

Review Article

Aberrant Salience Inventory: A meta-analysis to investigate its psychometric properties and identify screening cutoff scores

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Introduction

The Aberrant Salience Inventory (ASI) is a useful tool to measure salience abnormalities among the general population. There is strong clinical and scientific evidence that salience alteration is linked to psychosis. To the present day, no meta-analysis evaluating ASI's psychometric properties and screening potential has been published.

Materials and Methods

PubMed, Google Scholar, Scopus, and Embase were searched using terms including “psychosis,” “schizophrenia,” and “Aberrant Salience Inventory.” Observational and experimental studies employing ASI on populations of non-psychotic controls and patients with psychosis were included. ASI scores and other demographic measures (age, gender, ethnicity) were extracted as outcomes. Individual patients' data (IPD) were collected. Exploratory factor analysis (EFA) was performed on the IPD.

Results

Eight articles were finally included in the meta-analysis. ASI scores differ significantly between psychotic and non-psychotic populations; a novel three-factor model is proposed regarding subscales structure. Theoretical positive predictive values (PPVs) and negative predictive values (NPVs) were calculated and presented together with different cutoff points depending on preselected specific populations of interest.

Discussion

PPV and NPV values reached levels adequate for ASI to be considered a viable screening tool for psychosis. The factor analysis highlights the presence of a novel subscale that was named “Unveiling experiences.” Implications regarding the meaning of the new factor structure are discussed, as well as ASI's potential as a screening tool.

Key words: Psychotic disorders, psychometric, early medical intervention, psychopathology, meta-analysis.

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INTRODUCTION

In the last decade there has been an increase in data regarding salience alterations and their relevance to psychosis psychopathology (Godini *et al.*, 2015; Kapur, 2003). Salience is not a new concept; the observation and description of some of the features associated with this entity date back to Jaspers and Conrad (Mishara, 2010; Mishara & Fusar-Poli, 2013; Sass & Ratcliffe, 2017).

Salience is nowadays defined in psychology and neuroscience as the “relevance” that a perceived object acquires for the subject who perceives it. This process involves raw sensorial stimuli as well as cognitive or emotional states (Damiani *et al.*, 2020). Salience is what allows individuals to correctly distinguish between important and negligible internal and external inputs. In neuroscientific terms, salience regulation is often attributed to the VTA (ventral tegmental area) system and its dopamine interplay with basal ganglia (Lin, Liang & Luo, 2021).

According to Kapur (Kapur, 2003), many symptoms of psychosis might be framed as epiphenomena of salience alterations; for example, delusions can be described as attempts to fit abnormally salient experiences within one's own world view.

In that way, salience alterations pertain to the spectrum of positive psychotic symptoms (Azis *et al.*, 2021; Chun, Brugger & Kwapil, 2019), which constitute some of the best estimators to predict the onset of psychosis (Fusar-Poli *et al.*, 2020; Oliver *et al.*, 2020). Hallucinations might originate from a similar psychopathological process as well, reflecting a direct experience of the aberrant salience of internal representations. Neuroscientific evidence also supports this theory (Duek, 2021; Gregory *et al.*, 2021). Moreover, antipsychotic treatment seems to partially reduce these brain connectivity changes (Gregory *et al.*, 2021).

In the past few years, a significant amount of quantitative data has been gathered on salience alterations. One of the main tools employed to investigate this phenomenon is the Aberrant Salience Inventory (ASI; Cicero, Kerns & McCarthy, 2010): Its psychometric properties seem to make it a suitable instrument for early detection of psychosis as evaluated in different settings (Pelizza *et al.*, 2021; Raballo *et al.*, 2019) and countries (Golay *et al.*, 2020; Rodríguez-Testal *et al.*, 2022). ASI is clinically relevant in ultra-high-risk subjects (UHR) as well, with no differences in scores with first-episode-of-psychosis (FEP) patients (Azzali *et al.*, 2022; Poletti *et al.*, 2022); furthermore, its

usefulness is underlined by the fact that attenuated positive symptoms are the principal risk factors for psychosis onset in high-risk individuals (Oliver *et al.*, 2020).

ASI's score is highly correlated to quantitative measures of schizotypy, such as the Perceptual Aberration Scale (Chapman, Chapman & Raulin, 1978) and the Magical Ideation Scale (Eckblad & Chapman, 1983), as shown in recent literature (Cicero *et al.*, 2010). Because schizotypy is the prelude to overt psychosis in many instances (Fonseca-Pedrero *et al.*, 2021), the value of this scale as a screening tool for psychosis proneness might prove to be coherent.

