, and AF, among those with SIS>4 at baseline). Cases overlap in at least 2 domains (shaded dark grey).