Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria
Brazilian Psychiatric Association
Fully open access
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(article published as accepted)

Original Article

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http://doi.org/10.47626/1516-4446-2026-5002

Submitted: 30-Apr-2026

Accepted: 28-Sep-2026

This is a preliminary, unedited version of a manuscript that has been accepted for publication in the Brazilian Journal of Psychiatry. As a service to our readers, we are providing this early version of the manuscript. The manuscript will still undergo copyediting, typesetting, and review of the resulting proof before it is published in final form. The final version may present slight differences in relation to the present version.

SoundPics: visual and auditory psychophysics reveals distinct sensory profiles that differentiate schizophrenia from bipolar disorder in early psychosis across three independent Brazilian public health clinical samples

Running title: Early sensory markers for psychosis

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ABSTRACT

Psychosis assessment relies mostly on top-down cognitive and behavioral evaluations. We investigated whether low-cost visual and auditory

psychophysical tests can detect early sensory alterations. Participants (schizophrenia [SCHZ] n = 45, bipolar disorder [BIP] n = 36, first-episode psychosis [FEP] n = 39) recruited from three independent Brazilian public mental health facilities (SUS) were independently compared to age-matched healthy controls (pooled N = 94). The Pictorial Size Test (PST) measured perceived image size in degrees of visual angle (dva). The Sound Appreciation Test (SAT) measured sound discomfort levels (SDL) across pure-frequency sweeps. SCHZ and FEP patients exhibited significantly larger perceived pictorial sizes relative to controls (d = 0.76, p = 0.0057; and d = 0.58, p = 0.013, respectively), whereas BIP patients did not differ from controls. Elevated hearing discomfort was present across all groups but was most pronounced in BIP (d = 1.16; p < 0.0001), followed by FEP (d = 0.70; p = 0.0057) and SCHZ (d = 0.51; p = 0.028). Empirical cutoffs derived from chronic cohorts created the hierarchical rule-based algorithm SoundPics-(V3). SoundPics differentiated schizophrenia from bipolar disorder yielding 70.8% accuracy among clinically determined cases (72 of 81) and demonstrated convergent classification in an independent FEP group. Early psychophysical screening is viable in clinical triage in public mental health settings.

Keywords: Auditory discomfort; Pictorial size; Schizophrenia; Bipolar disorder; First-episode psychosis; Early psychosis; SoundPics

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Introduction

Schizophrenia is a severe and disabling disorder that typically emerges between the ages of 15 and 35 years and profoundly affects cognition, occupational functioning, and quality of life. Its course is associated with widespread neuroanatomical, neurophysiological, biochemical, and proteomic brain alterations.[1–15] However, it remains unclear to what extent these alterations are already present before the onset of psychosis or develop progressively during the course of recurrent psychotic episodes.

At the genesis of schizophrenia lies the clinical phenomenon of psychosis. Rather than being defined by a single manifestation, psychosis is characterized in DSM-5-TR[16] and ICD-11[17] by a cluster of symptoms in which hallucinations and delusions occupy a prominent position, together with disorganized speech, behavioral disturbances, and cognitive impairment. Yet, these clinically

recognizable manifestations describe the psychotic state once it has become apparent; they do not necessarily identify the processes through which that state develops.

A first-person account of entering and leaving psychosis

The theoretical framework underlying the present study originated from a first-person account of the process of repeatedly entering and leaving psychotic episodes.[18] It was not initially derived from an abstract theoretical model, but from the internal observation of more than five successive cycles of developing psychosis and subsequently recovering from it. Importantly, these experiences were observed by a researcher with doctoral training in sensory perception, allowing particular attention to changes in perceptual functioning across successive transitions.[18] Sensory phenomena that progressively developed and repeatedly reproduced themselves across episodes became a central observation from which the present framework emerged.

From this first-person perspective, the development of psychosis does not necessarily appear as an abrupt and discontinuous behavioral event, although its progression may sometimes be rapid. Rather, it may evolve along a continuum involving successive failures of the organism to adapt and readapt to unpredictable adverse environmental events, major social changes, personal losses, or other events perceived as highly relevant to survival.[18]

Within this framework, successive failures of adaptation are proposed to promote neuroplastic changes accompanied by shifts in sensory sensitivity across modalities. Increasing sensory sensitivity may amplify emotional responses and contribute to an increasingly unstable internal processing environment. As sensory input, emotional responses, memory, and reasoning progressively interact under these conditions, the construction of a stable representation of reality may become increasingly vulnerable.

The framework is concerned primarily with this process of developing psychosis rather than with the idiosyncratic content of individual hallucinations or delusions. The particular beliefs, values, memories, social experiences, and personal history of an individual may shape the specific content of psychotic experience, but they are conceptually distinct from the sensory and cognitive processes proposed here to accompany the transition toward psychosis.[18]

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Distinguishing sensory alterations from cognitive manifestations

A central distinction in this framework is made between the sensory and cognitive domains. Sensory perception refers here to the continuous reception and transduction of internal and external stimulation through which the organism obtains information about its environment. Cognition, in contrast, is considered to involve the integration of this information with memory, expectations, acquired knowledge, and social and cultural values, particularly when meanings are attributed to objects and events.

This distinction is particularly relevant to hallucinations and delusions. Although hallucinations are commonly described as perceptual phenomena, the sensory alterations considered in the present framework should not be equated with hallucinations. Instead, hallucinations and delusions are conceived as higher-order interpretations or misinterpretations occurring when sensory information is integrated within an increasingly unstable cognitive environment.[18,19] Under psychosis, the attribution of meaning to otherwise unrelated or random events may become increasingly unstable, allowing spurious relationships and meanings to acquire subjective plausibility.

Accordingly, the sensory phenomena of interest here are more elementary changes in perceptual sensitivity. The first-person observations suggested that sensitivity may begin to shift across sensory modalities before more evident cognitive malfunction becomes apparent.[18] These changes were experienced predominantly as heightened visual and auditory sensitivity and were repeatedly observed during transitions toward psychosis. This observation generated a testable proposition: if changes in sensory sensitivity precede overt cognitive manifestations, they should be amenable to direct psychophysical measurement.

From top-down assessment to early sensory measurement

Current psychiatric assessment, however, is predominantly directed toward manifestations that have already reached the clinical or cognitive level. Instruments such as the Clinical Global Impression (CGI),[20] Brief Psychiatric Rating Scale (BPRS),[21] Positive and Negative Syndrome Scale (PANSS),[22] and Comprehensive Assessment of At-Risk Mental States (CAARMS),[23] as well as cognitive screening instruments such as the Addenbrooke's Cognitive

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Examination-Revised (ACE-R),[24] Mini-Mental State Examination (MMSE),[25] and Montreal Cognitive Assessment (MoCA),[26] primarily assess symptoms, behavior, cognition, and functional impairment.

From the perspective proposed here, this creates an important temporal gap. If alterations in sensory sensitivity arise before clinically evident cognitive dysfunction, assessment strategies focused predominantly on top-down manifestations may overlook an earlier stage of the psychotic process. This possibility is consistent with a growing bottom-up literature identifying sensory-processing abnormalities as core or trait-like features and potential endophenotypes of severe mental illness.[19-40] Studies of schizophrenia-spectrum disorders have demonstrated abnormalities involving early visual processing, contrast sensitivity, cortical magnification, and surround suppression,[27–33] whereas bipolar disorder has been associated with generalized sensory over-responsivity, including heightened auditory sensitivity, sound intolerance, and suprasensory experiences.[37]

The purpose of sensory testing in this context is therefore not to replace clinical diagnosis or established psychiatric assessment, but to investigate whether relatively elementary perceptual alterations can provide objective information complementary to conventional top-down evaluation.

From first-person observation to experimental psychophysics

The first-person observations described above progressively motivated an experimental program aimed at determining whether the proposed sensory changes could be objectively measured. Over approximately two decades, our laboratory has systematically investigated perceptual responses associated with schizophrenia and other psychiatric conditions. Studies of visual perception began by examining alterations in perceived pictorial size,[38–40] and were subsequently complemented by studies of auditory discomfort in individuals with established neuropsychiatric disorders and in patients presenting early psychotic symptoms.[34,35]

This research led to the development of two portable psychophysical probes. The Pictorial Size Test (PST) measures the size of the first pictorial region perceived within visual scenes, expressed in degrees of visual angle.[38–40] The Sound Appreciation Test (SAT) measures sound discomfort levels across

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controlled auditory stimuli after individual adjustment for hearing sensitivity.[34,35] Together, these visual and auditory measures constitute the SoundPics battery.[18,41–46]

Since 2019, these procedures have also been applied to patients experiencing first-episode psychosis (FEP), allowing direct comparison of early-stage sensory responses with those observed in healthy controls and in patients with established schizophrenia (SCHZ) or bipolar disorder (BIP).[41–46] Thus, SoundPics represents the progressive operationalization of observations that originated in the first-person experience of psychosis into experimentally measurable visual and auditory variables.

Empirical evidence of two distinct disorder-specific sensory profiles

Measurements obtained across these studies produced two unexpected patterns. Although schizophrenia and bipolar disorder may both involve psychosis, patients with these diagnoses did not exhibit identical patterns of visual and auditory responses. Instead, chronic schizophrenia and bipolar disorder showed distinct sensory profiles on the SoundPics measures.