The relationship between aberrant salience measurement and cognitive processes such as reward processing has also been investigated, with non-definitive evidence showing that aberrant salience might also be related to effort expenditure toward low probability, low rewards opportunities as compared with controls (Neumann, Glue & Linscott, 2021). Moreover, there is evidence supporting that tetrahydrocannabinol, a known psychotomimetic substance, might alter both reward and salience processes (Gunasekera, Diederer & Bhattacharyya, 2022). This relationship between aberrant salience and reward processing, though, is still under debate; as an example, it has not been confirmed in a general population sample (Neumann & Linscott, 2018).

Other questionnaires investigating similar psychological phenomena can be employed in the evaluation of patients with psychosis or UHR, most prominently the Perceptual Aberration Scale (Chapman *et al.*, 1978; Fornasari *et al.*, 2015) and the Referential Thinking Scale (Lenzenweger, Bennett & Lilienfeld, 1997); however, as the ASI's main scope is nominally Aberrant Salience, it is arguably the most indicated and up-to-date questionnaire to evaluate this construct. In fact, both the Perceptual Aberration Scale and the Referential Thinking Scale refer to a related but different construct, namely schizotypy (Coleman, Levy, Lenzenweger & Holzman, 1996; Lenzenweger *et al.*, 1997). In addition, the Salience Attribution Test (Schmidt & Roiser, 2009) is a reaction time game that assesses implicit and explicit measures of adaptive and aberrant salience measures, but results concerning association between explicit aberrant salience and schizotypy are controversial.

Aims

To date, no meta-analysis summarizing ASI's studies on patients with psychosis has been conducted. The main objectives of the present study are the following:

- Confronting ASI scores from controls and patients with psychosis
- Evaluating the factor structure of ASI
- Detecting the potential presence of publication bias and estimating heterogeneity across studies
- Understanding ASI's potential as a screening tool for psychosis

MATERIALS AND METHODS

The present meta-analysis and systematic review follows PRISMA 2020 guidelines (Page *et al.*, 2021).

Eligibility criteria

Inclusion criteria were observational or experimental study, either cross-sectional or longitudinal, with at least one cohort of adult (>18 years old) subjects experiencing psychotic symptoms assessed with DSM-IV, ICD-10, or MINI criteria. Exclusion criteria were the study being a systematic review, a meta-analysis, an opinion article, a case report, an animal study, or methodological or technical contributions with no analysis over clinical data.

Information sources and search strategy

Several databases were used. Different strings were used for the databases, in order to optimize the search on different search engines; the Pubmed string was devised in order to select as much literature as possible, while the Google Scholar one was more stringent, as the latter database provides a larger data set of "gray" literature that we did not intend to include (Haddaway, Collins, Coughlin & Kirk, 2015).

("aberrant salience") AND (schizophrenia OR psychosis OR psychotic), Pubmed

("aberrant salience inventory") AND (schizophrenia OR psychosis OR psychotic), Google Scholar

("aberrant salience") AND (schizophrenia OR psychosis OR psychotic), Scopus

("aberrant salience") AND (schizophrenia OR psychosis OR psychotic), Embase

No limits were applied for language. The last search was run on 10 February 2023.

Selection process

Four authors (O.B.B., G.P.M., V.P., I.F.) independently assessed titles and abstracts of potentially eligible studies. Eligibility assessment was performed in an unblinded standardized manner. If there was doubt about whether the study was eligible for inclusion, the reviewers examined the full text of the articles. The published protocol required consensus in case the authors disagreed on the inclusion of a specific study. In case the opinion was not unanimous, a majority vote would have been taken between all authors. The authors agreed on all the eligibility assessments of the studies, and no consensus vote needed to take place.

Data collection and processing

Four authors (O.B.B., G.P.M., V.P., I.F.) independently extracted seven categories of data from each included study: study design (interventional, observational), sample size, diagnostic tool for schizophrenia and/or psychosis, control type, ASI scores for both the psychosis group and the control group (mean and standard deviation). Whenever the relevant data was not clearly shown, authors were directly contacted through email.

