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Late-life onset psychosis-like symptoms assessed in the Mild Behavioural Impairment framework are associated with impaired performance on the Stroop task

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ABSTRACT

Late-life onset psychosis and milder delusion-like ideation are known risk factors for cognitive decline and dementia. The Mild Behavioural Impairment (MBI) framework was developed to capture specific psychotic-like symptoms relevant to dementia prognosis in older adults. This study aims to investigate the cognitive deficits associated with MBI-psychosis and their implications for understanding the underlying mechanisms and potential treatment targets. The study recruited participants between November 2021 and July 2022 from the PROTECT study registry. Participants completed the Cambridge Gambling Task, Stroop, Trail Making, Paired Associates Learning, Verbal Reasoning, Digit Span and Self-Ordered Search. Psychotic symptom status was assessed using the Mild Behavioural Impairment Checklist (MBI-C), with participants categorized as MBI-psychosis if they or their study partner reported any psychotic symptoms. Out of 2,111 eligible participants invited, 417 consented to participate. There were no significant differences in age, sex, education level, or mental health history between the MBI-psychosis and No Psychosis groups. Participants with MBI-psychosis exhibited significantly worse performance on the Stroop task ($p=0.0002$, Cohen's $d=0.37$) compared to those without psychosis. There was also some evidence of impairment in verbal reasoning, though it did not reach significance after Bonferroni correction. No significant differences were found on other cognitive measures. This cross-sectional study provides insight into the cognitive deficits

associated with MBI-psychosis. The finding of impaired Stroop task performance in individuals with MBI-psychosis is noteworthy, as this deficit is commonly observed in earlier-life major psychotic disorders. Further research is needed to explore the neural underpinnings of these deficits and to determine whether they represent early markers of neurodegenerative disease or other factors.

Keywords: Mild Behavioural Impairment, psychosis, Stroop, Cambridge Gambling Task, executive function.

INTRODUCTION

Late-life onset psychosis and milder delusion-like ideation are established risk factors for cognitive decline and dementia, even in people with no prior history of psychotic disorders[1][2][3]. The Mild Behavioural Impairment (MBI) framework was developed to capture the specific spectrum of symptoms that are relevant to dementia prognostication in older adults[4][5]. When psychotic symptoms are described in this context, we refer to them here as MBI-psychosis (noting that we are not referring to a clinical disorder but milder changes in thoughts and perceptions). In addition to psychosis, MBI also captures the domains of apathy, affective symptoms, impulse dyscontrol and socially inappropriate behaviour. MBI-psychosis is the least common of the five MBI domains, present in 1-5% of cognitively normal people[6][7].

Risk of global cognitive impairment and incident dementia associated with MBI-psychosis is the highest of the five MBI domains[3]. This risk warrants a detailed understanding of the symptom profile, but studies are limited due to the fact that symptoms are uncommon (so large-scale screening is needed to identify people) or often framed in the context of psychiatric disorders.

Our online longitudinal study of community dwelling adults over 50 has MBI data from over 20,000 people and is to our knowledge the largest sample in the world with these measurements. In this sample, we have previously shown longitudinal changes in cognition associated with psychosis, but these studies were largely focused on memory[1][8]. While undoubtedly an important domain in the field of psychosis, it is not known if people with MBI-psychosis exhibit the broader range of cognitive deficits associated with psychosis in clinical contexts earlier in life. A detailed understanding of the cognitive substrates of MBI-psychosis will lead to a better understanding of the transdiagnostic mechanisms underlying symptoms, which may guide possible psychological treatment targets to mitigate risk of cognitive decline and perhaps the emergence of more severe psychoses in dementia.

Psychosis earlier in life is consistently associated with deficits in Trail Making, Stroop, and the Cambridge Gambling Task. However, performance on these established tests with respect to later-life emergent and persistent psychosis, i.e., MBI-psychosis, is not known[9][10][11].

Therefore, in this study we tested the hypothesis that participants with MBI-psychosis would exhibit impairment on each of these tests compared to participants without MBI-psychosis.

METHODS

Study period

Recruitment took place between November 2021 and July 2022.

