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## The noise in our brain: A systematic review and meta-analysis of neuroimaging and signal-detection studies on source monitoring in psychosis

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### ABSTRACT

Objectives: Noisy thoughts or perceptions are characteristics of psychosis (PSY) and, they are deeply related to
source monitoring (SM) — the ability to discriminate the origin of internal/external experiences.
Methods: This MOOSE, PRISMA-compliant meta-analysis compared SM performances in PSY compared to healthy
controls (HC) focusing on signal-to-noise discrimination in order to: i) test whether neuroimaging procedures
(fMRI/EEG) might be a group-specific source of noise for SM; ii) compare error- and accuracy-based indexes; iii)
to meta-analyze signal-detection measures (i.e., discrimination index and response bias); iv) to determine the
best index capturing SM deficits in psychosis. We conducted a 3-level meta-analysis for each aim to estimate
pooled effect-sizes (Cohen's d). SM type, source discrimination and stimulus modality were used as meta-
regressors. Heterogeneity (I <sup>2</sup> ), publication bias (Egger's test) and multiple comparisons (Bonferroni correc-
tion) were considered.
Results: Sixteen neuroimaging, 44 error/accuracy-based behavioral and 7 signal-detection trials were included
(2297 PSY, age range = $18.78-52.6$ ; 1745 HC, age range = $21.1-53.3$ ). The noise generated by neuroimaging
procedures slightly influenced error, but not accuracy. Accuracy-based (d = -0.83), but not error-based, indexes
showed significant and large SM impairments in PSY compared to HC. Overall SM performance differences
between PSY and HC were larger in discrimination index (d = $-0.65$ ) and accuracy (d = $-0.61$ ), followed by
response bias (d = $-0.59$ , ns) and error-based (d = $0.35$ ) indexes.
Conclusion: Although both accuracy and discrimination indexes differentiate patients with PSY from HC,
discrimination index is more reliable and may better capture the bi-directional nature of the internal/external
source confusion

### 1. Introduction

The experience of a "tumultuous internal noise" is a prominent feature of psychosis, a clinical condition characterized by impairments in the ability to discern whether our experiences stem from internal mental processes or external stimuli (Fusar-Poli et al., 2022). The cognitive capacity allowing such discernment is referred to as Source Monitoring (SM) (Johnson et al., 1993). SM is a complex, but fundamental activity that plays a key role in differentiating two or more non-self stimuli (external source monitoring), self-generated stimuli from each other (internal source monitoring), or self-generated from other-generated stimuli (reality monitoring) (Mitchell, 2017).

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Several neurological and psychiatric conditions, such as Alzheimer's Disease, Autism and Schizophrenia alter the sense of self and reduce SM performance (Anselmetti et al., 2005; Damiani et al., 2021; El Haj et al., 2012), but with specific differences across conditions. For instance, patients with Alzheimer's disease are more susceptible to external SM errors (El Haj et al., 2012), while deficits in Autism are more linked to alterations in the free recall memory (ie. when no memory clues are presented) rather than to a specific SM type (Damiani et al., 2021). Psychosis, and Schizophrenia in particular, is the disorder in which SM has been most extensively investigated. The presence of psychosis is more linked to externalizing errors, wherein individuals attribute an internal stimulus to external sources, compared to internalizing errors, which involve attributing an external stimulus to internal sources (Brookwell et al., 2013). As an example, patients with psychosis often misattribute words that they have said to others. A recent meta-analysis from our group showed that SM deficits in psychosis are maximized for internal, imagined sources (Damiani et al., 2022). Accordingly, words that have been imagined, rather than spoken, are even more likely to be confused with words said by others. However, some questions are left open, leaving room for further investigation.

First, it has not been determined whether neuroimaging procedures have an influence on SM performance. For example, some auditory noise originating from the MRI scanner is present even when noise-cancelling devices are implemented, and the tactile solicitations from the EEG cap and gel may represent confounding and detrimental factors. Additionally, MRI and EEG procedures involve unusual contexts and require the participant to lie still during the recording, potentially interfering with the attentional processes. Second, the highest deficits in SM performance showed by patients with psychosis compared to healthy controls were observed for accuracy, rather than error measures (Damiani et al., 2022). While accuracy defines the percentage of answers where the source is correctly attributed, errors define the percentage of incorrect answers. At a first glance, accuracy and error measures may appear to be one the inverse of the other. However, according to the Signal Detection Theory accuracy can be measured as hits and/or correct rejections, while errors can be evaluated as false alarms and/or misses. As each of these four indexes may be governed by different neural substrates (Dijkstra et al., 2022), measures commonly used as indicators of overall "SM performance" might actually reflect distinct underlying processes. According to Dijkstra and colleagues, three main neurofunctional systems constantly interact to modulate SM performances. The first system is related to the bottom-up sensory processing operated by the primary sensory cortices (i.e., visuo-auditory cortices). The second system regulates the top-down cognitive control of sensory inputs: dorsolateral prefrontal cortex and orbitofrontal cortex are the main brain regions involved in this process. The third system, source attribution, integrates the previous two operating higher-order inferences, activating salience-related regions in the anterior medial prefrontal cortex. As alterations in each of these mechanisms may generate source confusions, the choice of specific indexes to measure SM performance in each study can significantly impact the observed outcomes.