The main outcome effect that was taken into account during the statistical analysis was Cohen's *d*. The meta-analysis and graph plotting were performed through the R package "meta," version 6.1-0 (Balduzzi, Rucker & Schwarzer, 2019). Meta-regression analysis was deemed not appropriate to be performed, as per the Cochrane guidelines (Cumpston *et al.*, 2019), since there were fewer than 10 studies at the end of the selection process; moderator variables and confounding factors were nevertheless discussed in a less formalized manner in the discussion. Cronbach's alpha was extracted from every study included, when reported, in order to evaluate ASI's reliability.

Differences in ASI scores among psychotic and non-psychotic patients were evaluated through common and random-effects meta-analysis that accounted for between-study heterogeneity. Between-study heterogeneity was assessed by standard χ^2 tests and the I^2 statistic. Statistical significance was set at the two-tailed 0.05 level for hypothesis testing.

The corresponding authors of the included studies were contacted through mail in order to ask for the raw data, with the intention of performing an Individual Patient Data (IPD) meta-analysis (Debray *et al.*, 2015). A ROC curve was computed and plotted on IPD using the R

package “pROC” (Robin *et al.*, 2011). Theoretical positive predictive values (PPVs) and negative predictive values (NPVs) were calculated according to different prevalence rates (Zimmerman, 2022), in order to estimate ASI’s efficacy for psychosis screening in different populations; prevalences were extracted from a previous meta-analysis on other screening tests for psychosis (Fusar-Poli *et al.*, 2015).

IPD data were employed in order to perform an exploratory factor analysis (EFA) through the R package “psych” (Revelle, 2013). Since previous studies (Golay *et al.*, 2020) showed that ASI items are positively correlated, an oblique rotation (“promax”) was chosen. The optimal number of factors was determined through the use of a Scree graph (Ledesma, Valero-Mora & Macbeth, 2015), plotted through SPSS 2.5 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp, 2020).

Risk of bias

Four authors (O.B.B, G.P.M., V.P, I.F.) independently assessed risk of bias for individual studies using the STROBE checklist for observational studies (von Elm *et al.*, 2007). In case the opinion was not unanimous, a majority vote would have been taken between all authors. The four authors agreed on all the eligibility assessments of the studies, and no consensus vote needed to take place. The risk of bias graphs (Supplementary Material S1–S3) were plotted through the R package “robvis” (McGuinness & Higgins, 2021). The publication bias was quantified formally through Egger’s test and funnel plots, plotted with the R package “meta” (Balduzzi *et al.*, 2019).

RESULTS

Overview

Overall, a total of 895 studies were found after running the search line. Among these, 172 were found on PubMed, 201 on Google Scholar, 202 on Scopus, and 320 on Embase. Four-hundred and seventeen of them were excluded as duplicates, and 453 were excluded after title/abstract screening and application of inclusion criteria. Twenty-five full-text papers were thus screened. Eight studies were finally selected (Ceaser & Barch, 2016; Cicero *et al.*, 2010; Golay *et al.*, 2020; Lelli *et al.*, 2015; Martinelli, Rigoli, Dolan & Shergill, 2018; Neumann *et al.*, 2021; Poletti *et al.*, 2022; Rodríguez-Testal *et al.*, 2022), all of them being observational studies (Fig. 1). In order to gather and integrate relevant data, it was necessary to reach out to the authors of two of the studies included, with satisfactory results.

The data extraction is shown in Table 1. Four authors provided raw data for the patient-level meta-analysis, for a total of 1,960 subjects, 294 of whom were in the psychotic group and 1,660 in the non-psychotic control group (Cicero *et al.*, 2010; Golay *et al.*, 2020; Lelli *et al.*, 2015; Rodríguez-Testal *et al.*, 2022). Risk of bias assessment is shown in Supplementary Material S1–S3.

Sociodemographic factors

The mean weighted age among the psychotic group was 34.22 years old (weighted *SD*: 10.78), while in the control group the mean weighted age was slightly lower (27.32, weighted *SD*: 3.86), in line with the current epidemiological evidence concerning overt psychosis incidence (McGrath *et al.*, 2016), but drifting away from the existing evidence about FEP (Kirkbride

et al., 2017). The percentage of males versus females was 59.08% male in the psychotic group and 32.9% male in the control group. Four studies provided data on the sample ethnicity; among these, 80.23% of the participants were of European descent, 14.97% African American, 2.82% Asian, and 1.41% Maori. No other data on ethnicity was obtainable from the other selected studies. Among the sample of patients affected by psychotic symptoms or schizophrenia, 217 (73.8%) were under antipsychotic medication, while no data was available for the remaining portion. One of the included studies performed an invariance analysis (Rodríguez-Testal *et al.*, 2022), showing that age, gender, and clinical condition do not modify the subject’s interpretation of ASI items. The gender invariance was also proved in the original validation study (Cicero *et al.*, 2010).

