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## Original Investigation

# Psychotic Experiences and Neuropsychological Functioning in a Population-based Sample

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**IMPORTANCE** Psychotic experiences in early life are associated with neuropsychological impairment and the risk for later psychiatric disorders. Psychotic experiences are also prevalent in adults, but neuropsychological investigations spanning adulthood are limited, and confounding factors have not been examined rigorously.

**OBJECTIVE** To characterize neuropsychological functioning in adults with psychotic experiences while adjusting for important sociodemographic characteristics and familial factors and investigating the effect of age.

**DESIGN, SETTING, AND PARTICIPANTS** The South East London Community Health (SELCoH) study is a population-based household survey of physical and mental health in individuals 16 years or older conducted from June 1, 2008, to December 31, 2010, in 2 London boroughs. The study included 1698 participants from 1075 households. Data were analyzed from May 6, 2014, to April 22, 2015.

**EXPOSURES** Psychotic experiences measured using the Psychosis Screening Questionnaire.

**MAIN OUTCOMES AND MEASURES** Neuropsychological functioning measured using tests assessing verbal knowledge (Wechsler Test of Adult Reading), working memory (Spatial Delayed Response Task), memory (Visual Object Learning Task), and processing speed (digit symbol coding task). A composite IQ score of general cognitive ability was calculated.

**RESULTS** A total of 1677 participants with a mean (SD) age of 40 (17) years were included in the analysis. Compared with the group without psychotic experiences, the 171 (9.7%) adults with psychotic experiences did not show a statistically significant impairment on mean (SD) measures of IQ (95.25 [16.58] vs 100.45 [14.77]; Cohen  $d$ ,  $-0.22$ ;  $P = .06$ ) or processing speed (40.63 [13.06] vs 42.17 [13.79]; Cohen  $d$ ,  $-0.03$ ;  $P = .73$ ) but were impaired on measures of verbal knowledge (31.36 [15.78] vs 38.83 [12.64]; Cohen  $d$ ,  $-0.37$ ;  $P = .003$ ), working memory (20.97 [4.12] vs 22.51 [3.26]; Cohen  $d$ ,  $-0.34$ ;  $P = .005$ ), and memory (43.80 [8.45] vs 46.53 [7.06]; Cohen  $d$ ,  $-0.28$ ;  $P = .01$ ). Only participants 50 years and older with psychotic experiences showed medium to large impairments in neuropsychological functioning (mean [SD]) on measures of IQ (81.22 [15.97] vs 91.28 [14.31]; Cohen  $d$ ,  $-0.70$ ), verbal knowledge (28.31 [13.83] vs 38.51 [11.50]; Cohen  $d$ ,  $-0.88$ ), working memory (19.11 [4.77] vs 21.99 [3.42]; Cohen  $d$ ,  $-0.82$ ), and memory (39.17 [8.23] vs 44.09 [6.51]; Cohen  $d$ ,  $-0.45$ ) after adjusting for socioeconomic status, cannabis use, and common mental disorders. Medium impairments (mean [SD]) on measures of working memory (21.27 [3.64] vs 22.62 [2.97]; Cohen  $d$ ,  $-0.45$ ) and memory (44.32 [5.84] vs 46.91 [5.74]; Cohen  $d$ ,  $-0.45$ ) were seen in those aged 35 to 49 years and on a measure of verbal knowledge (30.81 [14.17] vs 37.60 [10.48]; Cohen  $d$ ,  $-0.62$ ) in those aged 16 to 24 years. First-degree relatives of adults with psychotic experiences showed a small impairment on a measure of verbal knowledge (34.71 [12.10] vs 38.63 [10.97]; Cohen  $d$ ,  $-0.36$ ;  $P = .02$ ), and unrelated cohabitants showed no neuropsychological impairment.

**CONCLUSIONS AND RELEVANCE** The profile of cognitive impairment in adults with psychotic experiences differed from that seen in adults with psychotic disorders, suggesting important differences between subclinical and clinical psychosis.

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Schizophrenia has a lifetime prevalence of approximately 1% and combined psychotic disorders of approximately 3%.<sup>1,2</sup> A substantial minority of the general population also reports subclinical psychotic experiences, with the World Health Organization World Mental Health Surveys<sup>3</sup> reporting a lifetime prevalence of 5.8% worldwide and of 6.8%, 7.2%, and 3.2% in high-, middle-, and low-income countries, respectively. Evidence suggests that subclinical psychotic experiences may lie on a continuum with clinically significant psychotic symptoms and therefore be informative for research into the cause of psychotic illness. First, psychotic experiences and psychotic disorders share risk factors, including low IQ, childhood maltreatment, and stressful life events.<sup>4,5</sup> Second, imaging studies report pathophysiologic overlaps between subclinical and clinical psychosis, including hypofrontality, frontotemporal disconnection, and deficits in gray and white matter.<sup>6-8</sup> Finally, psychotic experiences in early life are associated with an increased risk for later psychotic illness<sup>9,10</sup> and in adulthood with later hospitalization for a psychotic disorder.<sup>11</sup> However, psychotic experiences are also associated with nonpsychotic psychiatric disorders, including anxiety, depression,<sup>12,13</sup> and suicidal thoughts and behavior.<sup>14,15</sup>