Altered pictorial size perception emerged prominently in schizophrenia, whereas pronounced auditory discomfort was particularly evident in bipolar disorder. This disorder-dependent sensory dissociation was not originally formulated as a diagnostic rule; it emerged from the accumulated psychophysical data. The observation subsequently motivated systematic comparisons across independent samples and raised the possibility that combining visual and auditory measurements could provide information relevant to differential diagnosis.

Emergence of the SoundPics algorithm

The SoundPics hierarchical classification algorithm subsequently emerged from these findings and was developed to operationalize these empirically observed response patterns. Thus, the conceptual framework preceded the psychophysical investigation, whereas the specific disorder-dependent visual and auditory dissociation and its implementation as a classification algorithm emerged from the experimental findings.

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The present study

The present study brings together results obtained with the same SoundPics psychophysical approach across healthy controls and independent clinical samples of patients with first-episode psychosis, schizophrenia, and bipolar disorder recruited from specialized Brazilian public mental health services.[41–46]

We investigated whether the sensory profiles identified in established clinical groups could also be detected during early psychosis and provide objective information complementary to conventional clinical assessment. Based on the distinct sensory patterns that emerged from previous observations in patients with chronic schizophrenia and bipolar disorder as well as on the converging psychophysical literature[34-40], we tested whether these distinct sensory patterns could be found in FEP patients.

Finally, we examined whether the emergent hierarchical rule-based SoundPics algorithm could integrate these two sensory dimensions and translate the observed psychophysical divergence into an interpretable adjunctive tool for early clinical triage and differential diagnostic classification.

Method

Participants

The present study involved 120 diagnosed patients and 94 healthy controls. Participants were between 15 and 70 years old. Thirty-nine patients formed the first-episode psychosis (FEP) group, 45 patients the schizophrenia (SCHZ) group, and 36 patients the bipolar disorder (BIP) group. Ninety-four participants formed the age-matched healthy control groups for each patient population (HC). Group characteristics are listed in Table 1.

Importantly, the three patient groups were recruited from three distinct types of mental health facilities: SCHZ predominantly from a forensic psychiatric hospital (HCTP) and community CAPS units; BIP exclusively from CAPS units in Recife and Alagoas; and FEP from a specialized first-episode psychosis outpatient clinic (AMPEP). This institutional independence supports cross-group comparisons and generalizability.

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First-episode psychosis patients

Thirty-nine participants with a provisional diagnosis of first-episode psychosis and a clinical suspicion of schizophrenia formed the FEP group. They were attending the mental health facility *Ambulatório de Primeiro Episódio Psicótico do Hospital das Clínicas da Universidade Federal de Pernambuco* (AMPEP-EBSERH-HC-UFPE). During the six-year period of the experiments, some of these patients received a definitive diagnosis and were transferred to either the SCHZ or the BIP group accordingly. Only those still under care at AMPEP remained in the FEP group sample. Not all FEP patients were medicated.

Schizophrenia patients

The SCHZ group (N = 45) was composed of 25 males diagnosed with schizophrenia at the forensic psychiatric hospital *Hospital de Custódia e Tratamento Psiquiátrico* (HCTP) from Caetés-PE, Brazil, and 11 patients diagnosed with schizophrenia at AMPEP-EBSERH-HC-UFPE. The remaining nine patients were from outpatient CAPS (*Centros de Atenção Psicossocial*) type-II units in Alagoas (AL), Brazil. All SCHZ patients were medicated.

Bipolar patients

The BIP group (N = 36) included 25 patients from four outpatient mental health facilities: CAPS-tipo-II *Espaço Azul*, CAPS-tipo-III *Galdino Loureto*, CAPS-tipo-III *David Capistrano*, and CAPS-tipo-III *Espaço Livremente*, all in Recife-PE, Brazil. Three patients were from CAPS-**t**ipo-II units in Alagoas (AL), and the remaining eight patients were diagnosed at AMPEP-EBSERH-HC-UFPE. All BIP patients were medicated.

Healthy controls

Volunteers for the HC group (N = 94) were recruited from the general population; 25 of them came from the school *Educação de Jovens e Adultos* (EJA) in Arcoverde-PE, Brazil.

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Age matching

Healthy volunteers were pooled from the total of 94 to be closely paired by age during group data processing. Pairing was rigorous and produced identical mean ages with similar standard deviations in each age-matched group pair. A small subset of controls was used in more than one age-matched pair when age ranges overlapped across patient groups. This does not affect the independent comparisons, because each patient group was compared only to its own matched control set. Generally, the same HC sample served for both PST and SAT comparisons within a given patient group, and independent HC groups were composed for each age group of each patient group. There were no missing cases.

Diagnostic procedures

All diagnoses were established by experienced psychiatrists (including the co-author, head of the AMPEP clinic) according to DSM-5 and ICD-11 criteria following the routine clinical practice of the Brazilian public mental health system (SUS).

Inclusion and exclusion criteria

Inclusion required that patients be regularly attending the mental health facility, be willing to participate, and be able to understand and follow the test instructions. There was no age restriction. Even a patient with a hearing aid was willing to participate and demonstrated adequate comprehension and task performance**.**

The main exclusion criterion was inability to understand instructions or agitation that precluded participation.

Main Instruments

(i) The Pictorial Size Test (PST)

The present version of the PST consists of 20 color photographs of natural rural scenes (15 cm × 10 cm) bound in a 20-page folder. Ten photographs have vertical symmetry axes and ten have horizontal symmetry axes. Stimuli were viewed at a standard distance of 30 cm using a portable apparatus[40] (Figure 1). Participants were instructed to circle the first image they perceived in a glimpse,

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after one training trial. The diameter of each circled area was measured in centimeters and converted to degrees of visual angle (dva) based on the fixed viewing distance.

(ii) The Sound Appreciation Test (SAT)

This version used only the 16 pure-tone frequency sweeps from the 20 sounds measured and reported previously elsewhere [34,35]. Participants were asked to listen to each sound and mark on a pad the intensity of their perceived hearing discomfort. The folder contained written instructions and 20 pages, each featuring a 10 cm visual analog scale ranging from “NOTHING BAD” (left, no discomfort) to “TOO BAD” (right, maximum auditory discomfort). Each stimulus was played once through high-resolution headphones with noise attenuation, connected via Bluetooth to a cell phone at intensities of approximately 65 dB (half scale). Prior to measurements, to consistently normalize hearing sensitivities across participants, the volume was adjusted to each individual's preferred listening level. This normalizes across individuals' auditory sensitivity, so that discomfort ratings reflect each participant's response intensity relative to their own baseline comfort level rather than absolute loudness.

Procedures

After obtaining signed agreements from the public mental health institutions where the research took place and receiving approval from the Ethics Committee (Plataforma Brazil under CAEE registration numbers #23665419.5.0000.8807, #74757323.7.0000.5208, #57166622.0.0000.5208, #59516722.0.0000.5208, #70836723.0.0000.5208, and 70836723.0.3001.8807), individual experimental sessions began. The session sequence was identical for every experimental group and HC.

After a thorough explanation of the procedure and confirmation that the participant (and/or responsible sponsor) fully understood the research steps, written informed consent was obtained. This was followed by a sociodemographic questionnaire to record personal and family medical history, and by the Mini-Mental State Examination (MMSE). Whenever available,

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complementary data were obtained from medical records. Basic visual and auditory functions were then assessed before the PST and SAT measurements.

Instructions were printed and read aloud by the experimenter at the beginning of each psychophysical test. Each test started only after the experimenter was assured that the volunteer had fully understood the instructions. Further details can be found in the Supplementary material and in previous studies[34,40].

Preliminary Statistical Analysis of PST and SAT

Mann-Whitney U tests for independent samples were used to compare group characteristics and mean differences between experimental groups and their respective controls. Analyses of variance (ANOVA) were run individually for each patient group and their corresponding controls, with Bonferroni corrections for multiple comparisons. Normality tests were performed prior to parametric analyses. All statistical analyses were conducted using Statistica Ultimate Academic and GraphPad Prism 10.

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Table 1. Sociodemographic and clinical characteristics of experimental and control groups

Group	N	Age (years) Mean (SD)	Education (years) Mean (SD)	Marital status (S/M/NI)	Visual acuity Mean (SD)	Smoker (N)	Antipsychotics (N)	MMSE Median (IQR)	*p* vs. HC
FEP-PST	39	26.1 (9.63)	11.2 (2.92)	21 / 4 / 14	0.99 (0.08)	1	ARI 1, OLA 6, RIS 10, HAL 5	30 (30–30)	NS
HC-PST	39	26.3 (8.96)	12.2 (2.61)	30 / 3 / 6	0.99 (0.08)	0	–	30 (30–30)	–
FEP-SAT	38	25.5 (8.98)	11.4 (2.78)	21 / 3 / 14	0.93 (0.17)	1	ARI 1, OLA 6, RIS 10, HAL 5	–	–
HC-SAT	38	25.8 (8.43)	12.1 (2.58)	30 / 2 / 6	0.99 (0.08)	0	–	–	–
SCHZ	45	34.4 (11.2)	8.1 (3.05)	43 / 2 / 0	0.61 (0.25)	23	ARI 3, OLA 7, RIS 26, HAL 12	21 (18–24)	< 0.0001
HC-SCHZ	42	34.2 (12.05)	11.6 (3.62)	23 / 5 / 13	0.88 (0.21)	2	–	30 (28–30)	–
BIP (PST and SAT)	36	37.8 (12.39)	10.5 (3.81)	32 / 4 / 0	0.70 (0.31)	6	ARI 1, OLA 6, RIS 10, HAL 5	23 (20–26)	< 0.0001
HC-BIP (PST)	36	37.8 (12.92)	12.7 (3.34)	17 / 8 / 11	0.94 (0.13)	1	–	29 (27–30)	–
HC-BIP (SAT)	36	37.7 (12.84)	12.1 (4.28)	15 / 11 / 10	0.88 (0.19)	2	–	–	–

• MMSE = Mini-Mental State Examination (median, interquartile range).
• For FEP, MMSE was available for 39 participants (no difference vs. controls).
• Addenbrooke's Cognitive Examination (ACE-R) was available only for FEP (n = 14) and HC-FEP (n = 14): FEP = 80.5, HC-FEP = 91.4, p = 0.0155.
• Abbreviations: ARI, aripiprazole; HAL, haloperidol; OLA, olanzapine; RIS, risperidone; S, single; M, married; NI, non-informed; NS, not significant; SD, standard deviation; IQR, interquartile range.
Layout formatting assisted by AI (DeepSeek, Claude AI); no AI-generated content.