Several research groups tried to overcome this issue leveraging the signal-detection theory, by which SM is defined as the ability to effectively segregate signals from noise (discrimination index). As opposite, stands systematic response bias, the specific tendency to systematically attribute the same source (either meaningful signal or noise) to all the presented stimuli. These indexes may represent more comprehensive and standardized measures of SM than the ones exclusively based on error and accuracy (see Methods). Furthermore, discrimination index and systematic response bias should better capture SM alterations and their possible underlying mechanisms when patients with psychosis are compared to healthy controls (Rossi et al., 2016). Nevertheless, the results on this topic coming from the empirical literature have never been critically summarized yet. Therefore, there are no definitive conclusions concerning how signal-noise discrimination and/or systematic response bias may account for SM deficits in patients with psychosis compared to

the general population. On the one hand, SM plays a key role in psychosis as a core psychopathological mechanism characterizing this clinical condition (Griffin and Fletcher, 2017). On the other hand, its implementation for clinical purposes remains limited. To bridge this gap, there is a need for a quantitative, comparative synthesis of the literature, encompassing different study designs and experimental contexts and indexes. This would not only help reduce heterogeneity in study designs but also aid in selecting the most suitable outcome measures for assessing treatment approaches for psychosis. Moreover, a meta-analysis of different methodological frameworks for the estimation of SM performances allows to compare indexes and SM systems in order to highlight the most representative psychopathological mechanisms for psychosis.

### 1.1. Aims

According to the previous considerations, the current study aimed at:

- i) summarizing results of SM performances of patients with psychosis (PSY) compared to healthy controls (HC) within EEG and fMRI studies. Our hypothesis was that psychosis may increase the susceptibility to the auditory and tactile noise produced by these experimental contexts due to the presence of sensory gating deficits (Bailey et al., 2021). Wider gaps in SM performance between PSY and HC during neuroimaging procedures should support that SM deficits among PSY patients could be ascribed to alterations of bottom-up sensory processing (Dijkstra et al., 2022);
- ii) comparing error- and accuracy-based indexes concerning SM performances of patients with PSY. The results of this contrast should provide suggestions regarding which SM mechanism between top-down cognitive control of sensory signals (i.e., error rates) and source attribution (i.e., accuracy rates) (Dijkstra et al., 2022) could be more affected in psychosis;
- iii) meta-analysing studies using signal-detection indexes to assess SM deficits among patients with PSY compared to HCs. Metaanalytic results of discrimination index and systematic response bias should reflect the capacity of signal-detection indexes to encompass the main mechanisms underlying SM, including bottom-up sensory processing, top-down cognitive control of sensory signals, and source attribution.

Finally, we aimed at comparing meta-analytic results of signaldetection and error/accuracy-based indexes to evaluate which measure could be considered the gold standard for evaluating SM performances in patients with PSY. This comparison should identify the best index for assessing the efficacy of clinical interventions in psychosis, considering the core psychopathological mechanisms contributing to the onset and persistence of this clinical condition.

### 2. Methods

This study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, 2020) and Metaanalyses Of Observational Studies in Epidemiology checklist (MOOSE) (eTable 1).

### 2.1. Literature search and inclusion/exclusion criteria

Articles were identified on MEDLINE and Web of Knowledge (all databases) from inception until April 30th, 2023. Two researchers (AD and CG) conducted a computerized search using the following search string: "(source monitoring OR reality monitoring OR self-monitoring OR self-related) AND (psych\* OR schizophreni\*)". Endnote X20 version was used to organize and collect data. A manual search by citation chaining was conducted on the relevant studies and additional

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### Table 1

Meta-analytic results of EEG and fMRI studies.

Level 2 N of comparisons	Level 3 <i>N</i> of studies	Moderator	$F (df_{1}, df_{2})$	b	d <sub>w</sub> (95% CI)	Q (df)	τ2 Level 2 <i>I2</i> Level 2	τ2 Level 3 <i>I2</i> Level 3	AIC	BIC	χ <sup>2</sup> (1)	Egger's coefficient 95% Bootstrap CI
Error-based index												
15	6				.26 (19–.71)	24.41* (15)	.00.00%	.14 53.93%	23.87	25.79	5.43*	1.75* (.70–2.95)
15	not considered				.17 (1346)		.11 48.18%		27.31	28.40		
Stimulus modality												
15	6	Auditory Performed Visual	.43 (2, 12)		.49 (25–1.23) .39 (31–1.09) .07 (–.83–.90)	15.62 (12)	.00 .00%	.16 58.76%	23.27	25.26		
Accuracy-based	index											
29	11				83** (-1.31 to34)	98.71*** (28)	.08 14.3%	.41 75.19%	73.88	77.88	6.20*	-1.51** (-2.58 to70)
29	not considered				69** (97 to40)		.33 85.01%		78.08	80.74		
Source discrimination												
29	11	External	4.70* (2, 26)		54* (-1.00 to08)	74.99*** (26)	.07 16.51 %	.29 69.77%	66.22	72.51		
		Internal			$-1.03^{***}$ (-1.38 to							
		Mixed			08) -1.79* (-3.12 to46)							

\*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001.

