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Validation of a novel Psychosis-Implicit Association Test (P-IAT) as a diagnostic support tool

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ABSTRACT

Despite significant advances in early-intervention services for psychosis, delays in identifying patients continue to impede the delivery of prompt and effective treatments. We sought to develop and preliminarily validate a self-administered psychosis implicit association task (P-IAT) as a screening and diagnostic support tool for identifying individuals with psychotic illness in community settings. The P-IAT is a response latency task, designed to measure the extent to which individuals implicitly associate psychosis-related terms with the "self." The P-IAT was administered to 57 participants across 3 groups: healthy controls (N=19), inpatients hospitalized with active psychosis (N=19), and outpatients with psychotic disorders (N=19). Mean D-scores (the output of the task) differed significantly between the illness groups and healthy controls (Mann-Whitney U=138, $p<.001$). A receiver operating curve was plotted to assess the performance of D-scores in predicting a psychosis diagnosis, yielding an area under the curve of 0.81. When participant D-scores exceeded -0.24, the test achieved a specificity of 100% (sensitivity: 47%), with all 18 participants scoring above this threshold belonging to the illness groups. The discriminant performance of the P-IAT suggests its potential to augment existing screening instruments and inform referral decision making, particularly in settings with limited access to specialist providers.

1. Introduction

As there are currently no objective tests or biomarkers that can confirm a diagnosis of psychosis (Kapur et al., 2012), the diagnostic assessment for psychotic illness in clinical care settings relies heavily on non-standardized interviews and patient self-report (Fusar-Poli et al., 2016). Correctly diagnosing psychosis often requires time-intensive nuanced evaluations that are most effectively conducted by clinicians with extensive formal training and expertise (Griswold et al., 2015; Kline et al., 2015; McDonald et al., 2019; Silverman et al., 2015). Prior work has demonstrated that individuals with first episode psychosis often have several clinical contacts before they receive accurate diagnoses and effective treatment (Birchwood et al., 2013; Cabassa et al., 2018; Marino et al., 2020). While many factors likely contribute to these findings, the difficult nature of eliciting psychotic symptoms from patients coupled with the relative scarcity of specialist psychiatric providers who can readily conduct diagnostic interviews (Jacob et al., 2007; Satiani et al., 2018) undoubtably complicate pathways to care for individuals with psychosis. These avoidable treatment delays have immediate adverse effects on the quality of life of individuals with psychotic illness and are associated with potential danger to patients and those around them (Addington et al., 2015a; Fusar-Poli et al., 2013; Marshall et al., 2005; Nielssen et al., 2012). Thus, the development of standardized self-administered psychosis assessment instruments that can be employed in the absence of specialist psychiatric providers would represent a valuable advance.

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To date, all available self-administered screening and diagnostic assessment instruments for psychosis rely heavily on the subjective self-report of patients. While self-administered instruments such as the PRIME Screen (Miller et al., 2004) or the Brief version of the Prodromal Questionnaire (PQ-B) (Loewy et al., 2011) have proven useful for screening purposes (Addington et al., 2015b), there has long been hesitation in employing self-report instruments in psychosis due to concerns that anosognosia may affect their validity. Patient-administered assessment instruments that are insensitive to insight, and can reliably provide useful diagnostic information, offer the potential to enhance current assessment models and improve pathways to care in first episode psychosis.

The testing of implicit cognition through the Implicit Association Test (IAT) has been widely employed to measure individual biases and preferences without relying on the subject's introspective awareness or insight (Nock et al., 2010; Nosek et al., 2007; Tello et al., 2020). In the two decades since it was first introduced, the IAT has garnered considerable interest in the social psychology literature as a means measure implicit biases related to sensitive topics such as race, gender, and age, where social desirability bias is likely to affect explicit self-report assessments (Glenn et al., 2017; Greenwald et al., 2003). While the degree to which the race or ethnicity IAT scores are useful in predicting behavior at the individual level remains the subject of considerable debate (Greenwald et al., 2015; Oswald et al., 2015, 2013), various adaptations of the IAT continue to be explored as a means to capture information that may be inaccessible to traditional self-report methods. In clinical research settings, the IAT has been adapted and utilized as a predictive tool in evaluating individuals at risk for engaging in suicidal and self-harm related behaviors, where purposeful concealment and limited insight affect the validity of self-report approaches (Glenn et al., 2017; Kene, 2017; Millner et al., 2019; Nock and Banaji, 2007; Tello et al., 2020). A wide range of IATs covering several topics have been made available to the public at https://implicit.harvard.edu/implicit/.