Participant characteristics and group comparisons

Table 1 shows the relevant statistical profiles of participants. Mann-Whitney U tests for independent samples were used to assess group characteristics and mean differences between experimental groups and their respective controls. Sex distribution was unbalanced due to the predominantly male population of the participating mental health facilities. For differences in MMSE group scores, see Table 1.

Participants were matched for age with controls within each experimental group and within each sensory test. For SCHZ and BIP, all patients completed both PST and SAT; for FEP, the numbers differed slightly because not all patients performed both tests. Age means were exactly matched when rounded to integer. Formal education differed significantly between SCHZ and HC_SCHZ ($p < 0.0001$) and between BIP and HC_BIP ($p < 0.05$), but no such differences were found for FEP. Visual acuity was worse for SCHZ ($p < 0.0001$) and BIP ($p < 0.001$) relative to their controls, whereas FEP showed no difference. Smoking was strongly overrepresented in SCHZ compared to FEP and BIP ($p < 0.0001$). Regarding medication, only the active drug of antipsychotics was recorded.

Preliminary Raw data handling

Questionnaires and PST data were entered into Excel spreadsheets. PST values were the diameters of the circled areas (measured in centimeters) and converted to dva. Figure 2 illustrates raw data from one healthy control and one SCHZ participant. There were no missing data; differences in group sample sizes were treated by handling statistics of each experimental group separately against its own matched control group.

SAT data are described as Sound Discomfort Level (SDL), rated on a continuous 0–10 visual analog scale. Sound stimuli were organized by modulation envelope (sawtooth, sine), order (ascending, descending), duration (4 s, 8 s), and frequency range (0.050–8 kHz, 2–8 kHz) for each participant and group.

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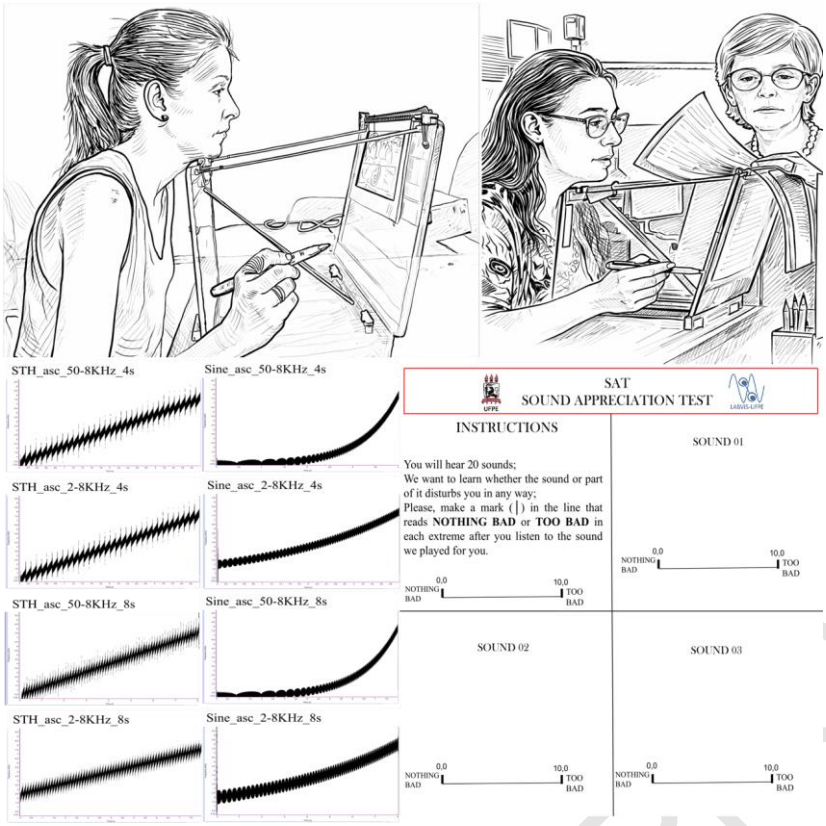


Figure 1 Setups for PST and SAT. ***Top***: Instances of the Pictorial Size Test (PST) experimental setup. Participants were instructed to circle the first image they perceived in a rural scene at 30 cm distance, after a single training trial using the visual apparatus illustrated in the picture. The diameter of each circled area was measured in centimeters and converted to degrees of visual angle (dva) . ***Bottom***: The Sound Appreciation Test (SAT) frequency sweep profiles and instruction page. Participants were asked to mark their level of auditory discomfort on a 10-cm visual analog scale (0 = NOTHING BAD, 10 = TOO BAD) after hearing each of 20 sound stimuli, one page per stimulus (the example includes prints of the instruction page and of single pages for first three stimuli extracted from the experimental folder used, bottom right). The procedure includes a volume adjustment step to normalize for individual auditory sensitivity.

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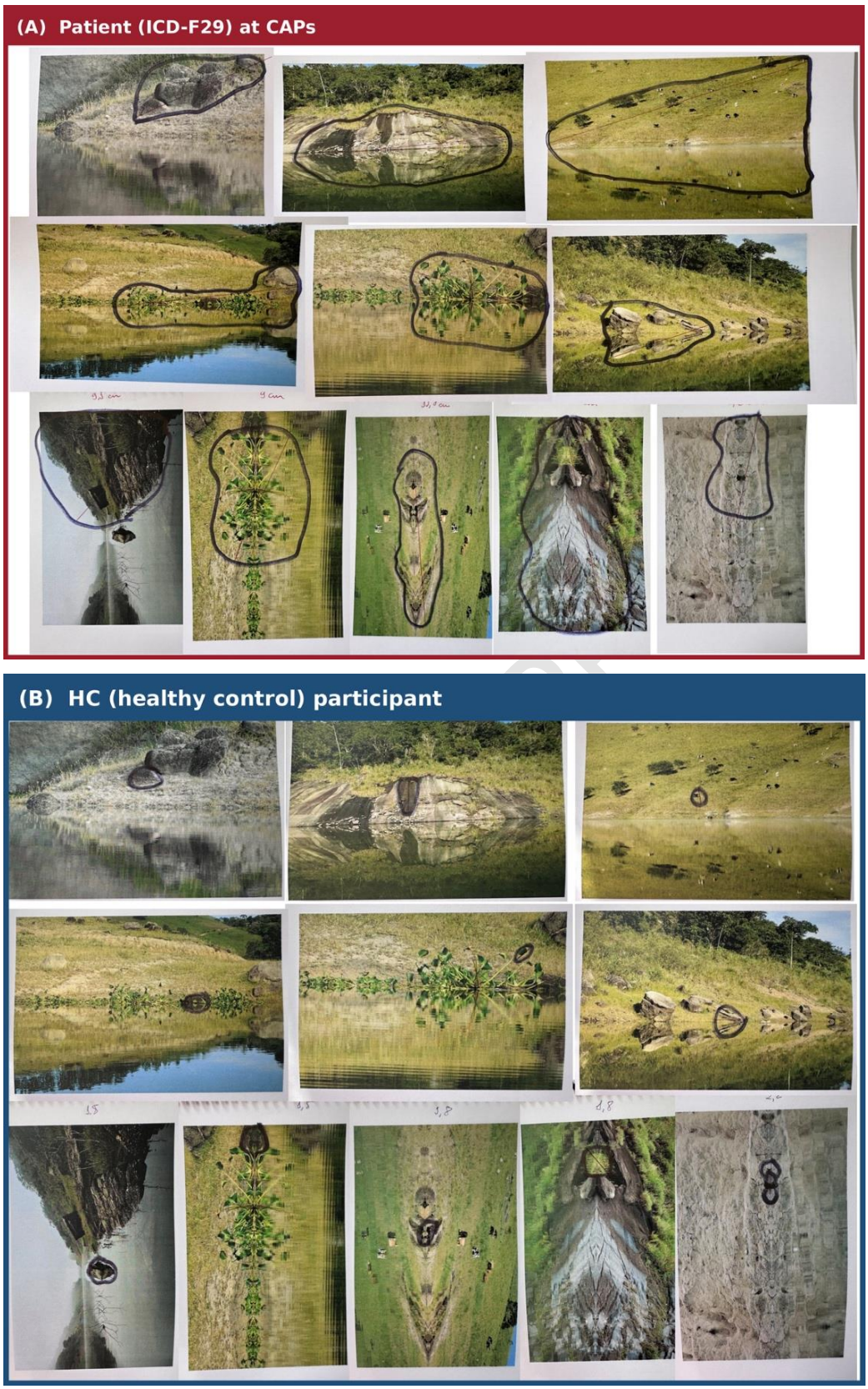


Figure 2 Representative PST responses: (A) Patient with first-episode psychosis (ICD-10 F29, unspecified psychosis) circled large areas, reflecting the augmented visual pictorial size perception characteristic of schizophrenia-spectrum disorders. (B) Healthy

control participant circled small areas indicating normal pictorial size perception. Circles were drawn by the participants in black ink.