AIC: Akaike Information Criterion; **BIC:** Bayesian Information Criterion; τ2: heterogeneity variance; ESM: external source monitoring; ISM: internal source monitoring; RM: reality monitoring.

references were included. Inclusion/exclusion criteria were applied following the Population, Intervention, Comparison and Outcomes and Study tool (PICOS)(Amir-Behghadami and Janati, 2020). Inclusion criteria were: i) populations that included subjects with a diagnosis of Schizophrenia Spectrum and Other Psychotic Disorders or Unipolar/Bipolar Mood Disorders with Psychotic Features according to DSM-III/IV/5 or ICD-10/11. Psychosis can be conceptualized as a clinical construct with delusions, hallucinations, and thought disorder as core clinical features (Gaebel and Zielasek, 2022). We included all the diagnoses of psychosis except for the "Schizotypal personality disorder" and the "Psychotic disorder due to another medical condition" DSM-5 categories. The former category includes by definition subthreshold psychotic symptoms, while the latter group of conditions includes dementia, lupus, and other disorders with no aethiological overlap with the Schizophrenia Spectrum (see eMethods for included DSM/ICD codes); ii) studies that administered tasks designed as internal SM, external SM, or reality monitoring; iii) studies should report a comparison between PSY subjects and a control group of healthy individuals; iv) SM tasks should identify a clear source and, they should report accuracyand/or error-based, or signal-detection outcome measures; v) studies included were written in English. Exclusion criteria were represented by: i) studies involving organic/neurological psychosis; ii) unsuitable task paradigm, such as source monitoring studies where only confidence was measured; iii) ineligible groups (i.e., no healthy controls or PSY group with diagnosis other than the codes accepted in eMethods); iv) no clear source differentiation involving external or internal stimuli; v) abstracts, posters and unpublished studies. Corresponding authors were contacted for papers that lacked sufficient statistical data (i.e., mean and SD). Discrepancies were resolved through consensus after involving a third reviewer (SD).

### 2.2. Data extraction

Two independent authors (IB and VG) worked independently and in duplicate to read the full texts and collected the following data: groups characteristics and diagnosis, number of subjects, gender (males %), mean age, instruments used for the evaluation of the clinical and cognitive profiles, duration of illness, and presence of old/new recognitions tasks (ONRT). In these specific tasks, participants were tasked with differentiating between previously presented stimuli (old) and newly presented stimuli during the recognition phase. New stimuli were as external sources as they were not self-generated. Hence, in certain ONRT designs, such as those in which all the old sources were internal, distinguishing between the old/internal sources and the new/ external sources requires performing a SM task. For this reason, as mentioned in inclusion/exclusion criteria, studies where ONRT did not prevent a clear source discrimination between old and new stimuli were included among SM studies. See Fig. 1 for further information.

Task descriptions and main SM findings from each study were systematically collected. Behavioral findings were systematically reviewed in signal-detection and neuroimaging studies.

### 2.3. Measures of SM performance

First, we considered SM performances on a measure level that was based on the stimulus source and on the final answer given by the participant (source discrimination). When considering the self as signal reference, error-based measures capture false alarms (e.g., source = external; answer = internal) and misses (e.g., source = internal; answer = external) responses. Conversely, accuracy measures are focused on the correct identification of sources, namely hits responses (e.g., source = internal; answer = internal) and correct rejections (source = external; answer = external). SM measures that considered both external and internal sources in the same error/accuracy parameter were included as additional category (e.g., some studies summed the accuracy of internal sources to the accuracy of external sources and reported a single accuracy parameter, which we named 'mixed').

With reference to the signal-detection measurements, the discrimination index  $d^{\circ}$  is a sensitivity measure (e.g., hits – false alarms). The higher the  $d^{\circ}$  value, the better the ability to discriminate signal (the real source of stimuli administered during the task) from noise (any other internal or external stimulus that could interfere with the correct identification of source). On the contrary, the response bias  $\beta$  or c captures the systematic tendency to identify signals rather than noise (hits + false alarms). For a detailed description of different methods for computing  $d^{\circ}$ ,  $\beta$  and c see Stanislav and Todorov (Stanislaw and Todorov, 1999). A



Fig. 1. Description of the error, accuracy and signal detection indexes according to how the original stimulus (Source) is recognized (Answer). Please note that \*signal-detection parameters use rates, not absolute values, for each measure.

visual and formal representation of accuracy, error and signal-detection measures is given in Fig. 1.