Lending support to this hypothesized psychosis continuum are the small neuropsychological impairments seen in people with psychotic experiences. (Table 1 and eMethods and eFigure 1 in the Supplement report results of a meta-analysis of previous population studies of neuropsychological functioning and psychotic experiences).<sup>4,5,16-40</sup> Neuropsychological impairment is a core feature of schizophrenia<sup>41,42</sup>; it emerges early and remains relatively stable throughout the course of the illness.<sup>43</sup> The most severe impairment is reported in processing speed,<sup>44,45</sup> but deficits in episodic memory and working memory have been proposed as core features.<sup>46</sup> A similar profile of impairment has been reported in people with psychotic experiences,<sup>19,20</sup> but most of the studies have focused on child and adolescent samples, despite evidence that psychotic experiences are prevalent across the life course.<sup>3,5,47,48</sup> Only 1 study in our meta-analysis investigated the neuropsychological correlates of psychotic experiences across adulthood<sup>5</sup> and reported on a single cognitive domain. Moreover, previous studies have not adjusted for key sociodemographic confounders, whose importance is highlighted by the World Mental Health Surveys' finding of higher prevalences of psychotic experiences in middle- and high-income countries compared with low-income countries.<sup>3</sup> Finally, the association between psychotic experiences and neuropsychological functioning may be confounded by shared familial factors.<sup>49</sup>

In the present study we examined subclinical psychotic experiences and neuropsychological functioning in adults from an ethnically and sociodemographically diverse population. Our study was unique in examining the effects of (1) important confounders, including cannabis use and psychiatric morbidity, (2) age, and (3) confounding by familial factors on the association between psychotic experiences and neuropsychological functioning. We hypothesized that psychotic experiences would be associated with a profile of cognitive impairment similar, yet milder, to that of schizophrenia, characterized

by specific deficits in processing speed and memory seen in the context of a generalized deficit.

## Methods

### Sample

The South East London Community Health (SELCoH) study is a population-based household survey completed in 2010 in the London boroughs of Lambeth and Southwark. The aim was to provide prevalence estimates of mental and physical health symptoms in an ethnically and socioeconomically diverse, geographically defined, inner-city community. A random sample of households was identified using the Small User Postcode Address File (<http://www.poweredbypaf.com/>), which has nearly complete coverage of private households in the United Kingdom. Introductory letters were sent to households, which were visited up to 4 times at different times of the day and the week. When contact was made, written informed consent was sought from as many eligible (aged  $\geq 16$  years) members of the household as possible; all study participants provided written informed consent. Contact was established with 2070 private households, of which 1075 had at least 1 member interviewed, representing a 51.9% household participation rate. Of 2359 individuals eligible within the participating households, 1698 (72.0%) participated (a detailed description can be found in Hatch et al<sup>50</sup>). This study was approved by the research ethics committee of King's College London.

### Procedure

Data were collected using a computer-assisted interview schedule, which was piloted to establish reliability, validity, and feasibility. Data were collected from June 1, 2008, to December 31, 2010. Participants received £15 for participation.

### Measures

#### Psychotic Experiences

The Psychosis Screening Questionnaire (PSQ)<sup>51</sup> was used to measure psychotic experiences. The PSQ is an interviewer-administered questionnaire that assesses psychotic experiences in the preceding year and consists of 5 sections covering hypomania, thought disorder, paranoia, strange experiences, and hallucinations. Items on hypomania were discarded because the focus was on psychosis. Each section has an initial probe, followed by secondary question(s), which establish the quality of psychotic experiences. The PSQ has been validated in 2 national surveys in the United Kingdom.<sup>52,53</sup> In this study, those participants who endorsed 1 or more secondary questions at the highest level on the PSQ were compared with those who did not<sup>5</sup> (eTable 1 in the Supplement).

#### Neuropsychological Functioning

Verbal knowledge was assessed using the Wechsler Test of Adult Reading (WTAR),<sup>54</sup> working memory with the Spatial Delayed Response Task (SDRT),<sup>55</sup> visual memory with the Visual Object Learning Task (VOLT),<sup>56</sup> and processing speed with a digit symbol coding task (DSCT)<sup>57,58</sup> (eTable 2 in the Supplement). Neuropsychological tests were administered using a

Table 1. Studies Investigating Neuropsychological Functioning and Psychotic Experiences

