Neuropsychological Studies in Geriatric Psychiatry

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Abstract and Introduction

Abstract

Purpose of Review: This review is a comprehensive summary of recent work in the field of neuropsychology that is relevant to geriatric psychiatry.

Recent Findings: Recent research identified neuropsychological predictors of functioning in geriatric samples, elucidated the neuropathology and neuropsychology of geriatric depression, further clarified the association between dementia and depression, contributed to advancements in the early detection and diagnosis of dementia, investigated emotion processing in aging, and adapted neuropsychological tests for severely impaired samples. There were encouraging trends indicating that neuropsychological investigations are becoming increasingly culturally diverse.
Summary: Recent research in neuropsychology will facilitate both the prediction of important clinical outcomes in geriatric samples and accurate differential diagnosis of psychiatric patients.

Introduction

Neuropsychological studies in geriatric psychiatry are increasingly advanced in their conceptual modeling, theoretical grounding, and reliance on neuroimaging technology. Over the past year, several trends are apparent in the literature. One pervasive theme is the prediction of important clinical outcomes, such as functional impairment and conversion to dementia - topics that are of critical importance in the clinical management of geriatric patients. Another theme has been the elucidation of brain and behavior associations in geriatric depression and dementia. Furthermore, there is encouraging evidence that research in geriatric neuropsychology is becoming more culturally diverse.

Neuropsychological Predictors of Functioning

Recent studies have demonstrated that cognitive abilities are significant predictors of daily functioning in diverse geriatric populations. Two investigations emphasized the importance of executive functions in the performance of activities of daily living. In one study, several neuropsychological measures of executive functions were compared in terms of their ability to predict instrumental activities of daily living in 50 geriatric patients, half of whom were suffering from dementia. Trail Making Test - Part B and the Wisconsin Card Sorting Test were the best predictors of instrumental activities of daily living.[1*] In another study,[2**] involving 45 out-patients with Alzheimer's disease, both executive cognitive and frontal behavioral impairments contributed independently to prediction of basic and instrumental activities of daily living. Similar results were reported in a study of 69 nursing-home residents,[3] which found that cognitive impairment and behavioral problems were significant predictors of functional status.

Two studies focused on functioning in geriatric psychiatry patients. In a chronically institutionalized sample (*n*=124), a 4-year longitudinal study[4] found that cognitive decline had the largest impact on functioning. Similarly, in an outpatient sample of geriatric patients with psychosis (*n*=111), dementia severity was significantly correlated with a performance-based measure of functioning.[5] In both studies, negative symptoms also were predictive of functioning, but to a lesser degree than cognitive abilities.

Geriatric Depression and Neuropsychological Dysfunction

In recent years, a great deal of attention has been devoted to geriatric depression, including associations between depression and executive functions, dementia, bereavement, and suicidal ideation.

Executive Functions

Associations between executive functions, brain structure, and geriatric depression have been the focus of many studies recently,[6*] and current research in this area continues to elucidate these associations further. In a 3-year longitudinal study,[7*] changes in white-matter hyperintensities and depression in one case was compared with those in 12 non-cases. The results indicated that white-matter hyperintensities were greater at baseline, and doubled in severity during the follow-up period for the case, during which time the patient experienced his first lifetime episode of major depressive disorder. A greater decline in executive functions also occurred during the study period. The authors hypothesized that both the depression and the deterioration in executive functions may have been caused by increased white-matter hyperintensities.

Another recent study characterized the neuropsychological presentation of geriatric depression, and found impaired executive functioning. Executive deficits were associated both with older age and depression, leading the authors to suggest that cognitive decline in aging may be compounded by geriatric depression.[8*]

Depression and Dementia

Depression is recognized both as a possible risk factor for dementia and also as a potential prodromal stage of the dementing process.[9,10] Recent research[11*] demonstrated that the peak incidence of depressive disorders occurred within 5 years preceding and 5 years following the onset of dementia in 147 participants with Alzheimer's disease, suggesting that both depression and dementia might be due to a common underlying neuropathology.