Considering that d' and  $\beta$  are given by hits and false alarms, they combine accuracy and error parameters. This feature did not allow to categorize external SM, internal SM and reality monitoring on a measure level. Thus, we determined the SM type on a study level by considering the alternatives given in the recognition phase by the task design. When the possible answers were all internal stimuli, the study was classified as internal SM. When the alternatives were all external stimuli, the study was classified as external SM. When both internal and external stimuli were available as alternatives, the study was classified as reality monitoring.

A separate categorization of SM stimuli is based on the stimulus modality (Damiani et al., 2022). External sources were presented as either auditory or visual stimuli (hearing or seeing a word, for example). On the other hand, internal sources were categorized as imagined or performed, encompassing activities like thinking about a word or writing it down, respectively.

### 2.4. Strategy for data synthesis

The current meta-analysis was based on the Cohen's d coefficient as an effect size measure. Values of d greater than or equal to 0.20, 0.50, and 0.80 were interpreted as small, moderate, and large effect sizes, respectively (Cohen, 1992). The index was primarily calculated using the descriptive statistics reported in the Results section of each study. Multiple experimental conditions were administered within each study generating multiple effect-sizes for each experimental context. Accordingly, a nested structured of data should be assumed. Therefore, we conducted a 3-level meta-analysis using the *metafor R* package in order to adequately estimate pooled effect sizes  $(d_w)$  taking into account interrelationships among the effect-sizes nested within a single study (Viechtbauer, 2010). The estimation of model parameters was based on the restricted maximum-likelihood method (Harrer et al., 2021). Starting from comparisons between PSY and HC (group - level 1), it was assumed that effects-sizes of each comparison (measure - level 2) were nested within each study (study - level 3). To further strengthen the reliability of the results, Bonferroni correction of p-values was applied when multiple contrasts were computed among the pooled effect-sizes

found through the application of multi-level approach. Heterogeneity in effect sizes was computed through Q statistic (Hedges and Olkin, 2014) and a multilevel version of  $I^2$  index (Cheung, 2014). The advantage of conducting a 3-level model was statistically demonstrated by comparing the Akaike (AIC) and Bayesian Information Criterion (BIC) as indexes for the best goodness of fit to data. To do so, we performed a Likelihood Ratio Test of a 3-level model with a reduced 2-level model, namely a model that assumes a null impact of specific experimental contexts on SM performances. This approach should effectively test whether SM performances of PSY might be modulated by specific experimental contexts or, alternatively, they are context-independent, suggesting their key role as core feature of such clinical condition.

In presence of significant heterogeneity in effect sizes, the 3-level, mixed-effect models were estimated to test the impact of several variables on effect-size. The same approach was used for the computation of  $d_w$  of studies that assessed signal-detection indexes.

Referring to the impact of experimental procedures (i.e., EEG/fMRI vs pure behavioral) on SM performances, we compared the goodness of fit of two distinct data structures. First, it was postulated that the effect-sizes of each comparison (level 2) related to error-based and accuracy-based measures were nested within experimental procedures (i.e., neuroimaging vs pure behavioral) (level 3). Alternatively, effect-sizes (level 2) were nested within each study (level 3) and experimental procedures were included as possible moderators of effect-sizes.

The considered moderators were: SM type of the task design (external SM, reality monitoring; no studies with pure internal SM were found in the literature), Source discrimination (external, internal, reality monitoring), stimulus modality (visual, auditory, performed, imagined), study/sample characteristics (year of publication, sample size, years of illness).

Egger's regression (Egger et al., 1997) was estimated to detect publication biases. Bootstrap methodology (i.e., bias corrected and accelerated) (Davison and Hinkley, 1997) was applied in computing the significance of the previous parameter. The Z-test procedure (Borenstein et al., 2021) was applied in order to compare pooled effect-sizes for each index reflecting differences between PSY and HCs in SM performances. To further strengthen the reliability of the results, Bonferroni correction of *p*-values was applied when multiple contrasts were computed among the pooled effect-sizes.

### 2.5. Quality assessment

The Newcastle-Ottawa Scale (NOS, see eMethods) was implemented to assess each study quality. It considers criteria of selection, group comparison and statistical analysis (maximum score = 9) (Wells et al., 2000).

### 3. Results

### 3.1. Systematic review

The literature search yielded 6645 records. Twenty additional studies were manually added (total n = 6088). After removing duplicates, we screened the title of 6540 citations and 351 abstracts were selected. Among these studies, 44 were included as clinical-behavioral SM studies with accuracy/error-based measures. Moreover, 51 full texts were assessed for eligibility in signal-detection (20 studies) and neuroimaging (31 studies). Twenty-three case-control articles were finally included for data extraction and systematic review, including 7 signal-detection (Anselmetti et al., 2005; Brebion et al., 2020; de Sousa et al., 2016; Harvey, 1985; Radaelli et al., 2013; Salomon et al., 2020; Schimansky et al., 2012), 12 MRI/fMRI (Allen et al., 2007; Fu et al., 2008; Garrison et al., 2017; Hawco et al., 2015; Kambeitz-Ilankovic et al., 2013; Kumari et al., 2010; Ragland et al., 2006; Subramaniam et al., 2012, 2017; Thoresen et al., 2014; Vinogradov et al., 2008; Wang et al., 2011) and 4 EEG (Abhishek et al., 2018; Nelson et al., 2020; Posada et al., 2007; Tikka et al., 2017) studies (PRISMA flow chart in eFig. 1).