Results

Psychophysical Results from Responses to PST and SAT

Group statistical analyses were carried out with Statistica Ultimate Academic and GraphPad Prism 10. Analyses of variance (ANOVA) were run individually for each patient group and respective controls, with Bonferroni corrections for multiple comparisons. Our main results are shown in Figure 3, organized as comparisons between each patient group and its age-matched HC.

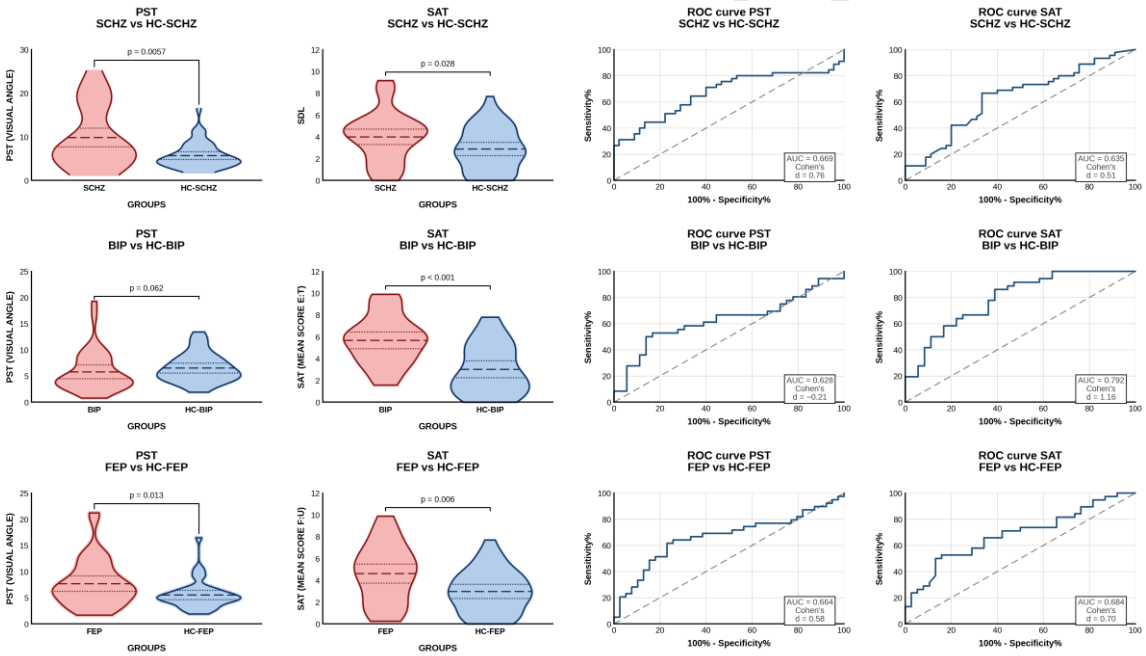


Figure 3 Distributions of Pictorial Size Test (PST; first column) and Sound Appreciation Test (SAT; second column) scores (violin plots) and respective ROC curves (PST, third column; SAT, fourth column) for each patient group versus its age-matched healthy controls: SCHZ vs HC-SCHZ (top row), BIP vs HC-BIP (middle row) and FEP vs HC-FEP (bottom row). Long-dashed lines indicate group means and dotted lines the 95% confidence intervals of the means; in the PST FEP panel, the open circle and error bar show the mean ± standard error. The diagonal dashed line in the ROC plots indicates chance performance (AUC = 0.5). P-values from Mann-Whitney U tests (two-tailed). Graphs were prepared using Microsoft Excel and Claude AI software

Pictorial Size Test (PST)

Figure 3 (first column) shows the first perceived pictorial size distributions and means and the statistical differences (Mann-Whitney U tests) for each experimental group versus its controls. SCHZ and FEP both circled significantly larger sizes than their respective HCs ($p = 0.0057$ and $p = 0.013$, respectively). BIP did not differ from HC_BIP.

Notably, the effect size for FEP ($d = 0.58$) although smaller than that for chronic SCHZ ($d = 0.76$), suggests that the visual size alteration is already present at the earliest stages of schizophrenia-spectrum disorders and may might become more pronounced with chronicity. The effect is already present regardless of FEP normal visual acuity.

Sound Appreciation Test (SAT)

Figure 3 (second column) shows SDL distributions and means. All three patient groups reported significantly higher auditory discomfort than their respective controls: BIP ($p < 0.0001$), FEP ($p = 0.0057$), and SCHZ ($p = 0.028$). Supplementary Figure 1 provides group means for each measurement and shows each significant difference found for specific sound sweeps.

PST and SAT additional parametric statistical treatments

To examine possible image symmetry effects in PST, three-factor ANOVAs (group × symmetry × scene) were performed separately for SCHZ, BIP and FEP after normality testing.

Significant group differences were found for SCHZ vs HC_SCHZ ($F_{1,44} = 13.37$, $p < 0.0007$) and for FEP vs HC_FEP ($F_{1,38} = 12.81$, $p < 0.0010$), but not for BIP. A light symmetry effect was present in the BIP group ($F_{1,35} = 4.629$, $p < 0.0384$). No symmetry × group interactions were observed for SCHZ or FEP; however, a three-way interaction (group × symmetry × scene) was found for SCHZ ($F_{9,396} = 3.236$, $p = 0.0008$). Supplementary Figure 2 illustrates differences in first pictorial sizes and symmetries for SCHZ and BIP.

For SAT, two-factor ANOVAs revealed significant group differences for all three comparisons: SCHZ vs HC_SCHZ ($F_{1,44} = 7.619$, $p < 0.0084$), FEP vs HC_FEP ($F_{1,37} = 7.609$, $p < 0.0090$), and BIP vs HC_BIP ($F_{1,35} = 30.39$, $p <$

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0.0001), with the largest magnitude for BIP. A Group × Sound interaction was found only for SCHZ ($F_{15,660}$ = 2.101, p < 0.0086).

Supplementary Figure 1 (bottom panels) shows that most PST values for SCHZ and FEP lie well above their respective HC 95 % confidence intervals, whereas BIP differs from HC_BIP in only 5 out of 20 stimuli.

Bonferroni corrections in PST and SAT data

Bonferroni corrections for PST and SAT were carried out. The distribution of first perceived pictorial sizes in SCHZ and FEP was found to be very similar, but the magnitude is higher for SCHZ. Values for BIP in PST yielded no significant difference.

PST and SAT Receiver Operating Characteristics (ROC) and power analyses

Figure 3 (third and fourth columns) shows ROC curves for each patient group versus respective controls. PST distinguished SCHZ (AUC = 66.9%, p = 0.0057) and FEP (AUC = 66.4%, p = 0.013) from their controls, but not BIP (AUC = 62.8%, p = 0.062). SAT distinguished BIP well (AUC = 79.2%, p < 0.0001), and also distinguished SCHZ (AUC = 63.5%, p = 0.028) and FEP (AUC = 68.4%, p = 0.0057) from controls, with somewhat lower discrimination than PST for SCHZ, and slightly higher discrimination than PST for FEP.

Power analysis calculations showed that PST has 94.5% power (d = 0.76, p = 0.0057) to distinguish SCHZ from HC, and 72.1% power (d = 0.58, p = 0.013) to distinguish FEP from HC. SAT has 99.8% power (d = 1.16, p < 0.0001) to distinguish BIP from HC, and progressively lower power for FEP (85.2%, d = 0.70, p = 0.0057) and SCHZ (67.2%, d = 0.51, p = 0.028).

SoundPics creation: The SoundPics Classification Algorithm

Given the strong statistical effects and the coupled specificity of PST and SAT for distinct pathologies, we have developed a psychophysical sensory-based classification algorithm, SoundPics (short for “Sound Discomfort & Picture Size”), for assessing schizophrenia or bipolar disorder sensory tendencies. Refer to Figure 4 for summary findings.