Domain by Source	No. of Participants	Age at Measurement of Cognition, y	Age at Measurement of Psychotic Experiences, y	Rate of Psychotic Experiences, %	Effect Size, Cohen <i>d</i>
<b>IQ<sup>a</sup></b>					
Polanczyk et al, <sup>4</sup> 2010	2127	5	12	5.9	-0.51
Kremen et al, <sup>16</sup> 1998	547	4 and 7	23	3.2	-0.61
Horwood et al, <sup>17</sup> 2008	6384	8	12	13.8	-0.08
Cannon et al, <sup>18</sup> 2002	789	3-11	11	14.7	-0.52
Pooled effect size	NA	NA	NA	NA	-0.40
<b>General cognition<sup>b</sup></b>					
Niarchou et al, <sup>19</sup> 2013	6784	8, 10, and 11	12	11.6	-0.05
Kelleher et al, <sup>20</sup> 2012	165	11-13	11-13	25.5	-0.03
Barnett et al, <sup>21</sup> 2012	2916	8, 11, and 15	53	22.3	-0.16
Gur et al, <sup>22</sup> 2014	4275	8-21	8-21	15.5	-0.42
Johns et al, <sup>5</sup> 2004	8520	16-74	16-74	5.5	-0.34
Pooled effect size	NA	NA	NA	NA	-0.19
<b>Processing speed<sup>c</sup></b>					
Niarchou et al, <sup>19</sup> 2013	6784	8, 10, and 11	12	11.6	-0.13
Kelleher et al, <sup>20</sup> 2012	165	11-13	11-13	25.5	-0.30
Gur et al, <sup>22</sup> 2014	4275	8-21	8-21	15.5	-0.29
Henderson et al, <sup>23</sup> 1998	870	78	78	7.5	-0.24
Ostling et al, <sup>24</sup> 2004	245	85	85	14.3	-0.56
Pooled effect size	NA	NA	NA	NA	-0.20
<b>Working memory<sup>d</sup></b>					
Niarchou et al, <sup>19</sup> 2013	6784	8, 10, and 11	12	11.6	-0.07
Kelleher et al, <sup>20</sup> 2012	165	11-13	11-13	25.5	-0.09
Gur et al, <sup>22</sup> 2014	4275	8-21	8-21	15.5	-0.29
Ostling et al, <sup>24</sup> 2004	245	85	85	14.3	-0.33
Pooled effect size	NA	NA	NA	NA	-0.18
<b>Memory<sup>e</sup></b>					
Kelleher et al, <sup>20</sup> 2012	165	11-13	11-13	25.5	-0.18
Gur et al, <sup>22</sup> 2014	4275	8-21	8-21	15.5	-0.32
Ostling et al, <sup>24</sup> 2004	245	85	85	14.3	-0.29
Pooled effect size	NA	NA	NA	NA	-0.31

Abbreviation: NA, not applicable.

<sup>a</sup> IQ measures include Vocabulary and Block Design subtests of Wechsler Preschool and Primary Scale of Intelligence-Revised<sup>29</sup> for Polanczyk et al<sup>4</sup>; Stanford-Binet Intelligence Scale (age 4 years)<sup>26</sup> and Information, Vocabulary, Digit Span, Comprehension, Block Design, Picture Arrangement, and Coding subscales of Wechsler Intelligence Scale for Children (WISC) (age 7 years)<sup>30</sup> for Kremen et al<sup>16</sup>; WISC III<sup>28</sup> for Horwood et al<sup>17</sup>; and Peabody Picture Vocabulary Test (age 3 years),<sup>25</sup> Stanford-Binet Intelligence Scale (age 5 years),<sup>26</sup> and WISC (ages 7, 9, and 11 years)<sup>27</sup> for Cannon et al.<sup>18</sup>

<sup>b</sup> General cognition measures include Picture Completion, Picture Arrangement, Block Design, and Object Assembly subtests of WISC III<sup>28</sup> for Niarchou et al<sup>19</sup>; Wide Range Achievement Test 4<sup>31</sup> for Kelleher et al<sup>20</sup>; Picture Intelligence, Reading, Sentence Completion, and Vocabulary (age 8 years), Arithmetic, Reading, Vocabulary, Verbal, and Nonverbal IQ (age 11 years), and Maths, Reading, Verbal, and Nonverbal IQ (age 15 years) from AH4 Group Test of Intelligence<sup>33</sup> for Barnett et al<sup>21</sup>; the Verbal Reasoning, Nonverbal Reasoning, and Spatial Processing subtests of the Computerized Neurocognitive

Battery (CNB)<sup>32</sup> for Gur et al<sup>22</sup>; and National Adult Reading Test<sup>34</sup> for Johns et al.<sup>5</sup>

<sup>c</sup> Processing speed measures include Sky Search Task from Tests for Everyday Attention for Children<sup>36</sup> and the Coding subtest of WISC III<sup>28</sup> for Niarchou et al<sup>19</sup>; Symbol Coding and Category Fluency in Trail Making Test from MATRICS neurocognitive battery<sup>35</sup> for Kelleher et al<sup>20</sup>; Symbol Letter Modalities Test<sup>37</sup> for Henderson et al<sup>23</sup>; and Identical Forms Test<sup>38</sup> for Ostling et al.<sup>24</sup>

<sup>d</sup> Working memory measures include Backward Digit Span and Arithmetic from WISC III<sup>28</sup> for Niarchou et al<sup>19</sup>; Spatial Span and Letter Number Span of Wechsler Memory Scale from MATRICS neurocognitive battery<sup>35</sup> for Kelleher et al<sup>20</sup>; Abstraction and Mental Flexibility and Attention and Working Memory subtests of CNB<sup>32</sup> for Gur et al<sup>22</sup>; and Digit Span for Ostling et al.<sup>24</sup>

<sup>e</sup> Memory measures include Hopkins Verbal Learning Test from MATRICS neurocognitive battery<sup>35</sup> for Kelleher et al<sup>20</sup>; Words, Faces, and Shapes subtests of CNB<sup>32</sup> for Gur et al<sup>22</sup>; and Thurstone Picture Memory Test<sup>38</sup> and Memory in Reality, Prose Recall, and Ten Word Memory Test<sup>40</sup> for Ostling et al.<sup>24</sup>

computer as in previous schizophrenia and bipolar disorder studies in which impairments of expected effect sizes were shown.<sup>59-63</sup> We calculated a general cognitive ability composite score as the first principal component of a factor analysis using all the neuropsychological tests administered.<sup>64</sup> Scores were transformed to an IQ-like score with mean of 100 and SD of 15.