### 3.2. Sample characteristics and study design

The overall sample included 731 PSY (403 in neuroimaging studies, 328 in signal-detection studies) and 570 HC (301 in neuroimaging studies, 269 in signal-detection studies). The age range was 18.78–41.06

#### Table 2

Error- and accuracy-based indexes together with effects of experimental contexts

for PSY and 21.09–45.00 for HC. Males were more prevalent than females: the mean percentage of males was 77.85% for PSY and 75.19% for HC. The instruments used for the evaluation of clinical and cognitive profiles were heterogeneous. Full details for each study are collected in eTable 2 and a systematic review of the included studies, other relevant descriptive statistics and categorizations of study designs are presented in eResults, eTable 3 and eTable 4.

SM tasks were structured in two phases. The first one was a presentation phase, where the stimuli were presented to participants and the second one was a recognition phase. For neuroimaging studies, the SM task was performed during fMRI or EEG (see eTable 5 for task descriptions). The overall quality of studies as assessed with NOS was high (mean NOS score 7.43 over 9, see eTable 6).

Data on studies implementing accuracy and error measures of SM performance were taken from our previous meta-analysis (1566 PSY and 1175 HC; age range: PSY: 19.9–52.6, HC: 21.1-53.3; % male: PSY: 65.9, HC 65.6; mean NOS = 7.41) (Damiani et al., 2022).

A detailed description of the group differences in neuroimaging and signal-detection studies can be found in the eResults section.

### 3.3. Meta-analysis

3.3.1. Aim 1: SM performances within fMRI and EEG studies – alterations of bottom-up sensory processing

Table 1 provides a synthesis of the results from the best fit metaanalytic models (for full results see eTable 7). Considering error-based measures, no significant differences between PSY and HCs. Effect sizes were heterogeneous across studies, but not within study. The best fit meta-analytic model included the characteristics of stimuli (i.e., auditory, performed visual) as moderators. The inclusion of these moderators explained the heterogeneity of results detected in the basic metaanalytic model. However, significant publication biases were detected (Egger's coefficient: 1.75 [0.70–2.95]; p = 0.02).

Looking at accuracy-based indexes, the analyses found large and

and accuracy-based indexes together with effects of experimental contexts.												
Level 2 N of comparisons	Level 3 N of studies	Moderator	F (df <sub>1,</sub> df <sub>2</sub> )	b	d <sub>w</sub> (95% CI)	Q(df)	τ2 Level 2 <i>I2</i> Level 2	τ2 Level 3 <i>I2</i> Level 3	AIC	BIC	χ <sup>2</sup> (1)	Egger's coefficient 95% Bootstrap CI
Error-based ind	ex											
218	40				.35*** (.20 - .50)	90.37 (217)	.00 .00%	.05 7.24%	618.36	628.50	8.02**	
218	not considered				.33*** (.21 - .45)		.05 7.38%		624.38	631.14		.33** (.1050)
Accuracy-based	index				,							
168	39				61*** (73 to 49)	344.54*** (167)	.10 44.42%	.03 14.05%	362.92	372.28	5.10*	-69** (97 to 43)
168	not considered				58*** (68 to 49)		.14 58.22%		368.02	377.37		
Stimulus modality					,							
168	39	Auditory			73*** (95 to 52)	301.24*** (163)	.07 28.87%	.06 27.56%	344.29	365.94		
		Imaginary	6.55***		-1.04*** (-1.37 to 71)							
		Mixed	(4, 103)		$93^{***}$ (-1.40 to							
		Performed			40) 66*** (87 to							
		Visual			–.45) –.38** (–.61 to –.15)							

\*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001.

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; 72: heterogeneity variance; ESM: external source monitoring; ISM: internal source monitoring; RM: reality monitoring.

significant SM deficits in PSY patients compared to HC ( $d_w = -0.83$ ; p = 0.001). However, the heterogeneity was significant, especially considering the between-study variability. Moreover, a publication bias was detected (Egger's coefficient: 1.51 [-2.58 to -0.70]; p = 0.006). The best fit model included the source of discrimination as moderators (i.e., external, internal, internal + external). No significant differences among pooled effect sizes related to the different source of discrimination were detected. The heterogeneity remained significant between studies.

*3.3.1.1. Aim 1: synthesis of the results.* The hypothesis that alterations of bottom-up sensory processing could sustain SM deficits among PSY patients was not supported considering error-based measures as shown by the absence of significant differences in SM performances between PSY and HC. On the contrary, the large difference found in accuracy-based indexes suggested that other mechanisms may better explain SM deficits characterizing PSY patients.

