Age-related decline is not uniform across cognitive domains. Some abilities, like vocabulary and general knowledge, can remain stable until very late in life. In contrast, attention, executive function, and memory abilities start to decline in middle adulthood and progress until death. Although such changes are well established, little is known about the pattern of intra-individual cognitive decline. For example, it is unclear whether all older adults exhibit memory decline or whether it is found only in those with persons with concurrent decline in other cognitive abilities.

Few studies have directly examined possible patterns of age-related cognitive decline, and existing studies suggest that isolated decline (ie, in one cognitive domain) is rare. For example, a study using cluster analysis identified 5 patterns of cognitive performance in older adults—2 clusters of persons with poor cognitive performance, 1 with average performance, and 2 with strong test performance. Similar patterns have been reported by other researchers. However, interpretation of these studies is complicated by their inclusion of participants with conditions known to impair cognitive test performance. Cardiovascular disease, diabetes, and depression are prevalent in older adults and independently associated with cognitive impairment. They are also linked to accelerated cognitive decline and may distort the pattern of normal aging.

As a result, it is unclear whether the patterns of cognitive decline reported in past studies are attributable to normal aging or pathological processes.

Therefore, the present study looked to identify patterns of cognitive performance in older adults without significant medical and psychiatric conditions. To do so, we first compared younger, middle-aged, and older adults on cognitive tests to identify age effects. Then, using these findings, we performed a cluster analysis in older adults and compared them with the clusters found in middle-aged adults. Drawing on the frontal aging hypothesis, we predicted that middle-aged and older adults would exhibit cognitive deficits relative to young adults, with the most consistent deficits emerging on tasks assessing executive function.
METHODS

Overview
This study used data from the International Brain Database, an archive of demographic, psychiatric, health, and cognitive data from healthy community-dwelling individuals. Exclusion criteria for the database include medical conditions known to affect cognitive performance, including traumatic brain injury, neurological disorder, and other medical conditions (e.g., hypertension, diabetes, cardiac disease, thyroid disease). Participants were also excluded for history of significant mental illness or drug/alcohol addiction. All participants signed a written informed consent form before participation and were assigned an 8-digit identification number for anonymity.

Participants
A total of 364 adults (age 21-82) were categorized into groups based on age, specifically, young (age 21-25, n = 84), middle-aged (age 26-49, n = 199), or older adults (age 50-82, n = 84). These age ranges were developed using a combination of statistical and theoretical rationale. Statistical examination of the relationship between test performance and age provided the upper limit for the young adult group. Using a sequential procedure starting with the youngest participants, individuals older than age 25 exhibited poorer performance than younger persons on at least 1 test. Use of this method was believed to provide an index of "cognitive middle age" in our sample. The lower age limit of the older adult group was chosen to be consistent with past studies that used cluster analysis to identify possible patterns of cognitive performance.

Procedure
Participants were seated in a sound-attenuated room, in front of a touch-screen computer (NEC MultiSync LCD 1530V). Cognitive tests were administered in a fixed order using prerecorded task instructions, and the touch-screen computer was used for answers. Participants were asked to refrain from caffeine and nicotine for at least 2 hours and from alcohol for at least 12 hours before testing.

Instrumentation
Five tests from the larger battery were chosen to represent the cognitive domains examined in past studies, namely, attention, executive functioning, memory, language, and motor skills.

Attention: digit span backward. Participants were shown a series of digits (e.g., 4, 2, 7 . . .) presented individually for 500 milliseconds and separated by a 1-second interval. The participant was then immediately asked to enter the digits on a numeric keypad on the touch-screen in reverse order. The number of digits in each sequence was gradually increased from 3 to 9. This test has good psychometric properties, including a test–retest reliability of $r = .63$. The dependent measure was the maximum number of digits the participant recalled without error.

Executive functioning: Switching of Attention task. This modified version of the Trail Making Test consists of 2 parts. The first required the connecting of numbers in ascending sequence (i.e., 1-2-3, etc). The second test, Switching of Attention–II, required the connecting of numbers and letters in an ascending but alternating sequence (i.e., 1-A-2-B, etc). The numbers 1-13 and the letters A-L were presented in circles on the touch-screen. This test is similar to Trail Making Test B and shows robust reliability ($r = .76$) and validity ($r = .65$). Time to completion for this second test was used as our measure of executive functioning.