Study level meta-analysis: Differences in ASI scores between psychotic and non-psychotic subjects

The pooled average ASI score in the psychosis group across all eight studies was 15.82. The overall psychosis sample comprised 501 individuals. The pooled control group included 1,829 individuals, with an average ASI score equal to 9.72. The Z test for overall effect has $p < 0.01$; thus, the present meta-analysis supports the hypothesis (ASI scores differ significantly between psychotic and non-psychotic individuals). The combined random effect size, measured through Cohen’s d , is equal to 1.14, while the common effect size is 1.19. Heterogeneity is quite high ($I^2 = 89\%$), suggesting relevant inter-studies variability (Fig. 2).

Publication bias analysis through a funnel plot (Fig. 3) and Egger’s test (Egger regression: $t = -0.38$, $p = 0.71$) did not show signs of bias.

IPD meta-analysis: Specificity, sensitivity, and theoretical positive predictive value of ASI

One-thousand nine hundred sixty IPD were collected from four of the eight studies; 294 made up the psychotic sample, while the remaining 1,666 constituted the control sample. A two-tailed, 95% CI t -test was performed on the two groups; there was a significant difference in ASI scores ($p < 0.001$, psychosis: mean 15.50, *SD* 7.15; control: mean 11.49, *SD* 6.82). A ROC curve was plotted on IPD for the 13.5 cutoff (Supplementary Material S6).

The area under the curve was equal to 0.74. This is considered an acceptable value for screening and even diagnostic tests (Mandrekar, 2010). Specificity, sensitivity, PPVs, and NPVs are displayed in Supplementary Material S4 and S5. We estimated the optimal cutoff value through maximizing the Youden Index; the highest Youden was 0.312, corresponding to an ASI cutoff of 13.5.

Reliability and factor structure of ASI

Regarding reliability, Cronbach’s alpha scores were extracted for the five studies in which it was available (data are shown in Table 1). As only three homogeneous Cronbach’s alphas were available, a formal meta-analytic calculation was deemed