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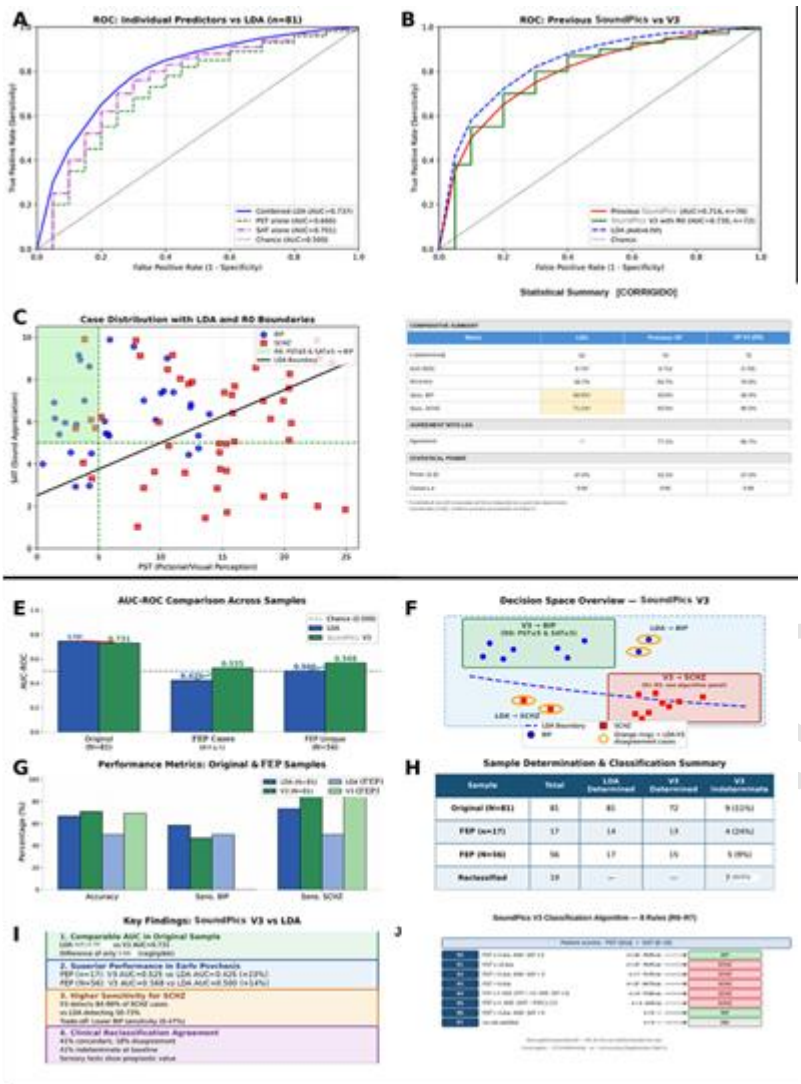


Figure 4. Comparative diagnostic performance of linear discriminant analysis (LDA) and the SoundPics rule-based classifier. **(A)** ROC curves for the individual predictors (PST alone, AUC = 0.660; SAT alone, AUC = 0.701) and the combined LDA model (AUC = 0.737) in the original sample (n = 81; 45 SCHZ, 36 BIP). **(B)** ROC curves for the previous SoundPics version (AUC = 0.714; n = 70 determined cases) and SoundPics V3 including rule R0 (AUC = 0.735; n = 72 determined cases), with LDA (AUC = 0.737) shown for reference. **(C)** Distribution of cases in the PST × SAT decision space, with the LDA boundary (solid line) and the R0 rule region (PST ≤ 5 dva and SAT ≥ 5; shaded green), which classifies cases as bipolar disorder. **(D)** Statistical summary comparing LDA, previous SoundPics and SoundPics V3 (R0) regarding determined cases, AUC-ROC, accuracy, diagnosis-specific sensitivities, agreement with LDA, statistical power (1−β) and Cohen's d.* **(E)** AUC-ROC comparison across three independent samples — original (N = 81): LDA 0.737 vs SoundPics 0.731†; early psychosis cases (FEP, n = 17): LDA 0.425 vs V3 0.525; first-episode psychosis unique

cases (FEP, N = 56): LDA 0.500 vs V3 0.568. **(F)** Schematic decision space with the LDA boundary and the main SoundPics V3 classification regions (R0 → BIP; R1–R5 → SCHZ); orange rings mark LDA–V3 disagreement cases. **(G)** Accuracy and diagnosis-specific sensitivities in the original and FEP samples. **(H)** Sample determination and classification summary, including the number and percentage of indeterminate cases under V3 per sample. **(I)** Key findings of the comparison. **(J)** The SoundPics V3 classification algorithm, composed of eight empirically derived rules (R0–R7) applied sequentially to PST and SAT scores: the first satisfied rule classifies the case (R0 and R6 → BIP; R1–R5 → SCHZ), and cases satisfying no rule remain undetermined (R7). Rule-specific case counts and accuracies are shown (Supplementary Table 3). *Diagnosis-specific sensitivities for LDA in panel D (BIP = 58.3%; SCHZ = 71.1%) were computed independently from the raw PST/SAT scores, as these values were not reported in the original analysis; they are consistent with the values shown in panel G. Abbreviations: PST = Pictorial Size Test; SAT = Sound Appreciation Test; AUC = area under the ROC curve; SCHZ = schizophrenia; BIP = bipolar disorder; FEP = first-episode psychosis. Figure prepared with the assistance of Claude AI and Kimi AI. †See note under panel E.

This is a hierarchical rule-based algorithm (SoundPics) derived exclusively from the SCHZ and BIP chronic patients' data. The algorithm uses eight hierarchical rules (Figure 4 J) with empirically defined cut-offs based on observed chronic patients' thresholds as well as thresholds from HC.

Initially we used cut-off points based on a dichotomic view of PST and SAT and generated SoundPics sets of rules V1 and V2. However, compared to those earlier cut-off versions, SoundPics-V3 improved overall agreement in concordance with established clinical diagnoses from 65.7% to 70.8% and bipolar sensitivity from 30.0% to 46.9% (Figure 4J). The algorithm returned 'undetermined' for 11.1% of cases (9 of 81), indicating that sensory profiles were inconclusive for differential diagnosis in a small subset of patients.

SoundPics-V3 classified 88.9% of cases (72 of 81 cases) and achieved 70.8% agreement with clinically established diagnoses among these classified cases, compared with 66.7% for linear discriminant analysis (LDA) applied to the same data (Figure 4). The ROC curve for the coupled SoundPics-V3

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algorithm yielded an AUC of 0.735, approaching the performance of LDA (AUC 0.737; Figure 4).

External validation using a second FEP group as an independent test set

Within a second independent sample of 17 FEP patients (not part of the main FEP group, N=39), the SoundPics-V3 algorithm showed a sensitivity of 90% for SCHZ and 69.2% agreement regarding provisional diagnoses. When both FEP samples were combined (N=39 + N=17, total N=56), overall agreement with established clinical diagnoses was 64.7%, and for SCHZ alone it was 76.8%. Further details are found in the Supplementary material in the session "Differential classification between SCHZ, BIP and undetermined".

The independently obtained PST and SAT psychophysical results from the FEP group (N=39) provided convergent validity for the SCHZ and BIP group findings. ROC profiles for both PST and SAT were very similar between FEP and SCHZ groups, even though the obtained measurements were totally independent.

We should emphasize that these are not psychometric measurements or predictions from theoretical latent constructs, but direct sensory psychophysical measurements from FEP patients that yielded concrete values in degrees of visual angle and in arbitrary units of hearing discomfort that are very similar to the responses from the SCHZ group findings. That similarity is consistent with the very origin of this FEP sample that was recruited from AMPEP-EBSERH-HC-UFPE, an outpatient service that selects patients clinically pre-classified as likely to develop schizophrenia.

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Discussion

This study introduces a novel psychophysical approach to the evaluation of early psychosis, prioritizing objective sensory measurements over conventional, top-down cognitive and behavioral evaluations alone. By directly assessing primary perceptual responses rather than inferring them from latent constructs, the Pictorial Size Test (PST) and the Sound Appreciation Test (SAT) operate as direct sensory probes capable of capturing early-stage processing anomalies. Consistent with the first-person phenomenological framework that originated this research program (Simas, 2018), repeated transitions into and

out of psychosis were accompanied by progressive shifts in visual and auditory sensitivity—alterations experienced as process-level changes in perceptual organization, distinct from the higher-order content of hallucinations and delusions. Crucially, these objective characteristics yield direct psychophysical quantification in degrees of visual angle and arbitrary units of discomfort, independent of the semantic variability of clinical phenomenology

Further, our findings revealed unexpected marked disorder specific dissociation in perceptual profiles across clinical groups where patients with schizophrenia (SCHZ) and first-episode psychosis (FEP) exhibited significant visual size enlargement on the PST, whereas patients with bipolar disorder (BIP) showed no visual size alteration. Conversely, while elevated auditory discomfort on the SAT was present across all patient groups, its magnitude was uniquely pronounced in bipolar disorder. Moreover, coupling these distinct visual and auditory signatures within the newly developed SoundPics-V3 hierarchical rule-based algorithm differentiated schizophrenia from bipolar disorder with 70.8% agreement with clinically established diagnoses leaving 11.1 % as undetermined.