PROTECT registry:

Participants were identified from the PROTECT study registry. Launched in 2015, PROTECT is an online study with the principal aim of determining risk factors for cognitive aging and dementia. People enrolled in PROTECT complete annual demographic, medical, mental health, and lifestyle questionnaires. They also complete an annual detailed cognitive test battery that focuses on domains pertinent to dementia risk (memory, attention, reasoning, and executive function)[12]. Informed consent to enrolling into PROTECT is obtained online and all participants give consent to be contacted for future research (Research Ethics Committee reference number 13/LO/1578). Participants may nominate a study partner who is required to know the participant well for at least 10 years. Upon enrolment into the PROTECT registry, participants confirm that they do not have a diagnosis of dementia, do have access to a computer and the internet, are age 50 years or older, and are able to read and write English.

Ethics

An additional ethical review and approval was obtained for this study, covering completion of the Cambridge Gambling Task which is not part of the core PROTECT study battery (University of Exeter College of Medicine and Health Research Ethics Committee, reference number: 19/11/231).

Measures

Demographic and medical history

Demographic data and medical history were collected by self-report questionnaire. Data from the PROTECT annual assessment closest to recruitment start were used. Self-reported history of diagnosis of any of the following psychiatric/mental health conditions was also recorded: depression, mania/bipolar depression, anxiety/generalized anxiety disorder, social anxiety disorder, agoraphobia, panic attacks, obsessive compulsive disorder, anorexia nervosa, bulimia nervosa, binge eating, schizophrenia, any other type of psychotic illness, personality disorder, autism spectrum disorder, attention-deficit/hyperactivity disorder, gambling and addiction. The presence of schizophrenia or any other psychotic disorder, addiction and gambling were used as exclusion criteria (see below) and the remaining were coded collectively as 'history of a mental health condition'.

MBI-psychosis

Psychotic symptom status was ascertained from the Mild Behavioural Impairment Checklist (MBI-C), which has been validated for online use. Both participants and their study partners provided ratings[4][6][13]. A total of 34 questions captures symptoms in five domains (mood, apathy, impulse dyscontrol, social inappropriateness, and psychosis). Each item is first rated as present or absent; if rated present, the severity of the item is then scored on a scale of 1 to 3.

To reflect MBI diagnostic criteria, the MBI-C is prefixed with the following instructions to participants (with wording amended accordingly for study partner ratings): "We would like to know if there have been any subtle changes in your behaviour such as changed interest in activities, altered mood, or impulsive behaviour." Answer options for the questions are as follows: "Yes: the behaviour has been present for at least 6 months (continuously, or on and off) and is a change from your longstanding pattern of behaviour. No: behaviour not present, or present for less than 6 months, no change from usual behaviour. Mild: noticeable, but not a significant change. Moderate: significant, but not a dramatic change. Severe: very marked or prominent, a dramatic change."

There are five MBI-C questions pertaining to psychosis; three questions cover delusion-type experiences, which includes overvalued ideas (paranoid, harm, and grandiose-type), and two cover hallucinations (visual and auditory). Ratings of participants and study partners had to be within 6 months of each other. Based on these ratings, two groups were created: MBI-psychosis and No Psychosis. Participants were classified as MBI-psychosis if they or their study partner rated any of the five psychosis items as present at their first visit. Participants were coded as No Psychosis if they scored zero on all five items on both participant and study partner ratings.

Cognitive tests

Cross-sectional cognitive tests results were drawn both from existing tests completed via participation in the PROTECT study and new testing specifically for the present study.

PROTECT Cognitive Test Package (CTP): Test results on Trail Making and Stroop were made available from PROTECT. For context we also included other tests which have been studied previously: Paired Associates Learning, Digit Span, Self-Ordered Search, Verbal Reasoning. Paired Associates Learning, Digit Span, Self-Ordered Search, Verbal Reasoning were introduced to PROTECT in 2015, while the Trail Making and Stroop were introduced in 2019.