### Confounders

The interview established ethnicity, age, and occupation classified according to the Registrar General<sup>65</sup> as professional (I), managerial/technical (II), skilled nonmanual (III-NM), skilled manual (III-M), semiskilled (IV), unskilled (V), and unclassified. Common mental disorders were assessed using the Revised Clinical Interview Schedule (CIS-R),<sup>66</sup> which asks about

the following 14 symptom domains during the previous week: fatigue, sleep problems, irritability, worry, depression, depressive ideas, anxiety, obsessions, subjective memory and concentration, somatic symptoms, compulsions, phobias, physical health worries, and panic. A score of 18 or more indicates the presence of a common mental disorder. Good reliability and validity of the Revised Clinical Interview Schedule have been reported.<sup>66,67</sup> Cannabis use in the past year was also reported. Ethnicity, occupation, cannabis use, and common mental disorders were correlated significantly with psychotic experiences and neuropsychological functioning, but minimally correlated with one another (eTable 3 in the Supplement). Interactions of group (participants with psychotic experiences or control participants) by confounder (ethnicity, occupation, cannabis use, and common mental disorders) with centered variables<sup>68</sup> on all tests were not statistically significant except for the group by ethnicity interaction on IQ ( $P = .03$ ).

#### Familial Factors

We investigated familial factors by dividing the cohabitants of participants with psychotic experiences into 2 groups. The first group included first-degree relatives (eg, biological child, biological sibling); the second, nongenetically related cohabitants (eg, spouse, nonbiological child).

#### Data Analysis

Data were analyzed from May 6, 2014, to April 22, 2015. Analyses were completed in STATA software (version 13; StataCorp). Appropriate survey commands (svy) were used to generate robust SEs. All analyses of SELCoH data accounted for clustering by household inherent in the study design and were weighted for within-household nonresponse.<sup>50</sup>

We used linear regression (adjusting for ethnicity, occupational class, cannabis use in the past year, and common mental disorders) to test the hypothesis that psychotic experiences would be associated with impairment in general cognitive ability (IQ). Because the profile of cognitive impairment in schizophrenia is characterized by specific deficits in processing speed and memory in the context of a generalized deficit and because different neural systems underlie performance on different neuropsychological tests, secondary analyses examined the association between psychotic experiences and individual neuropsychological test results. We applied a Bonferroni correction to adjust for multiple comparisons in the secondary analyses, yielding a corrected significance level of  $P < .007$  ( $0.05/7$ ). We computed Cohen  $d$  effect sizes using postestimation margins (effect sizes of 0.2, 0.5 and 0.8 represent small, medium, and large effects, respectively<sup>69</sup>).

To explore the effect of age on the association between psychotic experiences and neuropsychological functioning, local regression curves for age on the interaction of cognition by group were plotted for each test. To test the effect of age formally, we entered an interaction of group (psychotic experiences vs control) by age (continuous) with centered variables<sup>68</sup> into the regression model, adjusting for confounders as above. Linear regression analyses were subsequently stratified by age group (16-24, 25-34, 35-49, and  $\geq 50$  years), adjusting for confounders as above. Age categories were selected based on lo-

cal regression curves and to ensure sufficient power. Owing to the exploratory nature of the age-stratified analyses, Cohen  $d$  effect sizes with associated 95% CIs only are presented herein.

Confounding by familial factors was first examined by plotting local regression curves for age on the interaction of cognition by group (controls, participants with psychotic experiences, first-degree relatives, and unrelated cohabitants) for each test and subsequently using linear regression, as described above, across the whole sample to ensure sufficient power. We conducted sensitivity analysis using a different cut-off for the presence of psychotic experiences (ie, yes to  $\geq 1$  secondary question at any level<sup>70,71</sup>) using linear regression, as described above.

## Results

### Psychotic Experiences

Ten participants with missing PSQ data, 8 participants reporting a current or a past diagnosis of psychosis, and 3 participants currently taking antipsychotics were excluded from the analyses. The remaining 1677 participants were ethnically diverse (633 [37.7%] not white British), with a mean (SD) age of 40 (17) years (range, 16-90 years). Seven hundred thirty-three participants were male (43.7%).

Based on self-report and medication use, 11 participants (prevalence, 0.7%) had psychotic illness, which is consistent with previous reports of prevalence.<sup>1,2</sup> The 1-year weighted prevalence of psychotic experiences, defined as positive responses to all secondary questions in 1 or more categories on the PSQ,<sup>5</sup> included 171 participants (9.7%), which is consistent with findings from the World Health Survey.<sup>72</sup>

The group with psychotic experiences was more likely to be of a minority ethnic background, have a lower occupational status, have used cannabis in the past year, and have a common mental disorder (eTable 4 in the Supplement). Age differences in prevalence were not statistically significant.