The pronounced alteration in pictorial size perception observed in the SCHZ and FEP groups aligns with accumulating neurobiological evidence demonstrating anatomical and functional deficits in the early visual pathways of individuals with schizophrenia-spectrum disorders.[27–33] The enlarged perceived size (quantified objectively in degrees of visual angle) likely reflects disrupted early sensory processing, potentially involving a selective shift in the contrast sensitivity function toward lower spatial frequencies, altered cortical magnification mechanisms, and impaired surround suppression driven by cortical GABAergic interneuron dysfunction.[27,31,33,38–40] On the other hand, the effect size for visual size alteration was comparable between the FEP cohort (d = 0.83) and chronic schizophrenia patients (d = 0.76), despite the FEP participants presenting with intact visual acuity. This similarity indicates that visual size alterations are not secondary artifacts of disease chronicity, general cognitive decline, or long-term antipsychotic exposure. Instead, visual perceptual shifts appear to represent a stable, trait-like feature that is already fully expressed at illness onset and persists across the course of chronic illness. If the enlarged pictorial size perception reflected a low-level acuity deficit, the

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acuity-impaired SCHZ group would be expected to show the largest distortion; instead, the acuity-normal FEP group showed a marginally larger effect, arguing against basic visual acuity as the underlying mechanism.

Elevated auditory discomfort was present across all three patient groups—BIP, FEP, and SCHZ—suggesting that heightened sound reactivity may constitute a transdiagnostic marker of psychosis-related sensory dysregulation. However, its magnitude followed a clear hierarchy: most pronounced in BIP (d = 1.16), followed by FEP (d = 0.70) and SCHZ (d = 0.51). This hierarchy indicates that while auditory hypersensitivity is not exclusive to any single diagnosis, its severity is differentially distributed across disorders. The prominent auditory discomfort observed in the bipolar group provides empirical psychophysical confirmation of the generalized sensory over-responsivity and suprasensory phenomena documented in bipolar spectrum conditions[37]. Clinical phenomenological surveys have shown that individuals with bipolar disorder frequently report heightened, sharpened, or overwhelming sensory experiences across sensory modalities, including heightened auditory perception and low tolerance for noise, both during acute mood episodes and across baseline phases[37]. Because the SAT protocol standardizes individual baseline hearing thresholds by adjusting the volume to each participant's preferred listening comfort level prior to testing, the reported discomfort reflects central affective and sensory gating dysfunctions rather than peripheral auditory differences. Consequently, the selective prominence of heightened auditory reactivity in chronic, medicated bipolar patients indicates that extreme sound discomfort represents a stable, trait-like perceptual marker. Importantly, the diagnostic specificity of the SoundPics-V3 algorithm does not rest on the exclusivity of individual markers, but on their coupled configuration: the co-occurrence of normal visual size with extreme auditory discomfort characterizes the bipolar profile, whereas the co-occurrence of enlarged visual size with moderate, to high, auditory elevation characterizes the schizophrenia-spectrum profile. This profile-based logic is what enables the hierarchical rule-based classifier to operate with clinical interpretability.

Derived exclusively from the psychophysical response patterns of chronic patients with established diagnoses, the SoundPics-V3 classifier is empirically anchored rather than theoretically inferred: its rules emerged from observed

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thresholds in the data, not from a priori latent constructs. This data-driven origin is reflected in its agreement with established clinical diagnostic comparable to linear discriminant analysis (70.8% from SoundPics versus 66.7% from LDA) while maintaining clinical interpretability through explicit threshold rules. Furthermore, the algorithm's conservative designation of 11.1% of ambiguous cases as undetermined reflects a sound clinical safety threshold, prioritizing high classification specificity over forced diagnostic assignment.

These findings carry important translational implications, as the SoundPics-V3 algorithm demonstrates how coupling visual and auditory psychophysics can provide practical, low-cost adjunctive decision support in routine clinical psychiatry. Standard clinical assessment batteries rely heavily on clinical interview articulation and symptom self-reporting, which can be confounded during acute psychotic episodes.[20–26,47] In contrast, the PST and SAT take approximately 15 minutes to administer, rely on simple perceptual judgments, and require minimal portable equipment. .

A major strength supporting the validity of this framework is the external replication provided by the two independent FEP samples. Although recruited from a distinct clinical outpatient unit specializing in suspected schizophrenia (AMPEP) and evaluated independently from the chronic cohorts, FEP participants exhibited perceptual profiles and ROC curves remarkably similar to those of chronic schizophrenia patients. The convergence of direct visual and auditory psychophysical values between these independent cohorts confirms that the observed perceptual markers emerge at the very inception of the psychotic process, which supports the utility of the SoundPics-V3 framework as an early risk-stratification and screening tool in public health settings.[41–46]

Several methodological limitations of the present study must be acknowledged. First, all participants were recruited from specialized public mental health services within the Brazilian Sistema Único de Saúde (SUS) in Pernambuco, and the sample was male-predominant due to the demographic composition of the participating forensic and day-clinic facilities.[41–46] Second, baseline admission routines did not include standardized positive and negative symptom severity rating scales (such as PANSS or YMRS), which limited our ability to correlate perceptual alterations directly with specific syndromic symptom dimensions. From the perspective of the present framework, however,

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this absence does not weaken the central conclusion since the study targets elementary sensory processes rather than higher-order symptom content, the lack of correlation with syndromic dimensions is expected rather than problematic, though it remains an important direction for future research. Third, although perceptual patterns remained robust across medicated chronic patients and partially medicated FEP participants, systematic dose-response relationships and specific pharmacological class effects were not controlled. Finally, because the FEP cohort was drawn exclusively from a clinic dedicated to presumed schizophrenia, future validation requires the inclusion of early-stage cohorts with suspected bipolar disorder (e.g., from specialized bipolar clinics) to fully confirm the longitudinal predictive specificity of the auditory and visual markers.

In conclusion, low-cost psychophysical testing demonstrates that schizophrenia-spectrum disorders and bipolar disorders exhibit distinct sensory signatures at early and chronic stages of illness. The combination of visual pictorial size enlargement in schizophrenia and marked auditory discomfort in bipolar disorder provides an objective, brain-based dimension that complements traditional clinical evaluations.[18,37,48–50] By capturing pre-cognitive perceptual alterations within accessible testing formats, the SoundPics-V3 battery and its hierarchical algorithm offer a promising, scalable strategy for early screening, clinical triage, and diagnostic differentiation in psychiatric care.

Acknowledgements

We thank the Coordenação de Aperfeiçoamento de Pessoal do Nível Superior (CAPES) for support from the PROAP program and for the graduate fellowships to Mateus Monteiro de Gois Barros, Katherine Karla Souza da Silva, and Amanda Almeida Rodrigues e Silva, and PROPESQI-UFPE for the Scientific Initiation scholarship to Kayke Kauã de Siqueira**.** We also thank Maria Cristina Fortes Santos de Bustamante for making freely available a collection of photographs from her own authorship. We particularly thank Professor José Mauricio Haas Bueno for his comments and review of the manuscript.

Funding: Coordenação de Aperfeiçoamento de Pessoal do Nível Superior (CAPES); PROPESQI-UFPE

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Disclosure

None of the authors have conflict of interest.

Author contributions

Maria Lucia de Bustamante Simas *Idealized instruments, designed experiments, wrote the manuscript and performed statistics treatment and illustrations of data.*
Aline Mendes Lacerda *supervised part of data collection*
Joselma Tavares Frutuoso *supervised part of data collection*
Isabela de Fatima Pina de Almeida *Head of AMPEP public mental health service; supervisor & Clinical assessments*
Mateus Monteiro de Gois Barros *provided collected data from his master's thesis, prepared references, helped preparing documents for the ethics committee.*
Katherine Karla Souza da Silva *provided collected data from her master's thesis*.
Thays Macambira da Silva *provided collected data from her master's thesis*.
Giuliano Baltar Melo de Souza Ramos *provided collected data from his master's thesis*
Tamires Lima da Silva *provided collected data from her master's thesis*
Naianna Mocelin Ribeiro dos Santos *provided collected data from her master's thesis*.
Amanda Almeida Rodrigues e Silva *collected data, prepared references.*
Kayke Kauã de Siqueira *collected data*.

Edited by: Raffael Massuda

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SUPPLEMENTARY MATERIAL

1. Complementary information to METHOD

Supplementary Table S1

Table 1 shows scores on neuropsychological tests from experimental and healthy control groups. MMSE was available for 29 of 36 BIP patients and 29 of 36 HC-BIP; full sample sizes reported in main Table 1.

Group	N	MMSE median	*p*-value	N	Addenbrooke (ACE-R)	*p*-value
FEP/HC-FEP	39	30 / 30	NS	14	80.5 / 91.4	0.0155
SCHZ/HC-SCHZ	42	21 / 30	< 0.0001	-	-	-
BIPOLAR/HC-BIP	29	23 / 29	< 0.0001	-	-	-
SCHZ/BIP	42 / 29	21 / 23	0.0069	-	-	-

MMSE = Mini-Mental State Examination; ACE-R = Addenbrooke's Cognitive Examination; FEP = first-episode psychosis; SCHZ = schizophrenia; BIP = bipolar disorder; HC = healthy controls; NS = not significant.

Screening procedures

Other equipment and instruments

The experiment also involved the following equipment and instruments:

a. **Background questionnaire** – Sociodemographic data and medical background from patients were obtained either from medical records (with consent) and/or structured questionnaires.

b. **Screening test for cognition** – Cognitive functioning was evaluated with the Brazilian adaptation of the Mini Mental State Examination (MMSE) (Santos, 2010).

c. **Screening test for visual acuity** – The Android/iOS app *Smart Optometry* (by Smart Optometry) with varying sizes of Rasquim's "E" stimuli were presented either on cellphones or 8" tablets for near vision. Participants were asked to indicate the open side of the "E" either orally or by hand

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gesture. When more than 50% errors were made within the same size, the acuity corresponding to the size immediately prior to that was considered.

d. Screening test for hearing – Either the application *Test of audition* (developed by e-audiologia for Android) or *EasyHearingTest* (developed by Hiroaki Ito for iOS) was used to evaluate bilateral hearing of participants. A few participants wearing hearing aids and presenting expected age-standard hearing results were included in the study.