Cambridge Gambling Task (CGT, Cambridge Cognition Ltd.): This cognitive task evaluates decision-making and risk-taking behavior in a non-learning context. On the screen, participants are presented with a row of ten boxes, some colored red and others blue. The ratio of red to blue boxes changes between stages, but there is always one box containing a yellow token. The objective is to 'bet' on whether the yellow token is in a red or blue box. To make their choice, participants use the 'Red' and 'Blue' buttons located at the bottom of the screen.

Participants begin with 100 points and decide how many of these points to wager on their choice. A circle at the center of the screen displays the current bet value, which can either incrementally increase or decrease, depending on the chosen task variant. When this circle reaches the desired proportion of their score to bet, participants press the button, and their points are either added or deducted from their total score, based on the correctness of their choice and the actual location of the token. The following six CGT outcome measure were analysed in this study: 1. Decision making quality. 2. Risk adjustment. 3. Delay aversion. 4. Risk taking. 5.Median time to decision. 6. Overall proportion of points bet.

Inclusion/exclusion criteria

The PROTECT database was screened for participants meeting the following criteria (these data were available via PROTECT and were not collected during the present study).

Inclusion criteria

Active participant in the PROTECT study in the two years prior to the start of the study period (to ensure only those who are engaged in the platform are approached).

- Aged 50 or over.
- Have reported yes to experiencing any of questions 5.1, 5.2 or 5.3 on the Mild Behavioural Impairment Checklist questionnaire or no to all of these questions (this will determine the experimental groups).
- Has nominated a study partner who has also answered the above questions.
- Self and study partner MBI-C ratings are completed within one year of each other.

Exclusion criteria

- Diagnosis of dementia or neurodegenerative disease.
- Diagnosis of stroke or Mild Cognitive Impairment.
- Diagnosis of psychotic disorder (including schizophrenia).
- History of problem gambling.
- History of addiction to any substance.

Target sample size

Our sample of size of 417 has >80% power to detect a standardised mean difference (Cohen's d) of at least 0.4 between the MBI-psychosis and No Psychosis groups at a Bonferroni-corrected p=0.004 (0.05/12; the eight primary cognitive test comparisons plus the four secondary cognitive tests).

Recruitment procedure

Consent was obtained online within each eligible participant's account on the PROTECT UK platform. Briefly:

1. Eligible participants were sent an email explaining that they are suitable for a new study and that the study documents are available to review in their account.

2. Participants then enter the PROTECT account where they can view the Participant Information Sheet (PIS). The information sheet is presented in a printable format, and study participants were required to tick a box to confirm they had read and understood the relevant document.
3. Participants were then presented with a new website page with each consent item in the Informed Consent Form (ICF). They had to tick each item individually which activates a button to allow them to proceed to a new website page.
4. On the new website page, participants then had to tick a further box to confirm they consent to take part in the study which activates a button that they must select to continue. This process ensures consent cannot be given in error.
5. Consents were time- and date-stamped electronically and stored on the PROTECT study database, linked to study ID and pseudo-anonymised to allow for linkage to personal details in the event this information is required for future contact.
6. Once consent was given, participants were automatically sent a URL which connected them with Cambridge Cognition's website where they completed the CGT.

Eligible participants were grouped in the following: No Psychosis, self-rated MBI-psychosis only, proxy-rated MBI-psychosis only or both self- and proxy-rated MBI-psychosis. Email invitations were randomly sent out in batches with an approximately equal distribution across four groups, and on age, sex and education level and mental health history to balance recruitment.

Analysis

All cognitive test scores were centered to a mean of zero and standard deviation of 1 before analysis. The mean scores on each of the 6 PROTECT cognitive tests and the 6 CGT outcomes were compared between MBI-psychosis and No Psychosis. CGT Overall Proportion Bet, CGT Risk Taking and Verbal Reasoning were all normally distributed so a independent samples t-test was used. The Mann-Whitney U test was used for all remaining cognitive tests due to evidence of non-normal distributions across. The Kruskal-Wallis test was used for self and proxy group comparisons for the non-normally distributed tests and one-way ANOVA was used for normally distributed tests. Correlations between total MBI-psychosis score (the sum score of the five psychosis items ranging from 0 to 15) and cognitive test scores were done using the Spearman's rank correlation test. Effect sizes are expressed as Cohen's *d* and Bonferroni-corrected p=0.004 was used.