Memory: delayed verbal recall. Participants were asked to read and memorize a list of 12 words. Words were closely matched on concreteness, number of letters, and frequency. The list was presented 4 times, and participants were instructed to recall as many words as possible after each presentation. They were then presented with a list of distracter words and asked to recall those. Participants were then asked to recall the 12 original target words. Following a filled delay, participants were again asked to recall the original 12 target words. This measure of delayed verbal recall shows strong psychometric properties, including strong correlation with California Verbal Learning Test–Revised Long Delay Free Recall ($r = .63$). Total number of words recalled at long delay free recall was used as the dependent variable.

Language: animal fluency. For this task, participants were instructed to orally generate exemplars of animals within a 60-second time period. This measure of fluency has strong psychometric properties, including significant overlap with other measures of verbal fluency ($r = .76$). Responses were recorded, and the dependent measure was the total number of correct animals named.

Motor: motor tapping task. Participants were required to tap a circle on the touch-screen with their index finger as fast as possible for 60 seconds. Motor tapping performance is known to be both reliable and valid. The dependent variable was the sum of left- and right-hand taps.

RESULTS

Data Screening
Before analysis, the performances of all 364 individuals were examined for missing values and fit between distributions and assumptions. No participant had missing data. Assumptions of normality and possible extreme

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scores were then determined separately for each age group and variable. A slightly positive skew was detected for the executive function measure (Switching of Attention–II) in each age group. However, this minor violation is consistent with theoretical models of executive function and was not transformed.

Comparison of the Three Age Groups

Groups differed in age ($F_{2,361} = 706.48, P < .001$) but not years of education ($F_{2,361} = 2.87, P = .06$) or proportion of males/females ($\chi^2 = .07, P = .96$, see Table 1). Multivariate analysis of variance (MANOVA) revealed between-group differences in cognitive performance, with $\lambda = .68$ ($F_{10,714} = 15.33, P < .001$, partial $\eta^2 = .18$). Bonferroni-corrected posttests indicated significant differences on all cognitive tasks. In most cases, young adults performed better than middle-aged and older adults; however, middle-aged adults performed better than young and older adults on the memory task.

Cluster Analyses

Before cluster analytic procedures, raw test scores for middle-aged and older adults were transformed to $z$ scores, using the mean and standard deviation of the young adult group as a reference group. Based on past cluster analytic studies and the model proposed by Mesulam, we determined 3 clusters of cognitive performance in both middle-aged and older adults.

Middle-aged adults. Using an iterative procedure, a K-means cluster forcing 3 factors yielded the following results in middle-aged adults (see Table 2). Cluster 1 consisted of participants with intact performances on all tasks (Intact, $n = 91$). Cluster 2 consisted of participants with poor motor performance (Motor, $n = 19$). Finally, cluster 3 consisted of participants with reduced executive function performance (Executive, $n = 89$) (Figure 1).

Clustering with No Motor Performance

Groups differed in age ($F_{2,361} = 706.48, P < .001$) but not years of education ($F_{2,361} = 2.87, P = .06$) or proportion of males/females ($\chi^2 = .07, P = .96$, see Table 1). Multivariate analysis of variance (MANOVA) revealed between-group differences in cognitive performance, with $\lambda = .68$ ($F_{10,714} = 15.33, P < .001$, partial $\eta^2 = .18$). Bonferroni-corrected posttests indicated significant differences on all cognitive tasks. In most cases, young adults performed better than middle-aged and older adults; however, middle-aged adults performed better than young and older adults on the memory task.

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Older adults. Using an iterative procedure, a K-means cluster forcing 3 factors yielded the following results in older adults (see Table 4). Cluster 1 consisted of participants with weak executive function and otherwise intact performance (Executive, n = 54). Cluster 2 consisted of participants with poor motor performance, reduced attention, and executive dysfunction (Speed, n = 2). Cluster 3 consisted of participants with weak performances in all domains except memory (Global, n = 25) (Figure 2).

Clusters did not differ in sex (\(\chi^2 = 2.7, P = .26\)) or years of education (\(F_{2,78} = 1, P = .42\)) but did differ in age (\(F_{2,78} = 7.86, P = .001\)); participants in the Global cluster were significantly older than those in the Executive cluster. MANOVA also showed differences in test performance, with \(\lambda = .19\) (\(F_{10,148} = 19.07, P < .001\), partial \(\eta^2 = .56\), see Table 5). Bonferroni-corrected posttests revealed between-cluster differences in verbal recall, animal naming, and finger-tapping performance. Executive participants were superior to those with Global deficits on each of these tasks, with both Executive and Global participants outperforming Speed participants on the finger-tapping task.