### Association of Psychotic Experiences With Neuropsychological Deficits

Table 2 shows the relationship between psychotic experiences and neuropsychological performance before and after adjusting for confounders. The IQ impairment did not reach statistical significance when adjusting for confounders ( $\beta = -3.78$ ;  $t_{1261} = -1.91$ ;  $P = .06$ ; Cohen  $d = -0.22$ ). However, significant impairments were seen in the WTAR ( $\beta = -4.21$ ;  $t_{1347} = -3.02$ ;  $P = .003$ ; Cohen  $d = -0.37$ ), SDRT ( $\beta = -1.15$ ;  $t_{1385} = -2.84$ ;  $P = .005$ ; Cohen  $d = -0.34$ ), VOLT ( $\beta = -1.94$ ;  $t_{1455} = -2.59$ ;  $P = .01$ ; Cohen  $d = -0.28$ ), and VOLT delay ( $\beta = -0.66$ ;  $t_{1411} = -2.37$ ;  $P = .02$ ; Cohen  $d = -0.24$ ) scores. Impairments in the WTAR and SDRT scores remained statistically significant after correcting for multiple comparisons. No statistically significant impairment in the DSCT score was seen before or after adjusting for confounders.

We performed an exploratory analysis of the association between each psychotic experience (thought insertion, paranoia, strange experiences, and hallucinations) and neuropsychological performance. All experiences were associated with



Table 2. Group Means and Effect Sizes Before and After Adjustments

Cognitive Test	Mean (SD) Score by Group		Effect Size, Cohen $d^a$	P Value <sup>b</sup>	Effect Size, Cohen $d^c$	P Value <sup>b</sup>
	Psychotic Experiences	Control				
IQ <sup>d</sup>	95.25 (16.58)	100.45 (14.77)	−0.37	<.001	−0.22	.06
WTAR total <sup>e</sup>	31.36 (15.78)	38.83 (12.64)	−0.58	<.001	−0.37	.003
SDRT <sup>f</sup>						
Total	20.97 (4.12)	22.51 (3.26)	−0.46	<.001	−0.34	.005
Low load	11.32 (2.40)	12.02 (1.92)	−0.36	<.001	−0.27	.02
High load	9.66 (2.13)	10.49 (1.85)	−0.45	<.001	−0.33	.004
VOLT <sup>g</sup>	43.80 (8.45)	46.53 (7.06)	−0.38	<.001	−0.28	.01
VOLT delay <sup>h</sup>	14.27 (2.97)	15.14 (2.75)	−0.31	<.001	−0.24	.02
DSCT <sup>i</sup>	40.63 (13.06)	42.17 (13.79)	−0.12	.20	−0.03	.73

Abbreviations: DSCT, digit symbol coding task; SDRT, Spatial Delayed-Response Task; VOLT, Visual Object Learning Task; WTAR, Wechsler Test of Adult Reading.

<sup>a</sup> Indicates unadjusted.

<sup>b</sup> Results are statistically significant at the Bonferroni corrected level of  $P < .007$ .

<sup>c</sup> Indicates adjusted for ethnicity and occupational class, cannabis use in last year, and common mental disorders.

<sup>d</sup> Scores range from 40 to 160, with higher scores indicating better performance.

<sup>e</sup> Scores range from 0 to 50, with higher scores indicating better performance.

<sup>f</sup> Scores range from 0 to 24, with higher scores indicating better performance.

<sup>g</sup> Scores range from 0 to 60, with higher scores indicating better performance.

<sup>h</sup> Scores range from 0 to 20, with higher scores indicating better performance.

<sup>i</sup> Scores range from 0 to 94, with higher scores indicating better performance.

cognitive impairment, but effect sizes varied (eTable 5 in the [Supplement](#)). The frequency of individual symptoms did not allow stratification by age.

### Association Between Neuropsychological Functioning and Psychotic Experiences Stratified by Age

Previous studies have used samples consisting mostly of children and adolescents or of older adults, but inspection of Table 1 suggests that the association between psychotic experiences and neuropsychological functioning may differ by age. **Figure 1** shows an overall age-associated cognitive decline in both groups but also a difference in the severity of neuropsychological impairment associated with psychotic experiences at different ages. We found significant group-by-age interactions for all neuropsychological measures, including IQ ( $P = .006$ ), WTAR ( $P = .01$ ), SDRT ( $P = .03$ ), VOLT ( $P = .001$ ), VOLT delay ( $P = .02$ ), and DSCT ( $P = .01$ ) scores when adjusting for confounders.

After stratifying by age group and adjusting for confounders, group differences in mean (SD) IQ (81.22 [15.97] vs 91.28 [14.31]; Cohen  $d = -0.70$ ), WTAR (28.31 [13.83] vs 38.51 [11.50]; Cohen  $d = -0.88$ ), SDRT (19.11 [4.77] vs 21.99 [3.42]; Cohen  $d = -0.82$ ), VOLT (39.17 [8.23] vs 44.09 [6.51]; Cohen  $d = -0.45$ ), and VOLT delay (13.09 [2.74] vs 14.34 [2.40]; Cohen  $d = -0.52$ ) scores were medium to large in participants with psychotic experiences 50 years and older (**Figure 2**). Medium impairments in SDRT (21.27 [3.64] vs 22.62 [2.97]; Cohen  $d = -0.45$ ) and VOLT (44.32 [5.84] vs 46.91 [5.74]; Cohen  $d = -0.45$ ) scores were also found in participants aged 35 to 49 years with psychotic experiences and a medium impairment (30.81 [14.17] vs 37.60 [10.48]; Cohen  $d = -0.62$ ) and a medium advantage (44.80 [6.61] vs 38.63 [8.43]; Cohen  $d = 0.74$ ) in WTAR scores in those aged 16 to 24 and 25 to 34 years, respectively. All other impairments in those younger than 50 years were small.