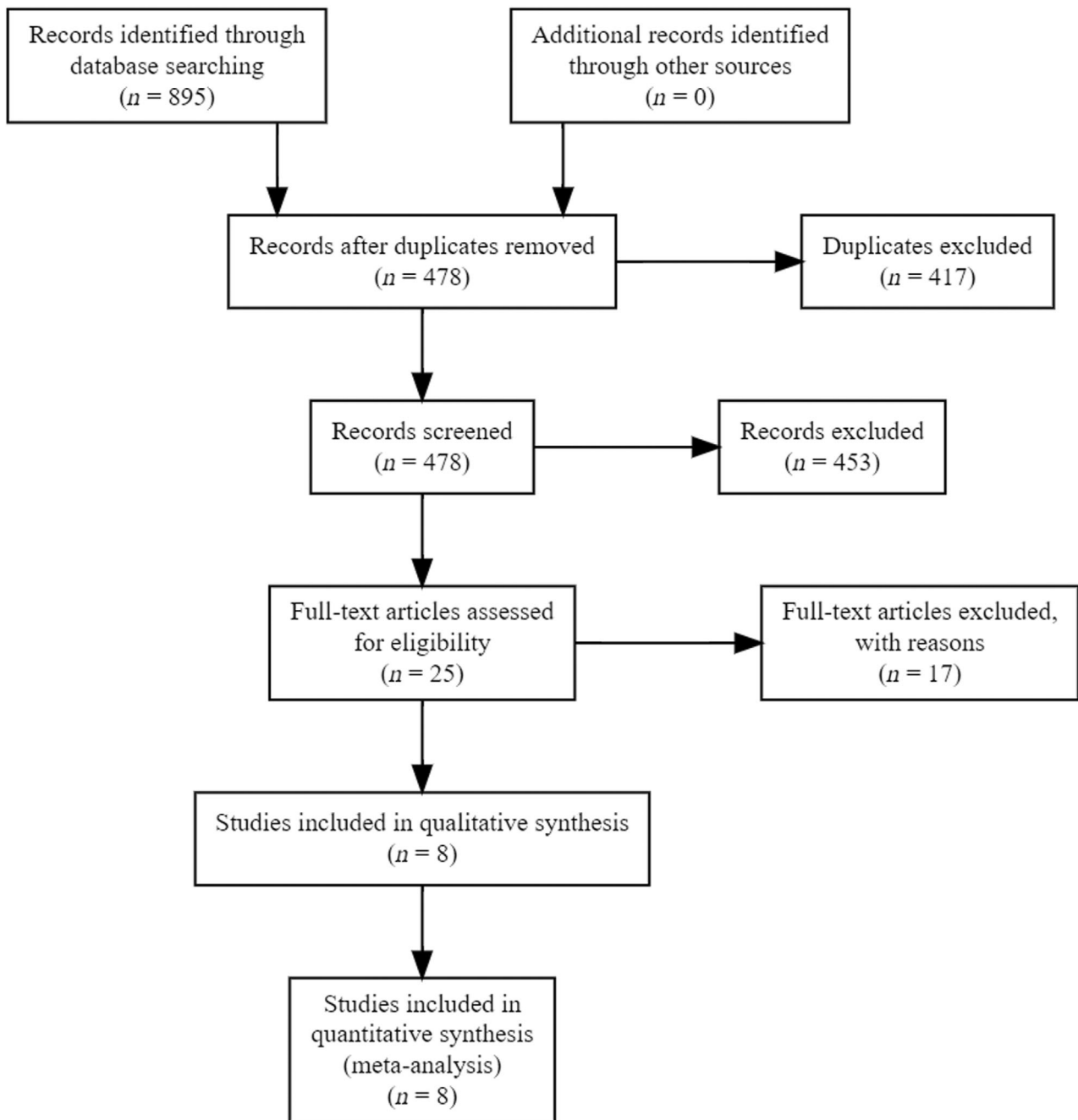


Fig. 1. Flowchart diagram.

unnecessary; all values available are above 0.89, suggesting good reliability (Tavakol & Dennick, 2011).

With regard to factor structure of the scale, the original authors of ASI (Cicero *et al.*, 2010) showed how the scale had a five-factor structure, which they named as follows: “Increased Significance,” “Senses Sharpening,” “Impending Understanding,” “Heightened Emotionality,” and “Heightened Cognition.” Another study (Golay *et al.*, 2020) found a simpler and better fitting model, with a three-factor structure: “Enhanced Interpretation and Emotionality,” “Sharpening of Senses,” and “Heightened Cognition.”

The present EFA showed a three-factor structure (Supplementary Material S7). ASI4 and ASI8 did not reach

significant loading on any factor and were thus excluded. Item loading was similar to Golay *et al.* with few differences in subscale composition (see Table 3 for more details).

Score differences among the new subscales were computed (Table 2). The group of patients with psychosis scored significantly higher on all subscales when compared with controls.

While two of the subscales from our analysis do not differ drastically from Golay *et al.*’s classification (two items or fewer), one of the subscales was renamed in order to better fit the content of its items. Thus, our proposal is to classify ASI in the following three subscales (as outlined in Table 3): “Unveiling Experiences,” “Enhanced Interpretation and Emotionality,” and “Sharpening of

Table 1. ASI meta-analysis results

| Reference | Design | Population (psychosis) | Population (controls) | Diagnostic tool | Results (psychosis) ^a | Results (controls) ^a | Effect size (Cohen's d) | Cronbach's alpha |
|------------------|--------|------------------------|-----------------------|-----------------|----------------------------------|---------------------------------|--|---|
| Ceaser, 2015 | OBS | 22 | 20 | DSM-IV | 13.59 (8.29) | 9.05 (6.88) | 0.6 | Missing data |
| Neumann, 2021 | OBS | 30 | 30 | MINI | 17.7 (4.03) | 9.5 (1.58) | 0.69 (calculated excluding the anxiety subgroup) | Missing data |
| Cicero, 2010 | OBS | 36 | 28 | DSM-IV | 15.17 (7.43) | 11.5 (5.35) | 0.57 | 0.91 in psychosis; 0.8 in controls |
| Lelli, 2015 | OBS | 30 | 64 | DSM-IV | 14.53 (7.29) | 7.52 (4.56) | 1.15 | 0.89 |
| Martinelli, 2018 | OBS | 20 | 20 | DSM-IV | 15.73 (5.99) | 10.36 (6.9) | 0.83 | Missing data |
| Golay, 2020 | OBS | 79 | 282 | ICD-10 | 16.13 (6.79) | 14.65 (6.53) | 0.22 | No overall Cronbach's alpha is available; factor's Cronbach's alpha range from 0.85 to 0.55 |
| Poletti, 2021 | OBS | 139 | 91 | DSM-IV | 13.93 (7) | 4.87 (5.46) | 1.44 (calculated excluding UHR data) | 0.925 |
| Testal, 2022 | OBS | 149 | 1,292 | DSM-IV | 17.79 (6.84) | 9.49 (5.49) | 1.34 | 0.89 |