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2. Complementary information to RESULTS

Supplementary Table S2 PST and SAT AUC, statistical power, Cohen's d, and 95% CI of the AUC with respective observed probabilities for SCHZ, BIP and FEP

GROUP	Test	AUC	*d*	Power	AUC 95% CI	*p*-value
SCHZ	**N = 45**					
	PST	**0.669**	0.76	**94.5%**	0.558–0.781	**0.0057**
	SAT	**0.635**	0.51	**67.2%**	0.520–0.749	**0.028**
BIP	**N = 36**					
	PST	**0.628**	−0.21	**14.2%**	0.499–0.757	0.062 (ns)
	SAT	**0.792**	**1.16**	**99.8%**	0.687–0.897	**< 0.0001**
FEP	**N = 39 (38 for SAT)**					
	PST	**0.664**	**0.58**	**72.1%**	0.544–0.784	**0.013**
	SAT	**0.684**	0.70	**85.2%**	0.565–0.804	**0.0057**

AUC = area under the ROC curve; *d* = Cohen's effect size; CI = confidence interval; PST = Pictorial Size Test; SAT = Sound Appreciation Test; SCHZ = schizophrenia; BIP = bipolar disorder; FEP = first-episode psychosis.

PST (degrees of visual angle, *dva*), SAT (0–10 sound discomfort level scale – arbitrary units).

Values in **red** indicate AUC values significantly greater than chance ($p < 0.05$; 95% CI not including 0.5), power > 99% and $p < 0.0001$. ns = not significant. AUC, its 95% CI (Hanley & McNeil method) and *p*-values (two-tailed Mann–Whitney *U* test) were computed from each participant's mean score; power refers to a two-tailed *t*-test (α = 0.05) for the observed *d*.

Sound Appreciation Test (SAT)

The sixteen sounds of SAT in an experimental design of subjective magnitude can be found at: http://www.fonae.org/audios (last accessed August 15, 2026).

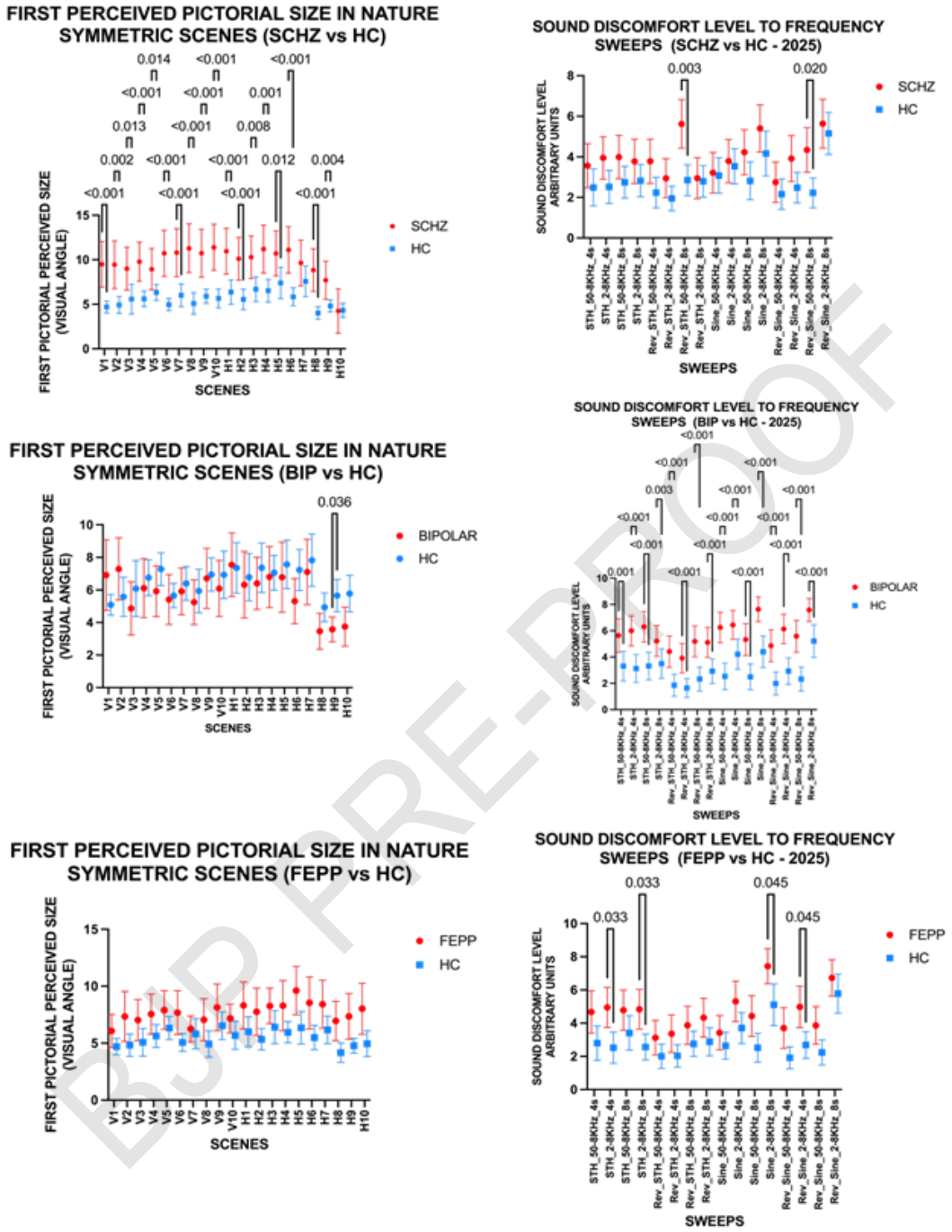
These sounds are hosted on the site of the National Forum on Schizophrenia, FONAE, second edition May 21–23, 2025, held every two years. Next edition, III FONAE, to be held on April 23rd-25th, 2027.

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Note: We measure 20 sounds in total. We report only on the 16 pure-tone frequency sweeps.

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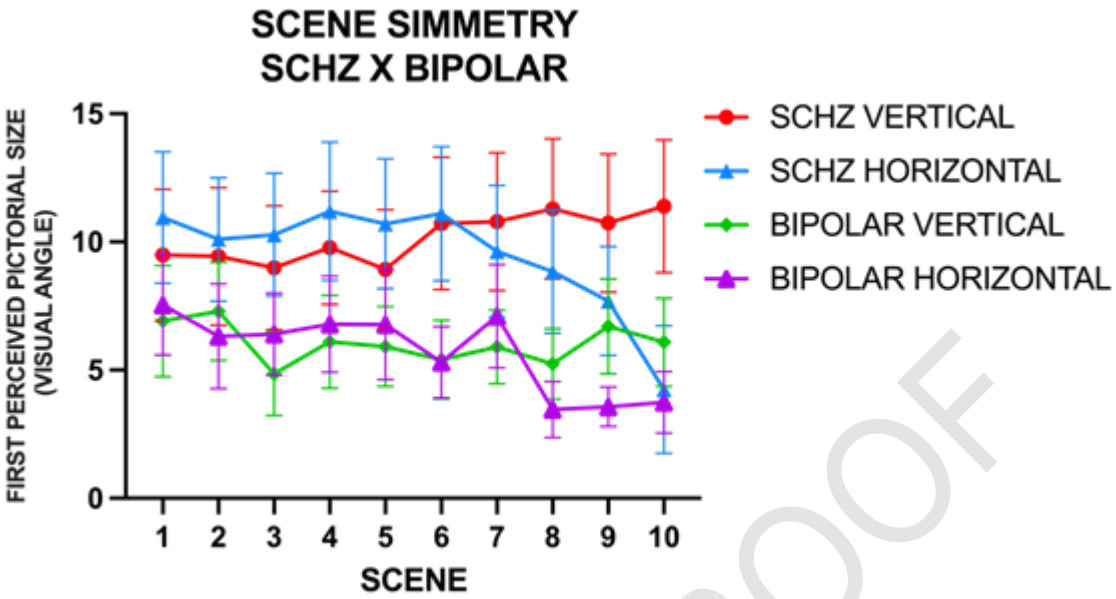
Supplementary Figure S1 PST (left) and SAT (right) means for each experimental group: SCHZ (top), BIP (middle), and FEP (bottom).



Error bars are 95% confidence intervals. Significant differences are illustrated.