Sensitivity analysis using a different cutoff for the presence of psychotic experiences<sup>70,71</sup> produced similar results

(eFigure 2 in the [Supplement](#)). Adjusting additionally for educational level (eTable 6 and eFigure 3 in the [Supplement](#)) also produced similar results.

### Association Between Neuropsychological Functioning and Psychotic Experiences by Familial Factors

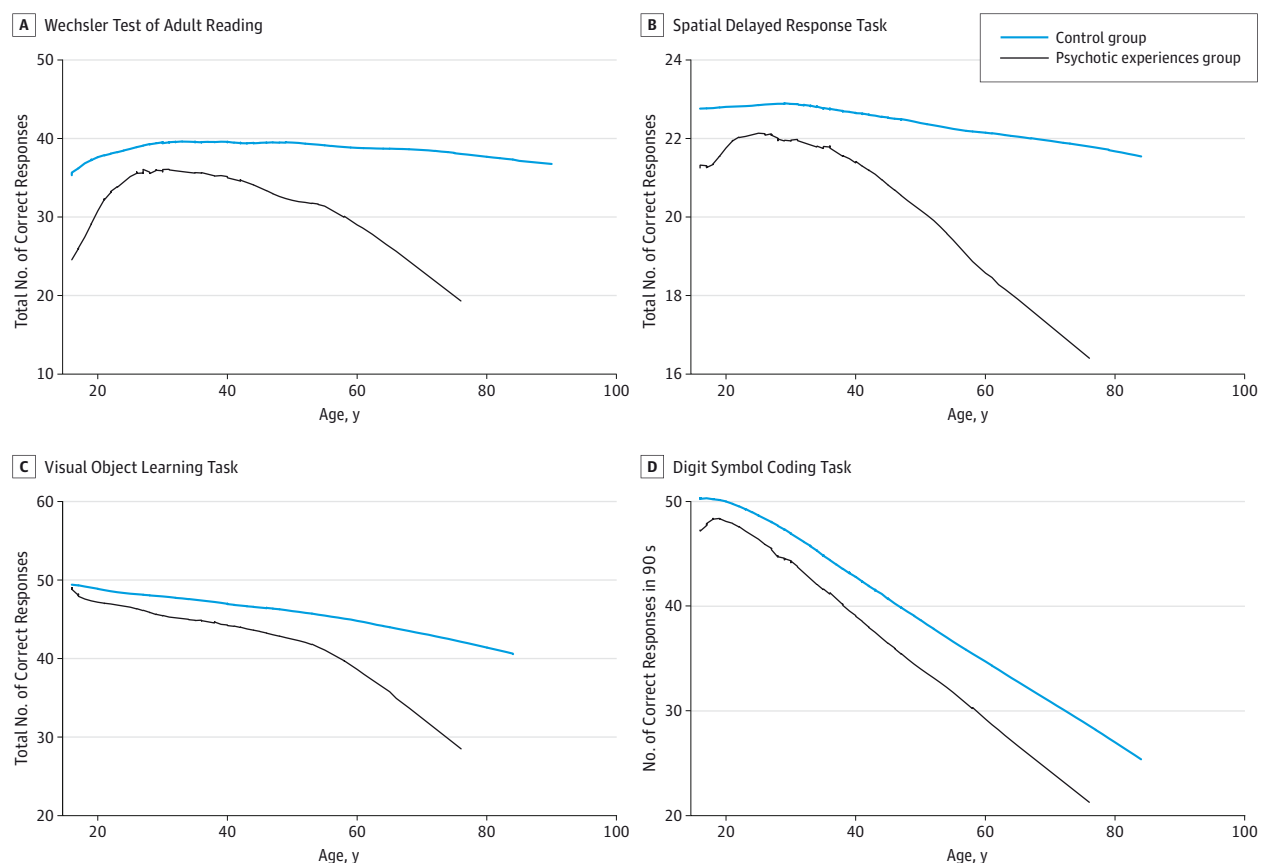
Characteristics of each group are shown in eTable 7 in the [Supplement](#). Exploratory analyses (eFigure 4 in the [Supplement](#)) suggested that WTAR performance was the most and VOLT performance was the least familial. First-degree relatives of probands were impaired on the WTAR score ( $\beta = -3.93$ ;  $t_{1347} = -2.33$ ;  $P = .02$ ; Cohen  $d = -0.36$ ) after adjusting for confounders (**Figure 3**). Nongenetically related cohabitants did not show statistically significant neuropsychological deficits.

## Discussion

This study provides evidence that subclinical psychotic experiences are associated with mild neuropsychological impairment in adults. The magnitude of impairment in specific domains suggests impaired verbal and memory functions but spared processing speed. Only older adults with psychotic experiences showed medium to large impairments in working memory and memory when adjusting for sociodemographic factors, psychiatric morbidity, and cannabis use. First-degree relatives of probands also had a significant verbal impairment, but not a significant memory impairment. Our findings introduce new knowledge and propose new hypotheses regarding the neuropsychology of psychotic experiences in adults.