# 3.3.2. Aim 2a: error/accuracy-based SM performances and effects of experimental contexts –top-down control of sensory signal and source attribution

Table 2 provides a description of the most representative metaanalytic results based on the combination of SM performances within pure behavioral (see eTable 3 and 4 for a description of the task designs), fMRI and EEG experimental contexts. Full results are reported in eTable 8.

Referring to error-based indexes, PSY patients performed worse than HC ( $d_w = 0.35$ ; p < 0.0001). Results were consistent between studies and within the same study. The Egger's regression suggested publication biases (Egger's coefficient: 0.33 [0.10–0.50];  $\underline{p} = 0.009$ ).

Results of accuracy-based indexes showed that hit rates were moderately lower in PSY compared to HC ( $d_w = -0.61$ ; p < 0.0001). However, there was a significant heterogeneity of findings between studies and, a small variability within each study. The best fit meta-analytic model included the stimulus modality as a moderator. Accordingly, the accuracy of PSY patients was worse for imagined stimuli compared to visual (Z = -3.17; p = 0.0007). However, a publication bias was found (Egger's coefficient: 0.69 [-0.97 to -0.43]; <u>p</u> = 0.001).

### 3.3.3. Aim 2a: synthesis of the results

No significant impact of the experimental context on SM performance was detected. This provides additional evidence against the hypothesis that alterations in the bottom-up sensory processing may determine SM deficit in psychosis. Conversely, the significant pooled effect sizes for error- and accuracy-based indexes suggested that alterations of cognitive control of sensory signals and source attribution could be mechanisms underlying SM deficits.

## 3.3.4. Aim 2b: comparisons among error- and accuracy-based measures of SM performance – top-down cognitive control or source attribution?

Overall, the differences between PSY and HC in SM performances were significantly larger for accuracy-based (i.e., hit-rates) than errorbased (i.e., false alarms and misses) (Z = 2.60; p = 0.004). With respect to the characteristics of stimuli, SM impairments reveled in PSY group were more severe for accuracy rates than error measures considering auditory (Z = 2.79; p = 0.002) and imagined stimuli (Z = 3.17; p = 0.0007), but less severe for performed (Z = 2.28; p = 0.010, not significant after Bonferroni correction) and visual stimuli (Z = 0.21; p = 0.420).

3.3.4.1. Aim 2b: synthesis of the results. As accuracy-based indexes in PSY were more impaired than the error-based ones, source attribution might be considered the most impaired systems in psychosis. However, the alterations of source attribution seemed to be a function of sensory characteristics of stimuli. Specifically, impairments for visuo-motor

stimuli were less evident compared to auditory-verbal and/or imagined stimuli.

3.3.5. Aim 3: SM performances and signal-detection: discrimination/ sensitivity index and systematic response bias as a comprehensive measure of SM mechanisms

Fig. 2A summarizes results of meta-analytic models concerning SM performances estimated by signal-detection indexes. PSY patients showed lower values of *d*' than HC ( $d_w = -0.65$ ; p = 0.0001). Results were consistent across studies and within the same study. The pooled effect-size of *d*' was not statistically different from the accuracy-based one (Z = 0.00; *ns*) and larger than the error-based one (Z = 1.76; p = 0.04, not significant after Bonferroni correction). Looking at  $\beta$  index, patients with PSY showed lower, albeit not significant, values than HCs (d = -0.59; *ns*). Results were consistent across studies and within the same study. Egger's regressions did not reveal publication biases. Fig. 2B shows pooled effect-size of SM performances and signal-detection indexes.

3.3.5.1. Aim 3: synthesis of the results. The consistency of results together with no significant differences between pooled effect sizes of signal-detection and error/accuracy-based indexes suggested that discrimination indexes and systematic response bias should be considered valid measure that reflect the integration of key mechanisms (i.e., top-down cognitive control and source attribution) involved in SM performances.

### 4. Discussion

The present work is the first to directly compare different indexes in SM while considering the different experimental procedures of each study. This was chosen in order to clarify which underlying mechanisms - bottom-up sensory processing, top-down cognitive control of sensory signals, source attribution - might be more representative for deficit in SM among patients with PSY. While accuracy deficits in PSY were stable across pure behavioral, EEG and MRI modalities, the differences in SM errors between PSY and HC could be slightly affected by the experimental procedures. Accuracy-based indexes are significantly more impaired than error-based indexes. The source of discrimination and characteristics of stimuli are moderators of accuracy performances, determining higher SM deficits in PSY patients compared to HC. On the one hand, d' index and accuracy measures showed moderate-to-large SM deficits among PSY patient compared to HC. On the other hand, these deficits are less evident considering  $\beta$  and error measures. Important considerations can be drawn from this evidence.