For the purposes of this study, the Psychosis-IAT (P-IAT) was developed collaboratively by investigators at Harvard University (Massachusetts, US) and The Zucker Hillside Hospital of Northwell Health (New York, US) in hopes that the test could reliably yield diagnostic information while being effectively insensitive to individuals' insight into illness. This study was designed to assess the potential utility of testing implicit cognition to gather useful diagnostic information about individuals with psychotic illness, a key first step in developing the P-IAT as a screening and diagnostic decision support tool. In order to assess the performance of the P-IAT we administered the task to a sample consisting of individuals who had been diagnosed with psychotic illness and healthy controls.

We hypothesized that subjects in the psychotic illness group would more readily associate psychosis-related stimuli with the "self" when compared to HC's. We further hypothesized that the strength of this association would be greater as the degree of acute psychotic symptom severity increased. Finally, we sought to evaluate the discriminant performance of the test output measure in differentiating subjects with primary psychotic disorders from HC's.

2. Methods

2.1. Participants

Participants were recruited from psychiatric clinical services at the Zucker Hillside Hospital (New York, US) from 2015 to 2019. Age-matched HC's were recruited by telephone outreach from the Zucker Hillside Hospital database of healthy control research volunteers. Inclusion criteria for the illness groups included: ages 18-65 years, chart diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, or schizophrenia spectrum disorders according to DSM-5 diagnostic criteria. Diagnoses of participants were obtained from patient medical records and confirmed with participants' primary psychiatric providers. Chart diagnoses were used in order to better approximate real-world clinical settings. All BPRS ratings were administered by trained research staff before subjects began the P-IAT. Exclusion criteria included: diagnosis of autism spectrum disorders, pervasive developmental disorder, estimated IQ < 70 based on history or clinical assessment, and current chart diagnosis of substance-induced psychotic disorder. Subjects satisfying the above criteria, were enrolled into one of two illness groups: inpatient or outpatient, depending on which care setting the participants were in at the time of consenting. To be eligible for the inpatient psychosis group, subjects were required to be currently admitted to an inpatient psychiatric unit and be rated as having a score ≥ 4 on one of the following Brief Psychiatric Rating Scale (BPRS) items (Woerner et al., 1988): grandiosity, suspiciousness, hallucinatory behavior, or unusual thought content. For the outpatient group, participants were required to be currently following in an outpatient setting and score no higher than 3 on any of the aforementioned BPRS items. These differential symptom severity criteria between the outpatient and inpatient groups were designed to assess whether the P-IAT was sensitive to acute symptom severity. The Feinstein-Northwell IRB approved all recruitment and study procedures.