RESULTS

2,111 recruitment invitations were sent to eligible participants between November 2021 and July 2022. Of these, 417 consented to the study online, completed the CGT task and had recent PROTECT cognitive test data. Participant characteristics are shown in Table 1, there were no statistically significant differences in age, sex, education level or mental health history between the MBI-Psychosis and No Psychosis groups.

Table 1. *Participant characteristics.*

	No Psychosis		MBI-Psychosis		P
N	178		239		
Sex (n, %)					
Male	48	27	57	24	0.5
Female	130	73	182	76	
Age (mean, SD)	68	6.8	68	6.4	0.6
Education Level (n, %)					
GCSE (left school at 16	21	12	28	12	0.6
A-Level (left school at 18)	18	10	27	11	
Voctional Qualification	25	14	45	19	
Undergradute Degree	66	37	91	38	
Postgraduate Degree	37	21	39	16	
Doctorate	11	6	9	4	
History of Non-Psychosis Any Mental Health Condition (n, %)					
No	99	56	121	51	0.4
Yes	79	44	118	49	

Cognitive testing

Results of the primary analysis comparing MBI-psychosis to No psychosis are shown in Table 2. The MBI-psychosis group had significantly worse performance on the Stroop task (p=0.0002, Cohen's *d*=0.37). There was evidence of a smaller impairment on verbal reasoning but this did not pass Bonferroni correction. There were no other significant differences across any of the other outcomes. There was also a statistically significant but modest correlation between sum score across the five MBI-C psychosis items (ranging from 0 to 15) and scores on these two tests (Stroop: rho=-0.18, p=0.0001; Verbal Reasoning: rho=-0.13, p=0.006).

Table 2. *Cognitive test scores, MBI-psychosis vs no psychosis.*

	No Psychosis		MBI-Psychosis		Cohen's d	95% CI		P
n	178		239					
CGT (mean, sd)								
Decision Making Quality	0.08	0.98	-0.06	1.01	0.14	-0.33	0.06	0.1
Risk Adjustment	-0.01	0.95	0.01	1.04	0.01	-0.18	0.21	0.7
Delay Aversion	-0.06	1	0.05	1	0.11	-0.09	0.3	0.5
Risk Taking	0.04	1	-0.03	1	0.06	-0.26	0.13	0.5
Median Time to Decision	-0.06	1	0.04	1	0.1	-0.09	0.3	0.6
Overall Proportion Bet	0.05	1	-0.04	1	0.08	-0.28	0.11	0.4
PROTECT CTP (mean, sd)								
Digit Span	0	1	0	1	0.01	-0.19	0.2	0.6
Paired Associates Learning	-0.04	1	0.03	1	0.07	-0.13	0.26	0.5
Verbal Reasoning	0.14	1	-0.11	1	0.25	0.06	0.45	0.01
Self-Ordered Search	0.04	1	-0.03	1	0.06	0.13	0.26	0.1
Stroop	0.21	1	-0.16	1	0.37	0.18	0.57	0.0002
Trail Making	-0.08	1	0.06	1	0.14	0.06	0.33	0.07

Post-hoc, we then explored whether there were differences between respondent types, results from this analysis are displayed in Table 3 along with the participant characteristics split by

group. Two subgroups were created from the MBI-Psychosis group, one where symptoms were rated present by self-report and absent on proxy report and one where symptoms were rated present on proxy report and absent on self-report. We excluded the group where both self and proxy were present (n=43) as our primary interest was differences between the two. The No Psychosis reference group remained the same (i.e., both self and proxy ratings were 0). In this analysis there were no between group differences on Verbal Reasoning, however performance on the Stroop task was worse in both self only and proxy only groups in comparison to the No Psychosis group (H=11.85, df=2, p=0.003).

