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Association Between Psychosis in Elderly Patients With Alzheimer Disease and Impaired Social Cognition

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Article Information

This cohort study assesses the association between psychosis in elderly patients with Alzheimer disease and social cognition in a longitudinal study.

Symptoms of psychosis in patients with Alzheimer disease may be the expression of a pathological subtype associated with an accelerated cognitive and functional deterioration portending a hastened mortality.[1] The proposed National Institute of Mental Health Research Domain Criteria initiative provides a framework for conceptualizing the common neurobiological underpinnings of symptom domains such as psychosis that transcend individual diagnostic categories to facilitate translational research.[2] Gur et al[3] suggest that highly implementable tasks measuring facial affective processing can be used to assay social cognitive integrity in psychotic disorders within the National Institute of Mental Health Research Domain Criteria framework. Although McLellan et al[4] report that facial affective processing is degraded in Alzheimer disease, to our knowledge no published studies have investigated the association between this impairment and the psychotic phenotype. We report on facial affective processing performance in a longitudinal cohort of healthy elderly control individuals and participants with mild cognitive impairment (MCI) or Alzheimer disease at baseline, with and without symptoms of psychosis over the course of the study.

Methods

Participants were recruited from Long Island and from the New York metropolitan area, in response to community outreach and direct referral by neurologists, psychiatrists, and geriatricians, for a longitudinal study investigating biomarkers of dementia. The study was approved by the institutional review board of the Northwell Health System and written informed consent was obtained. Assessments included the Mini-Mental State Examination (MMSE), the Comprehensive Affective Testing System Identity Discrimination and Name Affect subtasks, and the Neuropsychiatric Inventory psychosis subscales. The 92 recruited participants were followed up annually for up to 6 years. Psychotic symptoms in Alzheimer disease are a common but not ubiquitous manifestation of the disease, occurring in 30% to 40% of individuals over the course of the illness.[1] The 92 recruited participants were followed annually for up to 6 years, and divided into cohorts depending on whether psychotic symptoms emerged. For analysis, the cohort was divided into 3 diagnostic groups: participants with MCI or Alzheimer disease at baseline who would not become psychotic during the study (n = 38), participants with MCI or Alzheimer disease at baseline who would become psychotic during the study (n = 18), and cognitively healthy elderly controls (n = 36). Mixed model repeated measures analysis of variance used to determine if Comprehensive Affective Testing System performance differed across groups after adjustment for covariates (sex, age, group, educational level, MMSE score, and time [number of annual assessments]) (SAS, version 9.4; SAS Institute Inc).

Results

Of the 92 study participants (mean [SD] age 72.23 [11.2]), 50 were female (54%) (Table 1). On the Name Affect task, after adjustment for covariates, group differences in performance between impaired and nonimpaired groups were significant in the mixed model repeated measures analysis of variance (F_{2163} = 3.42; P = .03). Direct comparisons revealed that after adjustment for covariates including MMSE score, the presence of psychosis was associated with poorer performance when compared with the group without psychosis (change in score, −1.28 [95% CI, −2.57 to 0.007]; P = .05) and with the control group (change in score, −1.79 [95% CI, −3.16 to −0.42]; P = .01) (Table 2). In the unadjusted model, the group without psychosis differed from controls (change in score, −0.74 [95% CI, −1.43 to −0.05]; P = .03), but not significantly following adjustment for covariates (Table 2). MMSE score was independently associated

with performance on the Name Affect task across groups such that for each additional MMSE point there was an approximate increase of 0.11 (95% CI, 0.02-0.19; $P = .01$) score on Name Affect. As impaired affect recognition was associated with psychosis after adjustment for covariates, and as MMSE score was orthogonally associated with performance on the task, this suggests an association with the psychotic phenotype while highlighting the cognitive integrity required for adequate task performance.

On the Identity Discrimination task, after adjustment for covariates, with each year of additional age there was an approximate −0.03 ([95% CI, −0.06 to −0.01]; $P = .01$) reduction in score. Male sex was associated with poorer performance (change in score, −0.70 [95% CI, −1.3 to −0.1]; $P = .02$) on the task. MMSE score was also associated with performance with an approximate 0.22 (95% CI, 0.15-0.30; $P < .001$) increase in score for each additional MMSE point. In the unadjusted model, the psychotic group differed from controls (change in score, −2.70 [95% CI, −3.70 to −1.70]; $P < .001$) but this difference was not significant after adjustment for MMSE.