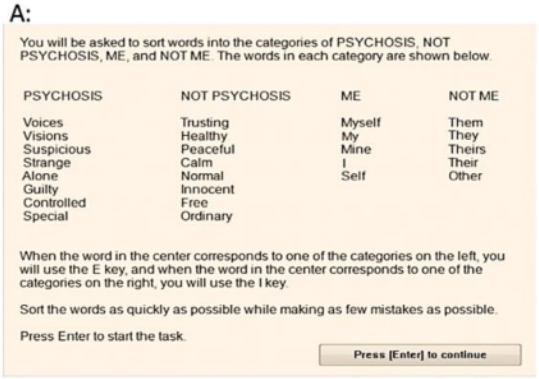
2.2. Assessment

The IAT is a computer-administered response latency test that relies on the assumption that subjects more readily associate related concepts as compared to less related concepts (Greenwald et al., 1998). The ease of association between conceptual constructs of interest can then be measured by recording an individual's differential response latencies observed across groupings of various concepts of interest. For example: a subject would be expected to have a longer response latency when the task requires the pairing of "insects" and "pleasant," then when the subject is prompted to pair "flowers" and "pleasant" (Greenwald et al., 1998). Similar to previously employed clinical IATs, the P-IAT sought to measure the degree to which participants associated psychosis-related stimuli with the self. As there had been no prior IAT developed for use in psychosis, the psychosis-related stimuli selected for use in the P-IAT (see Fig. 1A) were based on the best guesses of the authors who collectively had considerable experience working with individuals with psychosis and developing IATs for use in other clinical populations. Participants were accompanied by research personnel as they completed the P-IAT on a designated laptop computer. The test took roughly 10 minutes to complete. Fig. 1 presents an overview of the P-IAT structure and layout.

The test began with an instruction prompt presented on screen. A screen shot of the instruction prompt, which included a key linking the words (stimuli) participants would be asked to sort with their correct category pairings, is shown in Fig. 1A. The P-IAT is comprised of seven "blocks" which have been outlined in Fig. 1B. For each block, participants are asked to sort a sequence of words, which appear one at a time at the center of the screen, into different concept categories which appear at the top left and top right of the screen. The first block asks subjects to sort words based on their belonging to "Not Psychosis" or "Psychosis" categories. In the second block, words are sorted as belonging to "Not Me" or "Me" (illustrated in Fig. 1C). The 3rd, 4th, 6th and 7th blocks are the scored blocks, while blocks 1, 2, and 5 are practice blocks to allow subjects to develop familiarity with the task. In the scored blocks, categories (Psychosis, Not Psychosis, Me, and Not Me) are combined into "Not Psychosis/Not Me" and "Psychosis/Me" as shown in Fig. 1D. The fourth block recapitulates the third. Following the fourth block, "Psychosis" and "Not Psychosis" are moved to alternate sides of the screen. For blocks 6 and 7, "Psychosis/Not Me" and "Not Psychosis/Me" are paired (the inverse of blocks 3 and 4).

The output of the P-IAT is known as a "D-score," it is subject-level effect size measure that is conceptually similar to the Cohen's d. The P-IAT D-score reflects the degree to which subject's favor associations between the "self" and psychosis-related terms. IAT scoring

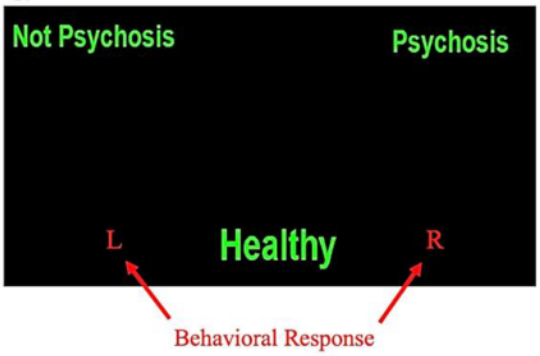
A:



B:

Block Number	Left Category	Right Category	Trials (N)	Output
1	Not Psychosis	Psychosis	20	Practice
2	Not Me	Me	20	Practice
3	Not Psychosis/Not Me	Psychosis / Me	20	Scored
4	Not Psychosis/Not Me	Psychosis / Me	40	Scored
5	Psychosis	Not Psychosis	20	Practice
6	Psychosis/Not Me	Not Psychosis/Me	20	Scored
7	Psychosis/Not Me	Not Psychosis/Me	40	Scored

C:



D:

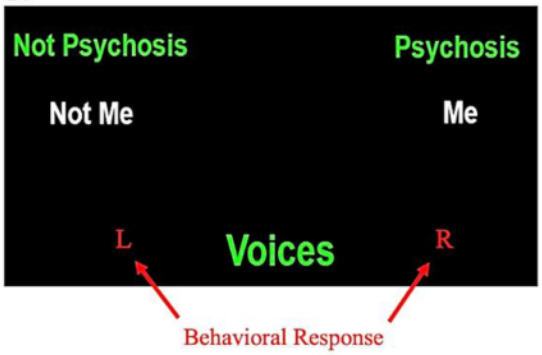


Fig. 1. Psychosis-IAT Overview. 1A. Instruction prompt; 1B. Structure of the P-IAT's seven blocks; 1C. Practice block layout illustration (Block 1); 1D. Scored block layout (Block 3).

recommendations and the development of the D-score have been explained in detail by Greenwald et al.,[22]. Briefly, a separate D-Score is calculated for each block pairing (block 3 and 6 are paired, and block 4 and 7 are paired). The first block in each pair tests a Not Psychosis/Me pairing while the second block in each pair tests a Psychosis/Me category pairing (illustrated in Fig. 1B). For each pair of blocks, a D-score is calculated by subtracting the mean response times recorded in the later block (e.g., block 6 – block 3) divided by the pooled standard deviation of response times across both blocks. The two D-scores obtained from each of the two block pairs are then averaged to yield a final summary D-score. D-scores range from -2.00 to 2.00. For the P-IAT, more positive D-scores correspond to stronger associations between the "Self" and "Psychosis," while more negative D-scores reflect stronger associations between the "Self" and "Not-Psychosis." Participants were compensated $20 if they completed the P-IAT. Readers interested in using the P-IAT in their research can contact the corresponding author (MKIRSCH@-NORTHWELL.EDU). The P-IAT will be made available at no cost to them upon request.

2.3. Data analysis

All statistical analyses were conducted with Statistical Package for Social Sciences Version 26 (SPSS, Chicago, Illinois, USA). The P-IAT has been designed to "flag" results when there are concerns about the integrity of a subject's responses. For the purposes of this study, only subjects assigned fast response flags were excluded from analysis. Fast flags were triggered if a subject responded to a stimulus in less than 400ms in greater than 25% of trials within a block, or greater than 10% of all the trials across the entire test. Responding in under 400ms, particularly in more than 10% of trials, is likely to indicate a participant is rapidly entering responses without attention to correctness of inputs[22, 23]. Prior to conducting analysis, we reviewed all data for fast flags and excluded those participants from analysis. One subject from each of the 3 groups (HC, inpatient, outpatient) recorded fast flags, thus these 3 subjects were excluded from analysis. This left 19 subjects in each group for our final analysis sample. Statistical significance cut-off was set at $p \leq 0.05$

To test our first hypothesis, which predicted that subjects in the psychotic illness groups would more readily associate psychosis-related stimuli with the "self" when compared to controls, mean D-scores in the three groups were compared using one-way analysis of variance (ANOVA). D-scores in each group were assessed for normality using the Shapiro-Wilk test. As the outpatient group D-scores were found to be non-normally distributed, post-hoc pair-wise testing was performed with the Mann-Whitney U test. To assess the diagnostic discriminant performance of the P-IAT D-score in predicting chart diagnosis of psychotic illness, a receiver operating characteristic (ROC) curve was plotted and the fitted area under the curve was recorded. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated at various D-score cut-off values to identify optimally performing diagnostic scoring thresholds. To test our second hypothesis, which predicted that patients with a greater positive symptom severity would show larger self-psychosis associations than would patients whose symptoms were less severe, we conducted linear regression analysis, restricted to the illness groups, in order to determine if individual D-scores were positively associated with overall BPRS score.

3. Results

Seventy-two patients consented to participate. Fifteen were excluded from the study for the following reasons: 7 were consented but did not meet BPRS criteria or had missing BPRS data, 3 were too ill to complete the task, 1 withdrew consent, and 1 was excluded as a result of diagnostic uncertainty. Three subjects completed the task but were excluded from analysis for fast flags, which are discussed in more detail in the

section below on data analysis. In all, 57 participants were included in analysis corresponding to 19 participants in each of the 3 groups (healthy controls, inpatients, and outpatients). Baseline characteristics of the 57 subjects included in analysis are presented in Table 1.