A recent longitudinal study[12**] was conducted to clarify the neuroanatomical association between depression and dementia in 115 non-demented elderly subjects. The results indicated that small left hippocampal volume at baseline was a risk factor for later dementia, indicating that depression may have been the heralding symptom of dementia in these patients. These results are complemented by findings from another study,[13] which indicated that greater depression severity at baseline was associated with a smaller improvement in cognitive functioning over a 1-year follow-up period. Patients with greater depressive symptoms may have been in a prodromal stage of a dementing process.

The association between 'subcortical brain syndrome' in dementia and symptoms of depression were investigated in 170 in-patients with dementia.[14] Subcortical brain syndrome was indicated by mental slowness, and bipyramidal, extrapyramidal and pseudobulbar signs. Patients with subcortical brain syndrome had a significantly higher frequency of depressive symptoms relative to patients with frontal, parietal, and global brain syndromes.

The results of an important study[15*] identified symptoms that are common to both depression and dementia in stroke patients, with and without dementia. A principal-components analysis indicated three groups of symptoms of dementia and depression: core mood symptoms, psychomotor symptoms, and vegetative symptoms. All three symptom clusters were strongly associated with depression, but the psychomotor factor also was associated with dementia. Thus, psychomotor symptoms may be due, in part, to neurological damage from stroke, rather than depression.

There is new evidence that the effects of depressive symptoms on neuropsychological functioning in the elderly are pervasive. In a sample of 66 elderly participants (over the age of 80) from Brazil,[16] the data indicated that bereavement is associated with cognitive impairment. Bereaved participants performed worse on some neuropsychological tests than non-bereaved individuals, despite the fact that there was no greater incidence of affective disorders in the bereaved group.

Suicidal Ideation

An innovative study[17*] examined associations between cognitive functioning and suicidal ideation in 90 elderly individuals without neurological impairment. The results of structural equation modeling indicated that cognitive impairment was associated with increased hopelessness, which was associated with greater suicidal ideation. Thus, cognitive impairment is a potential risk factor for suicidality, primarily because of increased symptoms of depression and hopelessness.

Alzheimer's Disease

Neuropsychological characterization of Alzheimer's disease has advanced the ability to detect preclinical cases with precision. Recent work also focused on neuropsychiatric symptoms, verbal memory, and cross-cultural research.

Early Detection of Alzheimer's Disease

Several studies combined neuropsychological and neuroimaging data to search for preclinical markers of Alzheimer's disease. In a study of 511 non-demented individuals aged 60-90,[18] the size of the head, body and tail of the hippocampus was measured, and associations with memory test scores were calculated. The size of the hippocampal head, rather than the body or tail, was associated with verbal memory performance and especially with delayed recall. The authors hypothesized that study results may lead to improved prediction of dementia, especially if future research demonstrates that there is early and selective involvement of the head of the hippocampus in Alzheimer's disease.

Another study[19] examined temporal lobe asymmetry in Alzheimer's disease, mild cognitive impairment, and a mixed neuropsychiatric sample. The results indicated left asymmetry in Alzheimer's disease, and mild cognitive impairment when the duration of the disease was less than 2 years, suggesting possible early lateralization in neurodegeneration.

Associations between apolipoprotein E, cognitive function, and metabolic change in the posterior cingulate cortex in 67 controls, 18 subjects with mild cognitive impairment, and 33 subjects with Alzheimer's disease were investigated.[20*] One measure of metabolic change in the posterior cingulate (*N*-acetylaspartate/creatine) appeared to be a non-specific marker for neuropsychological functioning in aging, while another measure (myoinositol/creatine) may be a specific marker for neurodegenerative disease. The latter measure may be useful in measuring the therapeutic effects of treatment or in predicting conversion from mild cognitive impairment to Alzheimer's disease.