## 4.1. Neuroimaging: the impact of external and internal noise on SM in healthy controls and psychosis

Our research question considered neuroimaging conditions as potential sources of external auditory and tactile noise while performing a SM task. This was hypothesized based on previous meta-analytic evidence that showed how noise stress significantly reduces cognitive performances in HC, including signal detection (Wright et al., 2014). This work also posited that patients with PSY may be even more susceptible to noise stressors than the general population, although the pilot trial designed to confirm this hypothesis found similar noise-induced deficits in schizophrenia and HC (Wright et al., 2016). Furthermore, other studies observed similar noise-induced deficits among individuals with high vulnerability to psychosis and HCs (Urbańska et al., 2019). Accordingly, the type of SM deficit may be detrimental to identify which type of noise has a greater impact in psychosis. Indeed, results showed that signal-detection and accuracy measures were not affected by EEG or MRI. Conversely, the number of SM errors slightly increased among HC, but not in the PSY group during

A)	Meta-analytic results of Signal Detection Theory indexes#										
Level 2	Level 3	d <sub>w</sub>	Q	$ au^2_{\text{Level 2}}$	$ au^2$ Level 3	AIC	BIC	χ <sup>2</sup> (1)	Egger's coefficient		
N of comparisons	N of studies	(95% CI)	(df)	$I^2$ Level 2	$I^2$ Level 3				95% Bootstrap CI		
Discrimination/sensitivity (d') index											
15	6	65*** (9436)	4.64 -14	0 0.00%	0 0.00%	31.93	33.84	0	-0.06 (4243)		
15	not considered	65*** (9436)		0 0.00%	-	29.93	31.21	0			
Response bias (β)											
	3	-0.59	0.58	0	0	42.27	44.19		-0.23		
15		(-1.2511)	-14	0.00%	0.00%				(5203)		
15	not considered	not estimated due to excessive heterogeneity									
***p<.001;						2					

**AIC:** Akaike Information Criterion; **BIC:** Bayesian Information Criterion;  $\tau^2$ : heterogeneity variance; #: Moderator, F(df1,df2) and b not estimated due to insufficient number of comparisons/studies.



**Fig. 2.** A) Meta-analytic results showing signal detection indexes. While discrimination index and response bias show similar magnitudes of effect sizes for SM performance differences (HC: healthy controls > PSY: patients with psychosis), only discrimination index is reliable across measurements and/or studies. B) Bar plot depicting the overall effect sizes indicating reduced source monitoring performance in HC compared to PSY.

neuroimaging procedures. This finding has a limited strength as it reflects a trend that was found only for error-based measures. However, it suggests that the ambivalence between imagination and reality may stem from an internal systematic noise, rather than external and contextual noise. Accordingly, this provisionally support the hypothesis that the neurofunctional system related to bottom-up sensory processing should be preserved among individuals with PSY. Consistently, our previous meta-analysis showed a specific SM deficit in psychosis for imagined stimuli (Damiani et al., 2022), which is further supported by the neuroimaging findings included in the current review: Abhishek et al. (2018) observed a significant reduction of the P300 amplitudes among individuals with PSY in several brain areas, but only during the internal SM task. Similarly, another study found that internal SM accuracy was systematically decreased independently of the mood induction to which the participants were exposed, while external SM deficits were more contextual. Indeed, external SM deficits in PSY were observed after neutral mood induction, but not after negative or positive mood induction (Fu et al., 2008; Subramaniam et al., 2017).

### 4.2. Comparison of error, accuracy and signal-detection measures

Accuracy-based measures better capture the SM performance deficits in patients with PSY compared to HC. signal-detection measures did not show different effect-sizes compared to accuracy indexes, but *d'* had a better reliability as shown by the high consistency of results across studies and the absence of a publication bias. Accuracy and error indexes measure a contextual error that considers whether the answer is correct or wrong. Conversely, signal detection indexes consider the *relationship* between the correct recognition of sources (hits) and the tendency to confound the noise for a signal (false alarms). According to the dramatic increase of cognitive and perceptual externalizations of inner thoughts characterizing patients with PSY, *false alarms* can be interpreted as the tendency of patients with psychosis to experience irrelevant stimuli, both internal and external, as actual signals. Therefore, the present data support the hypothesis that source attribution represents the core altered mechanism involved in SM deficits in psychosis.

Signal-detection measures may better detect this deficit as they correct accuracy rates by the false alarms rate. Indeed, signal-detection results were consistent both across studies and within the same study, and they did not show any evidence of publication biases. This was not the case for error/accuracy studies. Despite the small number of studies, the significant SM deficits revealed by the *d*' index further support the implementation of this measure as a standard proxy for the evaluation of SM among subjects with PSY. Similar findings in terms of effect-size have been observed for the  $\beta$  index. However, the number of studies. (n = 3) may have affected the statistical power of these last analyses.