Mean D-scores were calculated for HC [Mean D-score: -.80 (standard deviation: 0.34)], outpatients [-.30 (.56)], and inpatients [-.17 (.52)], and are graphically represented in Fig. 2.

One-way ANOVA for mean D-scores for the three groups showed significant between-group differences (F= 9.12, p<.001). Pairwise testing of group mean D-scores using the Mann-Whitney U test yielded significant mean differences between HC and inpatients (U= 56, p<.001), HC and outpatients (U=82, P=0.003), and HC vs the combined illness group comprised of inpatients and outpatients together (U= 138, p<.001). There was no significant difference detected between mean D-scores in the inpatient and outpatient groups. A ROC curve was plotted to further evaluate the discriminant performance of participant's D-scores in differentiating individuals in the psychosis groups from those in the control group and yielded an area under the curve (AUC) of 0.81 (95% confidence interval: 0.70-0.92, standard error = .056, p < .001). When employing a D-score cut off of greater than -0.24, the test achieved a specificity of 100%, with all 18 subjects above this cutoff having a psychotic disorder diagnosis. The sensitivity associated with the > -0.24 D-score cutoff was 47%. The sensitivities, specificities, PPV, and NPV associated with various D-score cutoffs are presented in Table 2.

To assess the relationship between D-scores and positive symptom severity as measured by the BPRS, linear regression was performed, but no significant association was found ($R^2 = 0.05$, B = 0.111, p = 0.177).

4. Discussion

In designing the P-IAT we sought to develop an objective, self-administered, diagnostic support tool for use in psychosis. The findings from this first validation study support the notion that the P-IAT can provide useful diagnostic information in the clinical assessment of psychotic individuals. In line with our expectations, between group differences in D-scores demonstrated that subjects with psychotic disorders more readily associated psychosis-related stimuli with the "self" when compared to healthy controls. The discriminant performance of the P-IAT D-score, reflected in the ROC-AUC of 0.81, is highly encouraging, yet the finding that most supports the further development of the P-IAT as a diagnostic support tool was that when individual D-scores were greater than -0.24, the test yielded 100% specificity in identifying psychotic individuals, with a corresponding sensitivity of 47%. To put these findings into context, the PQ-B is among the most studied and best performing self-administered screening instruments currently employed in screening for psychosis and clinical high-risk syndrome. The PQ-B, when a total score cut off of ≥ 3 is employed, demonstrates high sensitivity (89%) for differentiating individuals with acute psychosis or clinical high-risk psychosis status from those with no psychotic disorder, however the associated specificity at that cutoff is 58% (Addington et al., 2015b; Loewy et al., 2011). Thus, a remaining challenge in implementing a successful screening and triage program is to develop or adapt these scales to provide higher specificity and PPV to enable non-specialist providers to have greater confidence in decision making related to initiating treatment or facilitating appropriate referrals. The results of our study suggest that the P-IAT can serve as a valuable component of a multistep screening process whereby individuals who screen positive with the PQ-B, or similarly sensitive instrument, can then be subject to higher specificity testing with an instrument such as the P-IAT in order to generate a ranked priority order to drive referral decision making. Importantly, the PQ-B and P-IAT are both self-administered instruments and if combined, would take approximately 15 minutes to complete. Thus, these two instruments can be easily packaged in digital format and administered on smart phones or computers that can automate the scoring process and employ decision support algorithms to guide non-specialist health professionals in clinical decision making about treatment initiation and referrals to specialty care services.