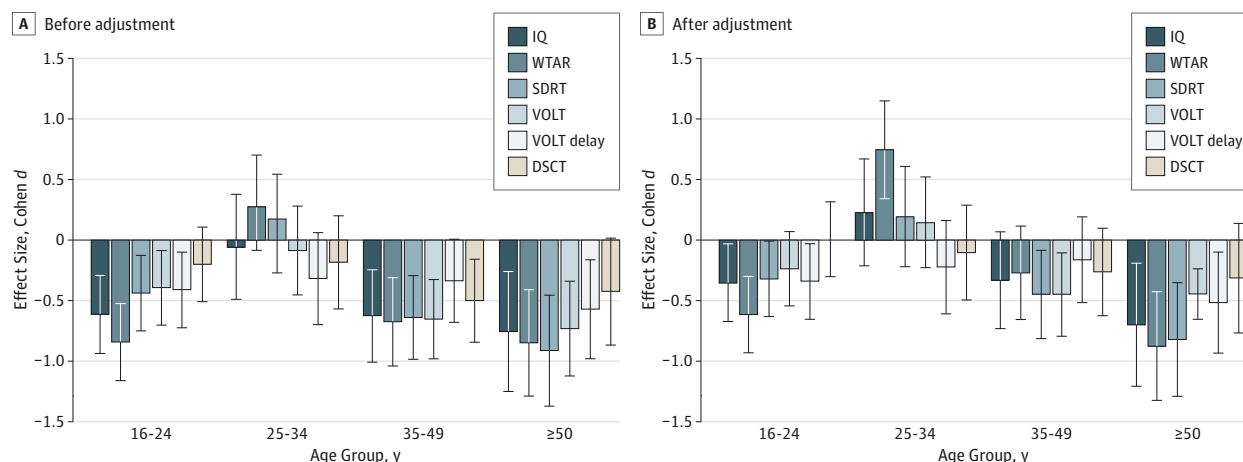
Our results are in line with those of the National Survey of Psychiatric Morbidity in Great Britain,<sup>5</sup> which reported a small verbal IQ deficit in adults reporting psychotic experiences. Although not directly comparable to those from other previous studies, which have mostly focused on younger or older samples,<sup>19,20,23,24</sup> the adjusted effect sizes we report

Figure 1. Local Regression Curves of Neuropsychological Functioning Domains



Domains are designated by the neuropsychological test used. Interaction of age by group is depicted on the graphs. The Wechsler Test of Adult Reading assessed verbal knowledge; the Spatial Delayed Response Task, working memory; the Visual Object Learning Task, visual memory; and the digit symbol coding task, processing speed.

Figure 2. Effect Sizes for Each Neuropsychological Domain by Age Group

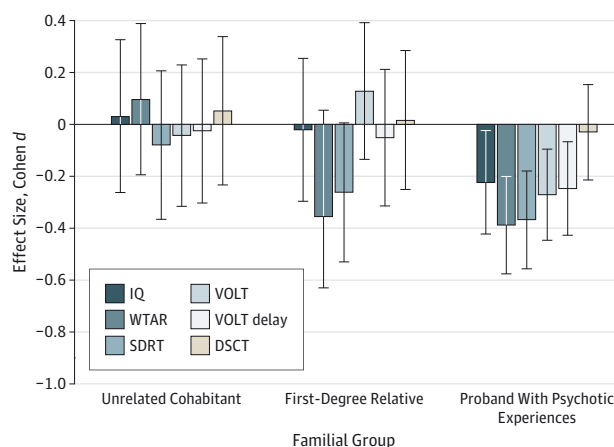


Data are depicted before and after adjusting for confounders. The Wechsler Test of Adult Reading (WTAR) assessed verbal knowledge; the Spatial Delayed Response Task (SDRT), working memory; the Visual Object Learning Task (VOLT), visual memory; and the digit symbol coding task (DSCT), processing speed. Error bars indicate 95% CIs.

closely approximate the pooled effect sizes in our meta-analytic summary (Table 1). Adjustment for confounders attenuated the processing speed deficit, suggesting that the sig-

nificant processing speed deficits reported in children and adolescents with psychotic experiences<sup>19,20</sup> may be partly confounded. Alternatively, the cause of processing speed defi-

**Figure 3. Effect Sizes for Each Neuropsychological Domain by Familial Group**



Effect sizes are adjusted for all confounders. The Wechsler Test of Adult Reading (WTAR) assessed verbal knowledge; the Spatial Delayed Response Task (SDRT), working memory; the Visual Object Learning Task (VOLT), visual memory; and the digit symbol coding task (DSCT), processing speed. Error bars indicate 95% CIs.

cits associated with psychotic experiences may differ between adolescence and adulthood. Indeed, a recent study that used a dimensional categorization of psychotic experiences also did not find differences in processing speed between adults with low and high levels of psychotic experiences.<sup>73</sup>

Our findings highlight similarities, but also differences, between neuropsychological dysfunction associated with psychotic experiences vs disorders. Meta-analyses have shown the most severe cognitive impairment in schizophrenia to be in processing speed.<sup>44,45</sup> We found only a weak association between psychotic experiences and DSCT performance. The discrepancy between a substantial processing speed impairment in psychotic disorder and a negligible impairment in psychotic experiences suggests that clinical psychosis is associated with increasing abnormality in processing speed.<sup>74</sup> Our findings add to a growing body of literature that challenges psychotic experiences as a subclinical phenotype of psychosis. Identification of factors associated with psychotic experiences that predict transition to psychotic disorder is needed if they are to be useful in the etiologic investigation of psychosis. Neuropsychological impairment, in processing speed specifically, may be one factor. Individuals with psychotic experiences and processing speed deficits may be most at risk for psychosis, and this combination of risk factors warrants further longitudinal study.