Two important studies[21**,22**] examined early markers of dementia in a large Mexican American population of individuals over 60 years of age, in an attempt to replicate findings from more highly selected samples. In one project,[21**] brain metabolism was measured by positron emission tomography in 93 participants divided into four groups: normal, memory impaired, cognitively impaired but not demented, and demented. Hypometabolism in the cingulate cortex was a more robust predictor of dementia than hypometabolism in the temporal or parietal neocortex. Hypometabolism in the cingulate cortex may be a good marker for early and/or preclinical Alzheimer's disease.[21**]

In another study[22**] with the same sample, cognitive function and brain structure on magnetic resonance imaging were measured. Cognitive function was assessed with the Spanish and English Neuropsychological Assessment Scales (SENAS) neuropsychological battery, which has psychometrically-matched Spanish and English versions. The results indicated that the combination of reduced hippocampal volume and increased white-matter hyperintensities more than tripled the risk of developing dementia, suggesting a synergistic effect.

Other research focusing on the hippocampus and behavior in Alzheimer's disease[23] found that left hippocampal volume and olfactory function were correlated in a sample of 13 patients with Alzheimer's disease and 22 controls. Since the mesial temporal lobe exhibits early neuropathology in Alzheimer's disease, associations between this region and olfaction indicate that odor identification is useful in the detection of early or preclinical Alzheimer's disease.

Neuropsychiatric Symptoms

Delusions and depression are common in persons with Alzheimer's disease, but their association is poorly understood. In a study of 303 outpatients with probable Alzheimer's disease,[24*] 75 patients exhibited delusions only; depressive symptoms in these patients were compared with those in 228 patients without delusions or hallucinations. There was a strong and significant association between delusions and depression, after controlling for several potential confounds, such as age, education, illness duration, cognitive impairment, and poor general health. The strong link between these two neuropsychiatric symptoms may be due to common underlying neurotransmitter changes in the cholinergic, noradrenergic, serotonergic, and/or dopaminergic systems.[24*]

Assessment and Diagnosis

Diagnosis of Alzheimer's disease often involves neuropsychological testing and neuroimaging, in addition to a comprehensive neurological examination. The expense and time involved in dementia evaluations may be reduced by eliminating redundant tests. A recent study[25*] reported that when patients exhibit impairment in orientation or on immediate recall items in the Mini Mental State Exam, the results of a scan using Single Photon Emission Computed Tomography did not contribute unique information to the diagnosis of Alzheimer's disease.

Other investigators adapted a popular test of executive functions for use with patients with Alzheimer's disease. In a study of 17 patients with Alzheimer's disease and 17 controls,[26*] the authors tested a simplified version of the Tower of London test, which measures planning and goal attainment. The performance of patients with Alzheimer's disease deteriorated with increasing complexity of the problems. The participants with Alzheimer's disease made more rule-breaking errors than controls, and made more of these errors as the complexity of the problem increased, indicating an inability to plan.

In a particularly timely study,[27*] the decision-making capacity of subjects with Alzheimer's disease was assessed by determining patients' willingness to participate in research. The results indicated that patients with Alzheimer's disease were able to recognize risk-benefit profiles of various research study scenarios. They became more sensitive to risk and made more conservative decisions as decisional abilities declined. These results are particularly important as increasing attention is paid to ethical issues surrounding informed consent in vulnerable populations.

Verbal Memory

Alzheimer's disease is characterized by impaired semantic memory processing. An innovative, longitudinal study[28**] sought to characterize the progression of this impairment. The results indicated dynamic degradation of semantic memory from lower to higher hierarchical levels in Alzheimer's disease,

beginning with loss of specific semantic features and progressing to shared properties. The initial loss of specific semantic information appears to have the paradoxical effect of temporarily increasing priming for higher-level semantic information. The results of this study may explain contradictory results in the literature regarding semantic priming in Alzheimer's disease.

In another important study,[29] verbal memory impairment in Alzheimer's disease was characterized in Chinese patients with the condition. The investigators examined both quantitative and qualitative aspects of memory deficits, and the results indicated poor performance on both recall and recognition testing in Alzheimer's disease, indicating an amnestic memory disorder. Semantic clustering distinguished mild from moderate Alzheimer's disease. The results replicate work that has been conducted on patients from other countries, and are consistent with the neuropathology of Alzheimer's disease.

Other Dementias

Recent neuropsychologcial studies of dementia with Lewy bodies (DLB), Parkinson's disease and frontotemporal dementia have discovered information that is useful for refining the assessment and diagnostic criteria for dementia.