The negative regression findings failed to support our second hypothesis that the P-IAT D-score would differentiate between individuals with a greater degree of acute positive symptoms from those with lesser severity symptoms. This suggests that the P-IAT does not appear to be particularly sensitive to symptom severity and is therefore unlikely to be useful in tracking treatment response or illness severity over time. Though counter to our expectations, this lends further support to the notion that the test has potential utility as a screening tool, considering that in help-seeking populations one would expect to observe a fair degree of variability in symptom severity, thus had the P-IAT been more sensitive to illness severity, it is likely to have been less successful in discriminating those with individuals with lower symptom severity burden from controls. The observed stability of the P-IAT's discriminant performance regardless of symptom severity in conjunction with the fact that the the IAT is relatively difficult to fake (Banse et al., 2001; Cvencek et al., 2010; Nock and Banaji, 2007) as compared to self-report, these negative findings additionally raise the prospect of using the P-IAT as a tool to better identify individuals who are falsely representing themselves as having psychotic disorders for secondary gain. Malingering is associated with substantial financial costs (Chafetz and Underhill, 2013) and represents a significant threat to the integrity of clinical trials evaluating new treatments (Devine et al., 2013; McCann et al., 2015; Resnik and McCann, 2015). The field of psychiatry, owing to its near exclusive reliance on patient self-report, is particularly vulnerable to malingering thus developing objective tools that can differentiate between individuals who are genuinely endorsing symptoms from those who are deceitfully doing so for secondary gain would represent a valuable advance. Though it is premature to suggest the P-IAT would be useful in countering the effects of deception and malingering, this application of the P-IAT appears to be a promising avenue for further research.

Table 1
Sociodemographic and clinical characteristics of the sample.

Variable	HC (N=19)	Outpatients (N=19)	Inpatients (N=19)
Age in years M (SD)	28.2 (10.2)	23.8 (5.6)	30.1 (12.0)
Sex (% male)	8 (42%)	11(58%)	10 (53%)
Race N (%)			
White	12 (63%)	6 (32%)	5 (26%)
Black	4 (21%)	7 (37%)	6 (32%)
Asian	2 (10%)	5 (26%)	5 (26%)
Other	1 (5%)	1 (5%)	3 (16%)
Employment Status N (%)			
Unemployed	2 (10%)	6 (32%)	8 (42%)
Employed	16 (84%)	4 (21%)	6 (32%)
Student	1 (5%)	9 (47%)	5 (26%)
Diagnosis N (%)			
Schizophrenia	NA	7 (37%)	10 (53%)
Schizoaffective Disorder	NA	2 (37%)	5 (26%)
Schizophreniform disorder	NA	1 (5%)	1 (5%)
Psychotic disorder NOS	NA	9 (47%)	3 (16%)
Psychopathology			
BPRS Total M (SD)	NA	25.5 (5.6)	42.5 (8.8)
BPRS Inclusion Criteria Domains M (SD)			
Grandiosity	NA	1.1(0.3)	2.9(2.0)
Suspiciousness	NA	1.4(0.7)	3.8(1.9)
Hallucinatory Behavior	NA	1.2(0.6)	3.5(2.1)
Unusual Thought Content	NA	1.2(0.4)	4.7(1.1)

HC: healthy controls; M: mean; NA: not applicable; NOS: not otherwise specified; SD: standard deviation.

4.1. Limitations

There are several limitations to our study. First, this was a preliminary validation study thus the sample size was relatively small and

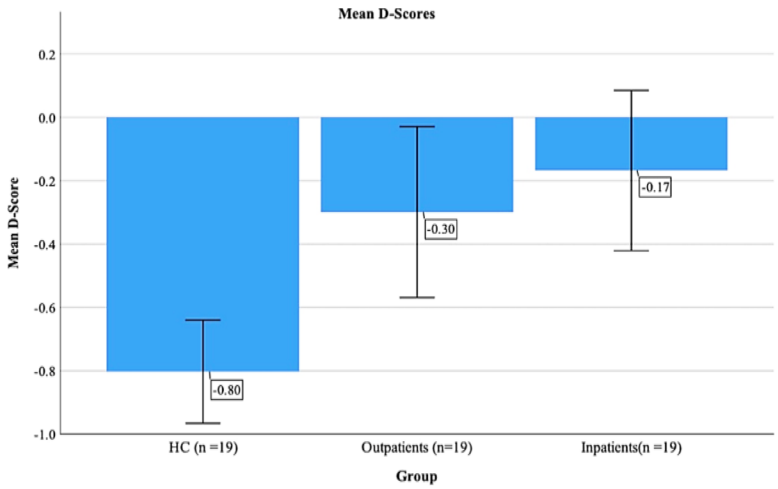


Fig. 2. Mean D-scores by study group.