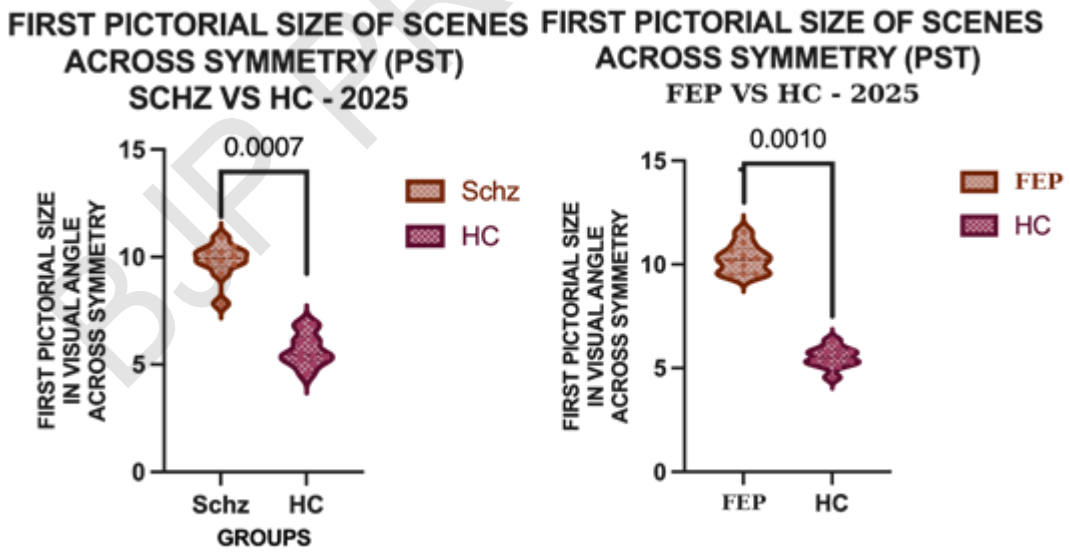
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Supplementary Figure S2 PST means for perceived pictorial sizes per symmetry direction (vertical vs. horizontal) for SCHZ and BIP groups



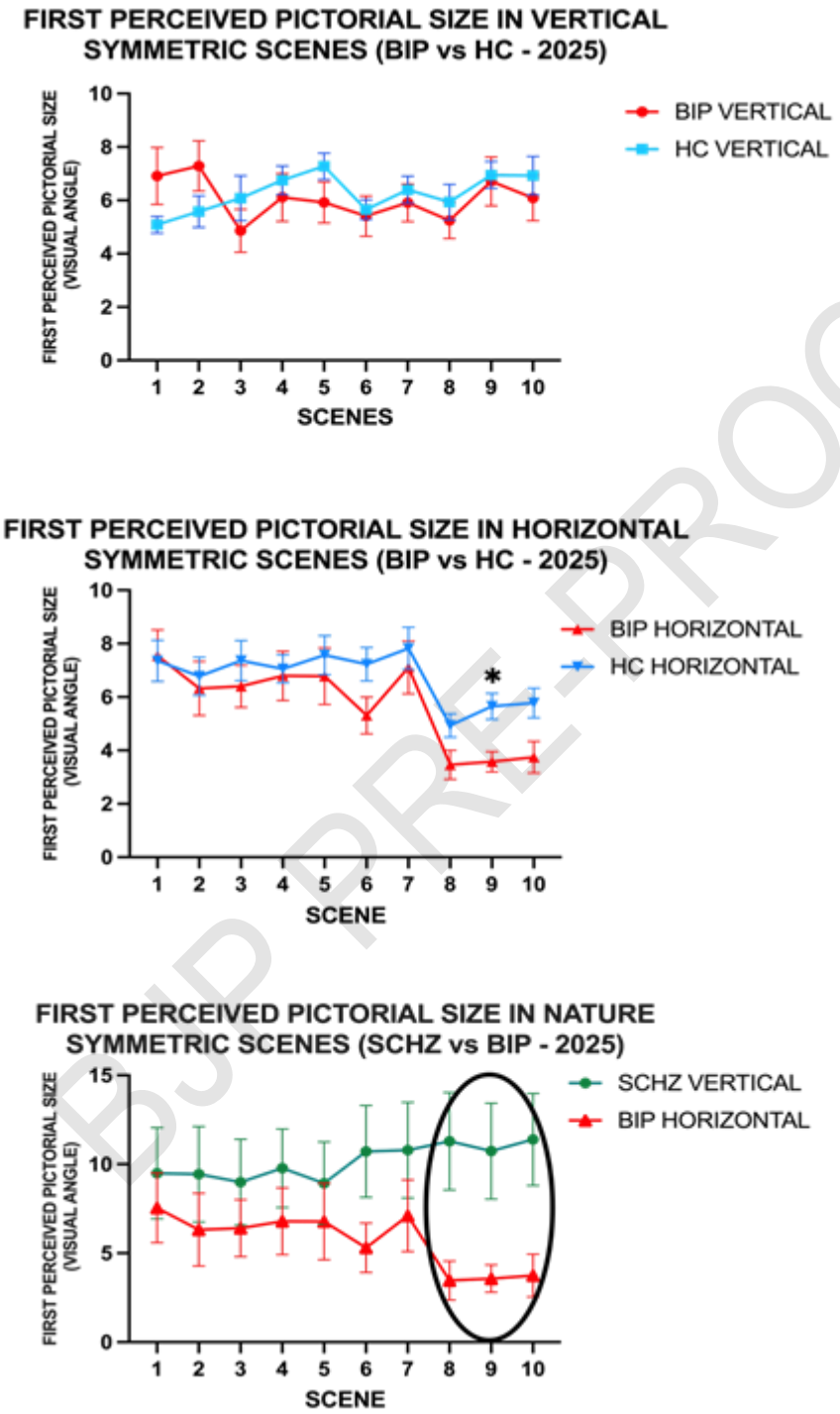
Error bars are 95% confidence intervals.

Supplementary Figure S3 PST means across symmetry conditions comparing SCHZ vs. HC-SCHZ and FEP vs. HC-FEP



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Supplementary Figure S4 PST responses to vertical and horizontal symmetric scenes for comparisons between SCHZ and BIP groups. These may be used for potential differential diagnosis



Error bars are 95% confidence intervals.

Differential classification between SCHZ, BIP and undetermined

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Supplementary Table S3 Empirically generated rules and their applications

Rule	Description	Prediction	Total	Correct	% correct
R0	PST ≤ 5 *dva* AND SAT ≥ 5	BIP	19	15	78.9%
R1	PST ≥ 10 *dva*	SCHZ	17	13	76.5%
R2	PST > 5 *dva* AND SAT < 3	SCHZ	7	5	71.4%
R3	PST > 6 *dva*	SCHZ	17	11	64.7%
R4	PST ≥ 4 *dva* AND (PST > 4.5 *dva* AND SAT ≤ 9)	SCHZ	9	7	77.8%
R5	PST ≥ 4 *dva* AND SAT ∈ [PST±2.5]	SCHZ	3	0	0.0%
R6	PST < 4 *dva* AND SAT > 5	BIP	0	-	-
R7	UNDETERMINED	-	9	-	-

PST = Pictorial Size Test score (degrees of visual angle, dva). SAT = Sound Appreciation Test score (0–10 sound discomfort level scale – arbitrary units).

Supplementary Table S4 Comparison after last rules adjustment: ***Previous*** SoundPics vs **SoundPics V3**

Metrics	Previous (R4 corrected)	V3 (with R0)	Difference
Cases (determined)	70	72	+2
Accuracy with clinical	65.7%	70.8%	+5.1%
Sensitivity BIP	30.0%	46.9%	+16.9%
Sensitivity SCHZ	92.5%	90.0%	−2.5%
Agreement with LDA	77.1%	84.7%	+7.6%
Undetermined	11	9	−2

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Supplementary Table S5 Comparison with linear discriminant analysis (LDA) considering only the results of SCHZ (*N* = 45) and BIP (*N* = 36) groups

Comparative summary – LDA vs SoundPics V3 (with new RULE R0)	**LDA**	**SoundPics V3**
Metrics		
Total # cases	81	81
Cases categorized	81	72
Cases correct	54	51
Accuracy (clinic diagnosis coincidence)	66.7%	70.8%
Undetermined	0	9
% undetermined	0%	11.1%
Sensitivities		
Sensitivity BIP	—	46.9%
Sensitivity SCHZ	—	90.0%
Agreement between methods		
Cases (agree)	61	84.7%
Cases (disagree)	11	15.3%
Cut-off points LDA		
PST isolated	5.0 *dva*	—
SAT isolated	5.6 (smaller → SCHZ)	—

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Comparative summary – LDA vs SoundPics V3 (with new RULE R0)	LDA	SoundPics V3
Formula combined	$Z = 0.089 \times PST - 0.271 \times SAT + 0.862$	—
Interpretation	$Z > 0 \rightarrow$ SCHZ; $Z < 0 \rightarrow$ BIP	—
AUC-ROC	0.737	—

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Supplementary Table S6 Diagnostic performance of the SoundPics V3 algorithm (PPV and NPV with 95% Wilson confidence intervals) by diagnosis

Diagnosis	True Positive (TP)	False Positive (FP)	False Negative (FN)	True Negative (TN)	PPV (95% CI)	NPV (95% CI)
SCHZ	36	17	4	15	67.9% (54.5%–78.9%)	78.9% (56.7%–91.5%)
BIP	15	4	17	36	78.9% (56.7%–91.5%)	67.9% (54.5%–78.9%)

TP = true positive; FP = false positive; FN = false negative; TN = true negative; PPV = positive predictive value; NPV = negative predictive value; CI = confidence interval (Wilson method); SCHZ = schizophrenia; BIP = bipolar disorder.

Values are derived from the confusion matrix of the 72 determined cases (SCHZ vs. BIP) classified by the SoundPics V3 algorithm against clinical diagnosis.

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