Table 3. *Participant characteristics, Stroop and verbal reasoning scores by self and proxy-rated MBI-psychosis.*

	No Psychosis		MBI-Psychosis Self Only		MBI-Psychosis Proxy Only		P
n	178		85		111		
Sex (n, %)							
Male	48	27	29	34	20	18	0.04
Female	130	73	56	66	91	82	
Age (mean, sd)	68	6.8	68	7	68	5.7	0.78
Education Level (n, %)							
GCSE (left school at 16	21	12	8	9	14	13	0.76
A-Level (left school at 18)	18	10	11	13	9	8	
Voctional Qualification	25	14	13	15	22	20	
Undergradute Degree	66	37	38	45	39	35	
Postgraduate Degree	37	21	12	14	22	20	
Doctorate	11	6	3	4	5	5	
History of Non-Psychosis Any Mental Health Condition (n, %)							
No	99	56	45	53	63	57	0.86
Yes	79	44	40	47	48	43	
Cognitive Tests							
Verbal Reasoning	0.14	1	-0.11	1	-0.05	1	0.09
Stroop	0.21	1	-0.15	1	-0.14	1	0.003

DISCUSSION

In this cross-sectional study, we set out to gain a detailed understanding of the cognitive substrates of MBI-psychosis. We did this by comparing performance on the Cambridge Gambling Task, Trail Making and Stroop.

MBI as a broad label (i.e., any of the five domains) is reliably associated with dementia and cognitive decline, as shown by a number of observational studies[14][15][16][17][18]. This study extends these findings to the specific domain of psychosis and a broader range of cognitive domains. People with MBI-psychosis performed worse on the Stroop task than those with No Psychosis. Similar deficits were observed for self-reported and proxy reported MBI-psychosis, reflecting the importance of capturing information on as wide a range of sources as possible[1][19][20]. Some evidence of worse performance on Verbal Reasoning was also found. We suspect a smaller effect size made our study underpowered to detect a difference on this test however we note it here because it is consistent with a previous larger study of which our sample

was a part[8]. There were no differences on any of the other measures. There was no relationship between MBI-psychosis and any measure on the CGT, this in contrast to deficits on this test being observed in earlier life psychoses[9][11] This study was only powered to detect a medium effect size so it is possible that a small effect is present and that this would be observed in larger studies. Accordingly, it may be the case that deficits in impulse control, decision making and risk taking are only associated with more severe psychoses, while processing speed and selective attention (as measured by Stroop) are more widely observed with a larger effect size across the psychosis spectrum.

Studies of late-life psychosis-like symptoms (especially in non-clinical samples) are uncommon and to our knowledge this is the first demonstration that deficits on the Stroop task, which are robustly seen in major psychotic disorders earlier in life are also present in the mild, later-life onset syndrome of MBI-Psychosis[10]. Further studies of the neural correlates of this finding are warranted however it is possible that the deficits observed here reflect impaired response inhibition, which is thought to be a key cognitive substrate of delusional ideation in earlier life psychoses.

While there is evidence linking MBI-psychosis to incident dementia, we do not know anything about the aetiology of the MBI-psychosis in this sample. Further research should incorporate AD biomarkers to help elucidate in whom the symptoms represent sequalae of neurodegenerative disease and whether our findings linking Stroop still hold. Psychosis in syndromic dementia due to AD is associated with a significantly worse disease course so targeting the emergence of psychosis early on in the neurodegenerative cascade could bring considerable patient benefit later. Indeed, just as cognitive deficits on Stroop are seen in younger people at high risk of psychosis[21], it would be interesting to explore whether the same applies to people at risk of psychosis in Alzheimer's disease.

The principal limitations of this study are the online format, which entails remote unsupervised completion of questionnaires and cognitive tests. While this could lead to inaccuracies, people reporting MBI-psychosis are relatively few (as symptoms are rare) and hard to reach as they may not be in contact with clinical services.

In summary, we show for the first time links between MBI-psychosis and impaired Stroop performance, which may reflect response inhibition, a key cognitive substrate of delusional ideation.

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Conflicts of interest/Competing interests: Adam Hampshire is owner and director of Future Cognition Ltd., a software company that produces bespoke cognitive assessment technology and that was paid to produce cognitive tasks for PROTECT.

Availability of material:
The data of this experiment can be found at https://doi.org/10.17633/rd.brunel.24442468

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