Table 2
Classification statistics for P-IAT predicting chart diagnosis of psychosis.

Positive Test D-Score If ≧	Sensitivity	Specificity	PPV	NPV
-1.14	*1.00*	*0.21*	*0.72*	*1.00*
-0.88	*0.89*	*0.42*	*0.76*	*0.67*
-0.71	*0.82*	*0.58*	*0.78*	*0.59*
-0.48	*0.63*	*0.84*	*0.89*	*0.53*
-0.24	*0.47*	*1.00*	*1.00*	*0.49*
0.00	*0.26*	*1.00*	*1.00*	*0.40*

NPV: negative predictive value; PPV: positive predictive value.

used healthy controls as a comparator. As the results of our study appear particularly promising for the screening application of the IAT, future work using the P-IAT would be better suited to evaluate the screening utility of the test in larger help-seeking samples that include active comparators with other psychiatric illnesses as opposed to healthy controls. Similarly, our sample was comprised of a 2:1 ratio of subjects with psychotic disorders to controls. While this may have led to over-performance of the test in our study, it is quite reasonable to expect that if the P-IAT were implemented as a follow up to a self-report psychosis screening instrument that the subsequent sample, being comprised of positive screens, would be similarly enriched with psychosis diagnoses. Furthermore, all the illness group study participants were in treatment (outpatient or inpatient) at the time the test was administered, and thus it remains unclear if the psychometric properties of the P-IAT would be replicable if the test were administered to individuals with psychosis prior to their ever engaging with psychiatric treatment. This is particularly relevant when considering the potential screening use case for this iteration of the P-IAT, as participants in this study were asked to sort stimuli into thematic categories labelled as "Psychosis" and "Not Psychosis." It is therefore plausible that the participants in our study had already developed some familiarity with the term psychosis, and that this may have impacted their performance on the test. Conversely, it is similarly plausible that having foreknowledge about the meaning of psychosis had little effect on the observed results, and the observed effects resulted from the associations participants were making between the self-related categories (i.e., "Me" and "Not Me") and the psychosis-related stimuli (e.g., voices, suspicious, etc.). As the scored blocks all contain combined category pairings such as "Psychosis/Me" or "Not Psychosis/Not Me," the degree to which the variance in D-scores between groups in our study was affected by this remains an open question, as this study was not adequately powered to assess the relative discriminant performance of individual categories or stimuli. These limitations make it difficult to determine the degree to which our study findings would be generalizable to clinical high risk or pre-treatment first episode psychosis populations. Further work, assessing the performance of the P-IAT in these populations will be necessary before making a judgement about whether the P-IAT can be of utility as a screening tool in clinical high risk or pre-treatment illness populations. Future work should consider alternative category names to "Psychosis" and "Not Psychosis," or a slight modification to the introductory prompt, that can include a brief definition of the term psychosis.

4.2. Conclusion

In conclusion, the findings from this study suggest that the P-IAT can offer useful diagnostic information that can be used to augment existing screening instruments and supplement clinical information to inform treatment and referral decision making processes, particularly in treatment settings with limited access to specialist providers. Further refinement and development of the P-IAT is warranted by the results of this study, which indicate that the P-IAT is likely to be most informative as a clinical decision support tool when paired with a self-report symptom screening instrument.

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Author contributions

M.A.K. served as the principal investigator of the study, oversaw data collection, analyzed the data, and composed the manuscript. J.M.K., L.V. L., M.K.N. developed the P-IAT, contributed to the study design, and assisted with the composition and editing of the manuscript. A.J.M. contributed to the analysis of the data and composition of the manuscript. A.F.A. and R.d.F. collected data, administered the P-IAT to participants, and contributed to the composition and editing of the manuscript.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of Competing Interest

The authors have nothing to declare.

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