Dementia with Lewy Bodies

In 1996, consensus guidelines for DLB were published.[30] The results of two recent studies[31*,32] may be useful for the refinement of these guidelines. On the basis of past evidence linking DLB with rapid eye movement sleep behavior disorder (RBD), patients with DLB were compared to patients with dementia and RBD, and to patients with Alzheimer's disease. The results indicated that RBD was neuropsychologically indistinguishable from DLB; however, both DLB patients and RBD patients were distinguishable from those with Alzheimer's disease. The authors argue that dementia associated with RBD is likely to be DLB, even when other key features of DLB, such as parkinsonism and hallucinations, are absent.[31*]

Another investigation[32] reported an 11-year case-study of a patient who initially presented with primary progressive aphasia, but who later developed hallucinations and parkinsonism. Autopsy revealed both Lewy bodies and Alzheimer's disease pathology. The case was unique because features of DLB were not evident until 6-8 years after symptom onset. The authors use this case to argue that the current diagnostic system for DLB is flawed. They argue in favor of a purely pathological definition, which is more amenable to recognition of the nosological links between Alzheimer's disease and DLB, presumably because this definition is not tied to clinical criteria, such as time of symptom onset.

Parkinson's Disease

The prodromal neuropsychological profile of Parkinson's disease was investigated in a longitudinal study.[33*] The results indicated that incident dementia was associated with greater perseverative errors on the Wisconsin Card Sorting Test, poorer performance on 'digits backward' (Wechsler Memory Scale - Revised), and less-efficient encoding and recognition in the California Verbal Learning Test. Thus, greater executive dysfunction in Parkinson's disease may be predictive of later dementia.

Frontotemporal Dementia

The pattern of neuropsychological impairments in frontotemporal dementia was investigated in 50 out-patients, and was compared with those of 30 matched patients with Alzheimer's disease.[34*] The results indicated that patients with frontotemporal dementia performed better than those with Alzheimer's disease in terms of word-list learning, delayed recall, and visuoconstruction. There were no differences for naming and verbal fluency. This study also investigated the prevalence of non-cognitive behavioral disturbances

in frontotemporal dementia. Apathy, speech abnormalities and loss of insight were found in over two-thirds of the frontotemporal dementia sample, whereas symptoms of depression were rare.

Geriatric Schizophrenia

Geriatric patients with chronic schizophrenia often exhibit severe cognitive impairments, and there are few neuropsychological instruments that do not exhibit floor effects with these patients. A study[35*] investigated if the Alzheimer's Disease Assessment Scale -Late Version Cog would provide reliable and valid assessment of cognition in patients with schizophrenia who had profound cognitive impairment (e.g. a Mini Mental State Exam score between 0 and 10). The results indicated that the Alzheimer's Disease Assessment Scale - Late Version Cog subtests (i.e. recall, remote memory, orientation, naming, commands, expressive language) had greater range, variability and internal consistency, and exhibited less of a floor effect, than the Mini Mental State Exam.

Emotion Processing and Aging

The effects of age on emotion processing are not well understood, but the results of a recent study[36*] inform this important topic. Two contrasting theories of emotion processing in aging were tested: the sociocognitive theory predicts improved emotion processing with age, whereas the neuropsychological theory predicts decreased functioning. Thirty young (Mean age=29.9 years) and 30 elderly (Mean age=69.2 years) participants were compared in terms of their ability to identify emotion information from verbal and visual cues. The results largely indicated that there is very little decline in emotion processing with age. However, older participants may have more difficulty in identifying sadness and anger from visual cues.

Conclusion

A strength of recent research is the focus on the external or ecological validity of neuropsychological tests, primarily in predicting functional impairment. Functional impairment is of critical importance because of the associated burdens placed on informal and formal caregivers and because of the limitations on independence for elderly patients.

There are several other promising trends in the current research. For example, the increasing integration of neuropsychological and neuroimaging data in dementia and depression studies is enhancing the accuracy of differential diagnosis, early detection, and determination of the etiology of these disorders. Another important trend is the increased recognition of cultural diversity in neuropsychological studies. Finally, tests are being adapted for populations that have been difficult to assess in the past.

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