**DISCUSSION**

Consistent with past studies, we found age effects in cognitive performance across the life span, with younger adults generally performing better than both middle-aged and older adults. Cluster analysis procedures identified distinct groups of older adults with executive dysfunction, those with reduced performance on tasks involving processing speed (attention, executive function, motor), and a group with global cognitive dysfunction. These clusters are similar to those found in middle-aged adults, although with greater levels of executive dysfunction. Several aspects of these findings warrant further discussion.

Even in our sample of very healthy individuals, no cluster of older adults exhibited intact performance in all cognitive domains. All clusters of older adults had reduced executive function relative to young adults. This finding is consistent with the "frontal aging hypothesis," which proposes that cognitive abilities mediated by the frontal lobe and its interconnecting neural circuitry are highly vulnerable to the effects of age.23,24 Because executive functioning is mediated by the frontal lobes and by frontal–subcortical circuitry, findings from the current study support selective aging-related decline in anterior brain systems, even in healthy older adults.25-27

As in past studies, we found no evidence for a cluster of individuals with isolated memory deficits in either
middle-aged or older adults. More striking is that all 3 clusters of older adults exhibited intact memory performance, even those with reduced performance in all other cognitive domains. Such findings support the notion that age-associated memory impairment is not part of healthy aging and may represent the consequences of medical conditions or early stages of a degenerative process.

A possible explanation for older adults having reduced executive function but intact memory is white matter disease. Even neurologically healthy older adults frequently exhibit subcortical hyperintensities (SH) on magnetic resonance imaging, and SH is associated with poor performance on executive function tasks. Although the exact mechanism by which white matter disease impairs cognition remains unclear, reduction in functional connectivity appears to play an important role. The relationship between white matter disease and cognition has not yet been explored in the International Brain Database, but that examination may provide insight into the underpinnings of age-associated cognitive changes in healthy adults.

The clusters identified in the present study differ somewhat from those from previous examinations. Past studies often cluster older adults into groups of persons with above-average, average, and impaired cognitive performance. Although it could be argued the present study also clustered individuals into groups with varying degrees of cognitive dysfunction, the degree of “impairment” was attenuated relative to past studies. Even when we compared older adults’ test performance to that of healthy young adults, the older adults in the present study produced few performances that would be considered clinically impaired (eg, >1.5 SD below mean). A possible explanation for different findings across studies is sample selection. In the current study, participants were rigorously screened and excluded for history of medical/psychiatric conditions associated with cognitive impairment, whereas past studies have often included these individuals. Exclusion of such persons likely reduces the proportion with pathological aging and may thus provide important information about healthy age-related cognitive decline.

Another possible explanation for differences across studies is the specific analytic techniques used. Given our goal of identifying patterns of healthy cognitive aging, we compared middle-aged and older adults to the performance of young adults. Past studies have used other approaches, including comparing older adults to other older adults. Each approach answers slightly different research question and may yield different results. Given our goal of determining age effects on clusters of cognitive performance, comparison to a young adult reference group appeared most appropriate.

The ability to generalize our findings to other samples is limited in several ways. One possible limitation is found in the operational definition of young, middle-aged, and older adults used in this study. As described in the Methods section, operational definitions for each group were based on a combination of statistical examination and the methods used in past studies. It is possible that use of other cut points would provide different results. A second possible limitation involves study methodology, because cross-sectional studies may be more susceptible to cohort effects than prospective studies. However, the large sample size and health of study participants suggest that these findings are robust, although replication in a large sample of older adults in narrowly defined age bands (eg, 60-70, 71-80, etc) would clarify these findings.

Taken in sum, the present study provides important information regarding age-related cognitive changes. Results show that significant decline in cognitive function characterizes the experience of older individuals, even very healthy older adults, with executive function abilities being most affected. Results also suggest that these cognitive changes begin to manifest in middle adulthood, possibly through changes in frontal brain regions. Further study of age-related cognitive decline in healthy adults is needed, because it may provide key insight into both healthy and pathological aging.

References