Discussion

Evidence suggests that impairments of facial affective processing are a feature of psychotic illnesses, including schizophrenia and bipolar disorder.[5,6] Deficits of affect recognition in a population with cognitive impairment may predispose such individuals to the erroneous decoding of the social signals of others, leading to delusional misinterpretations. Alternatively, the pathologic process responsible for the accelerated decline of individuals with Alzheimer disease and symptoms of psychosis may affect social neural networks recruited in affect recognition. In this sample the ability to discriminate faces–to determine whether 2 pictures show the same or different faces–was most closely associated with cognitive integrity as estimated with an MMSE score. The finding suggests that, in Alzheimer disease, networks responsible for facial identification may be more closely related to nonsocial cognitive or visuoperceptual domains. A limitation of this study is the number of patients with Alzheimer disease and psychosis. However, these data support the transdiagnostic relevance of social cognition in psychotic syndromes conceptualized within the National Institute of Mental Health Research Domain Criteria framework. Currently, the development of preclinical models of psychosis relies on a short list of behavioral paradigms with cross-species relevance, among them locomotor hyperactivity and disruption of sensorimotor gating.[1] Expanding this list to include social cognitive outcomes- paradigms that can be employed in murine models in the form of social learning and memory- may promote translational research and antipsychotic drug development.

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Figures and Tables

Table 1.

Baseline Covariates

Variable	Group		
	MCI/AD (n = 38)	MCI/AD+P (n = 18)	HEC (n = 36)
Female, No. (%)	21 (57)	10 (56)	19 (53)
Age, mean (SD), y	72.3 (9.1)	75.8 (10)	70.5 (13.3)
Educational attainment, mean (SD), y	15.5 (3.5)	15.7 (3.1)	16.4 (2.9)
MMSE score, mean (SD)[a]	24.7 (3.3)	20.2 (5.9)	28.9 (1.3)

Abbreviations: HEC, healthy elderly controls; MCI/AD, mild cognitive impairment or Alzheimer disease; MCI/AD+P, psychosis in MCI or AD; MMSE, Mini-Mental State Examination.

[a] $P < .001$ for the difference in scores among the 3 groups.

Table 2.

Fixed Effects for Identity Discrimination, Name Affect, and MMSE[a]

Group	Change in Score (95% CI)	P Value
Unadjusted Fixed Effects		
Identity discrimination		
MCI/AD vs HEC	−0.53 (−1.13 to 0.07)	.08
MCI/AD+P vs HEC	−2.70 (−3.70 to −1.70)	<.001
Name affect		
MCI/AD vs HEC	−0.74 (−1.43 to −0.05)	.03
MCI/AD+P vs HEC	−2.61 (−3.87 to −1.35)	<.001
Adjusted Fixed Effects		
Identity discrimination[b]		
Age	−0.03 (−0.06 to −0.01)	.01
Male	−0.70 (−1.3 to −0.10)	.02
MMSE	0.22 (0.15 to 0.30)	<.001
Name affect[c]		
MCI/AD+P vs HEC	−1.79 (−3.16 to −0.42)	.01
MCI/AD+P vs AD	−1.28 (−2.57 to 0.007)	.05
MMSE	0.11 (0.02 to 0.19)	.01

Abbreviations: HEC, healthy elderly controls; MCI/AD, mild cognitive impairment or Alzheimer disease; MCI/AD+P, psychosis in MCI or AD; MMSE, Mini-Mental State Examination.

[a]Results of repeated measures analysis of variance to determine if Comprehensive Affective Testing System Identity Discrimination and Name Affect subtasks scores differed over time across groups of HEC, patients with MCI or AD without psychosis, and patients with MCI or AD +P after adjustment for covariates (sex to age to group to education to MMSE and to time [number of annual assessments]).

[b]For age the estimates reflect change in score with additional year of age; for MMSE the estimates reflect change in score for each additional 1-point increase in MMSE.

[c]For MMSE, the estimates reflect change in score for each additional 1-point increase in MMSE.