This study was the first, to our knowledge, to investigate the effect of age on neuropsychological impairment associated with psychotic experiences in adults. Some studies suggest that these experiences are most prevalent in adolescence<sup>75</sup> and old age,<sup>76</sup> whereas meta-analyses have not found significant age differences.<sup>3,47,48</sup> In our sample, prevalence of psychotic experiences was greatest in the youngest group but remained sizable in the other age groups (eTable 4 in the Supplement). Only older adults showed medium to large deficits in IQ, verbal knowledge, working memory, and memory

after adjustment for multiple demographic and psychosocial factors. Medium impairments in working memory and memory were seen in the group aged 35 to 49 years and in verbal knowledge in the group aged 16 to 24 years. These findings highlight the heterogeneity of extended phenotypic expression associated with psychotic experiences throughout adulthood. Etiopathologic pathways to subclinical psychotic experiences and neuropsychological dysfunction may be age dependent (eFigure 5 in the Supplement). In young adults with psychotic experiences, neuropsychological impairment may signal a risk for general psychiatric disorders, possibly owing to psychosocial stress and/or substance use; however, in older adults, neuropsychological impairment may indicate vulnerability to accelerated cognitive aging. A faster trajectory of cognitive decline for patients with Alzheimer disease with concurrent delusions<sup>77</sup> and hallucinations<sup>78</sup> has been reported. Accelerated shrinkage of prefrontal and hippocampal regions seen in normal aging<sup>79,80</sup> may lead to disrupted dopamine release and psychotic phenomena<sup>81</sup> but also to more rapid cognitive decline.

By including cohabitants of participants with psychotic experiences, we explored potential mechanisms behind the association between psychotic experiences and cognition. First-degree relatives were significantly impaired on verbal knowledge, whereas unrelated cohabitants showed no impairment. Our findings suggest that a complex interplay of genetic, biological, and psychosocial factors lies behind the association between psychotic experiences and neuropsychological impairment. This pattern of verbal knowledge impairment suggests common genetic and/or family environmental factors. On the other hand, unimpaired memory functions in both groups of cohabitants support biological and/or psychosocial effects of psychotic experiences on memory consistent with a causal effect.

Although we hypothesize that sociodemographic factors, cannabis use, and common mental disorders are confounders, they could also be mediators or moderators. Mediation and confounding are identical statistically but can be distinguished conceptually.<sup>82</sup> Changes associated with the hypothalamic-pituitary-adrenal axis may be one area of investigation because the hypothalamic-pituitary-adrenal axis has been associated with all of these factors and with psychosis and cognition.<sup>83</sup> Shared genetic factors could be another area of investigation.<sup>84,85</sup> Examining interactions between multiple risk factors is important because complex multifactorial traits are likely to result from such interactions, and future studies with large samples are required for such investigations.<sup>86</sup>

The present study has a number of strengths. It is the first, to our knowledge, to use a large, heterogeneous, representative sample drawn from an urban community to investigate the effect of age and familial factors on the association between psychotic experiences and neuropsychological functioning while adjusting for important confounders. Nevertheless, several methodologic limitations require consideration. First, the 51.9% household participation rate was high, but we were not able to characterize nonresponders on demographic variables and rule out possible bias owing to nonparticipation. However, the sample was representative of the local population on most sociodemographic characteristics.<sup>50,71</sup>



Second, psychotic experiences are fairly common in old age, presumably owing to neurodegenerative processes,<sup>87</sup> and we could not exclude participants with dementia. However, most of the participants in the oldest category were aged 50 to 65 years, when dementia is rare,<sup>88</sup> and medium to large impairments in IQ, WTAR, SDRT, and VOLT scores (Cohen  $d > 0.50$  for all) remained when we excluded participants older than 65 years. Third, interpretation of effect sizes generally depends on the assumption of normality, which held true for all tasks except the WTAR, meaning that effect sizes in verbal knowledge may have been underestimated.

Moreover, those participants with poorer neuropsychological functioning may have been more likely to endorse psychotic experiences, and yet the association was not present at all ages or in all domains. We cannot infer from the current cross-sectional data that psychotic experiences lead to deficits in neuropsychological functioning. Another plausible explanation is that psychotic experiences and neuropsychologi-

cal functioning are manifestations of common underlying processes.<sup>89,90</sup> Finally, the timing and history of psychotic experiences cannot be established from the PSQ, meaning that some psychotic experiences may be long-standing. The present data provide valuable insight into potential pathways to adult psychopathologic disorders, but future longitudinal studies that are able to disentangle their temporal sequence and to determine whether these findings also apply to lifetime psychotic experiences are needed.

## Conclusions

The profile of cognitive impairment in adults with psychotic experiences differed from that found in psychotic disorders. Our findings highlight the importance of considering age, familial factors, and the psychosocial context in neuropsychological studies of psychotic experiences.

### ARTICLE INFORMATION

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