# 4.3. Integrating the present findings with the neural mechanisms of source monitoring

Novel theories focused on reality monitoring proposed that internal stimuli are normally characterized by lower neural strength/precision, stronger cognitive control, lower predictability and, they arise from different brain regions if compared to external stimuli (Dijkstra et al., 2022). Dijkstra and colleagues have stressed this point to emphasize that reality monitoring has a recurrent nature that is sensitive to imbalances at any level of the processing hierarchy. For instance, self-generated stimuli selectively recruit frontal cognitive areas, while sensory inputs directly impact primary sensory regions. However, the source of signal is transmitted to other areas on the base of a complex system of feedbacks and feedforwards among sensory regions that are secondarily activated by internal stimuli (Aitken et al., 2020). For the same mechanism, external stimuli can modulate the activity in higher control regions associated to imagined thoughts. Therefore, the direction of a stimulus' processing is crucial to discriminate its source (Dijkstra et al., 2020). Altered neuronal activations or dysconnectivity in the regions deputed

to SM may alter or reverse the information flow, resulting in ambivalence between internal and external sources (Mechelli et al., 2007; Wang et al., 2011). This is consistent with our hypothesis that World/Self Ambivalence is given by imbalances of internal and external pressures mirroring altered brain dynamics such as activation or connectivity. We also predicted that the main regions involved in this process pertain to default mode (DMN), salience, and primary sensory processing networks (Damiani et al., 2020). A recent systematic review on the neural correlates of SM deficits in schizophrenia outlined converging evidence for the involvement of medial prefrontal cortex (DMN/salience), hippocampus (DMN), anterior cingulate/paracingulate sulcus (salience network) and superior temporal gyrus (sensory)(Kowalski et al., 2021). As opposed to HCs, areas in the medial prefrontal cortex were not activated in response to the recognition of self-generated stimuli in patients with schizophrenia (Subramaniam et al., 2017; Thoresen et al., 2014; Vinogradov et al., 2008). Conversely, superior temporal gyrus (sensory region) showed a heightened activity in patients with schizophrenia compared to controls (Kumari et al., 2010; Wang et al., 2011). In these examples of SM tasks involving self-generated stimuli, the cognitive areas from which internal stimuli originate are less activated in schizophrenia compared to HC, while sensory areas are hyperactivated. Therefore, atypical information flow may derive from either of the two processes altering the regions deputed to segregate self signals from non-self noise.

These premises may explain why  $d^{*}$  is even more reliable than accuracy in detecting the SM deficits of patients with PSY compared to HC. Indeed, rather than simply describing the percentage of right or wrong answers, it considers the *distance* between the signal and the noise. The higher the distance, the better two sources can be discriminated. Hence, when the distance shortens, the ambivalence between the sources increases. More importantly, this distance may be reduced either by a reduced ability to capture the signal (<hits) or a higher sensitivity to noise (> false alarms). A combination of these parameters may reflect the neuronal recurrence between self, cognitive and sensory areas better than single accuracy or error measures (Fig. 3).

### 4.4. Limitations

The present study has some limitations. First, the meta-analyzed studies are heterogeneous and some parameters are underrepresented. For instance, no neuroimaging or signal-detection studies were designed to include only internal SM tasks. This did not allow to test whether internal SM is the most compromised SM type in psychosis in studies using neuroimaging procedures and signal-detection indexes. Similarly, systematic response bias has been underinvestigated and thus it could not be thoroughly discussed. On the one hand, a growing body of evidence is allowing to clarify the neurobiology of SM in the general population. On the other hand, very few studies including patients with PSY or similar conditions have been conducted in the last 2 years. Ultimately, almost no study directly compared error, accuracy and signal-detection indexes within the same sample. As guidelines for future research, studies should consider direct comparisons to select which indexes are more useful or applicable in the clinical context. Direct comparisons between different disorders may contribute to define the clinical specificity of SM deficits across psychiatric conditions.

### 5. Conclusion

The noise generated by neuroimaging procedures slightly influences error, but not accuracy. This provisionally excluded deficits in bottomup sensory processing. While both accuracy and discrimination indexes well differentiate patients with PSY from HC, results detected by discrimination index are more consistent and less heterogeneous. This could suggest that alterations in source attribution should be regarded as the primary mechanism in individuals with psychosis. Coherently, the discrimination index was the most reliable proxy of SM and it may



### **Example for source = internal stimulus**

Fig. 3. Visual representation of how alterations in the neuronal functioning may influence source monitoring. A) An internally-generated stimulus (i.e., a thought) is correctly recognized as originating from the Self, preserving the world-Self boundary. B) Deficits in different brain regions may act independently or in synergy to reduce the discrimination index. The impossibility to segregate internal from external stimuli and viceversa may thus result in symptoms linked to world/Self ambivalence such as delusions and hallucinations.

capture the recurrent, bi-directional nature of the source confusion.

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### Authors contributions

SD designed the theoretical framework and the logic of the study. MC analyzed the data and together with SD wrote a first draft of the

manuscript that was critically revised by AS, PP and PF. AD, CG, VG, IB and UP conducted the online research of studies. All authors approved the final version of the manuscript.

### Declaration of competing interest

Declare my interest in submitting the scientific paper titled The noise in our brain: a systematic review and meta-analysis of neuroimaging and signal-detection studies on Source Monitoring in psychosis" to Journal of Psychiatry Research. I affirm that I have no conflicts of interest, financial or otherwise, that could influence the objectivity and integrity of the research presented in this paper.

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### Appendix A. Supplementary data

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