RCT = randomized controlled interventional study; NRS = non-randomized interventional study; OBS = observational studies; UHR = ultra-high-risk.

^aMean (standard deviation).

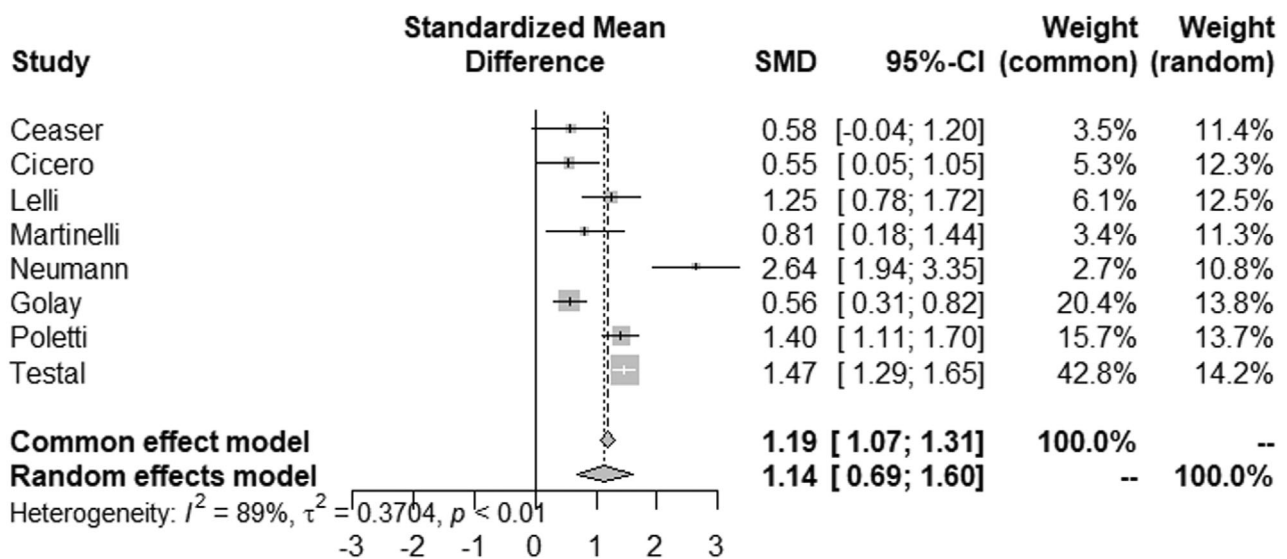


Fig. 2. Forest plot of comparison, psychotics vs. controls, outcome: ASI scores.

Senses.” Correlation coefficients between factors (see Table 4) are lower than in other proposed models (Golay *et al.*, 2020), demonstrating a robust factor structure.

DISCUSSION

ASI score comparison

The group of individuals diagnosed with psychosis shows a higher ASI score than the non-psychosis group, both at a study-level meta-analysis (psychosis: 15.82; controls: 9.72; $p < 0.01$) and in the IPD meta-analysis (psychosis: 15.50; controls: 11.49; $p < 0.001$). Thus, ASI could help identify people at risk for developing psychosis or already presenting with psychotic symptoms and perhaps improve prevention and early diagnosis in

both clinical and non-clinical assessments (van Os & Reininghaus, 2016). In fact, it should be considered that aberrant salience has a positive association with positive psychotic-like experiences in community samples and in UHR subjects (Livet, Navarri, Potvin & Conrod, 2020), while there is some evidence that patients with treatment-refractory persistent delusions show neither elevated aberrant salience nor an association between aberrant salience and delusions (Abboud *et al.*, 2016). A tool identifying aberrant salience should therefore be useful in subjects at risk of psychosis or in subjects with early psychosis.

Factor structure

The factor structure of the ASI is composed of three subscales, which differ slightly from the previous literature on the topic

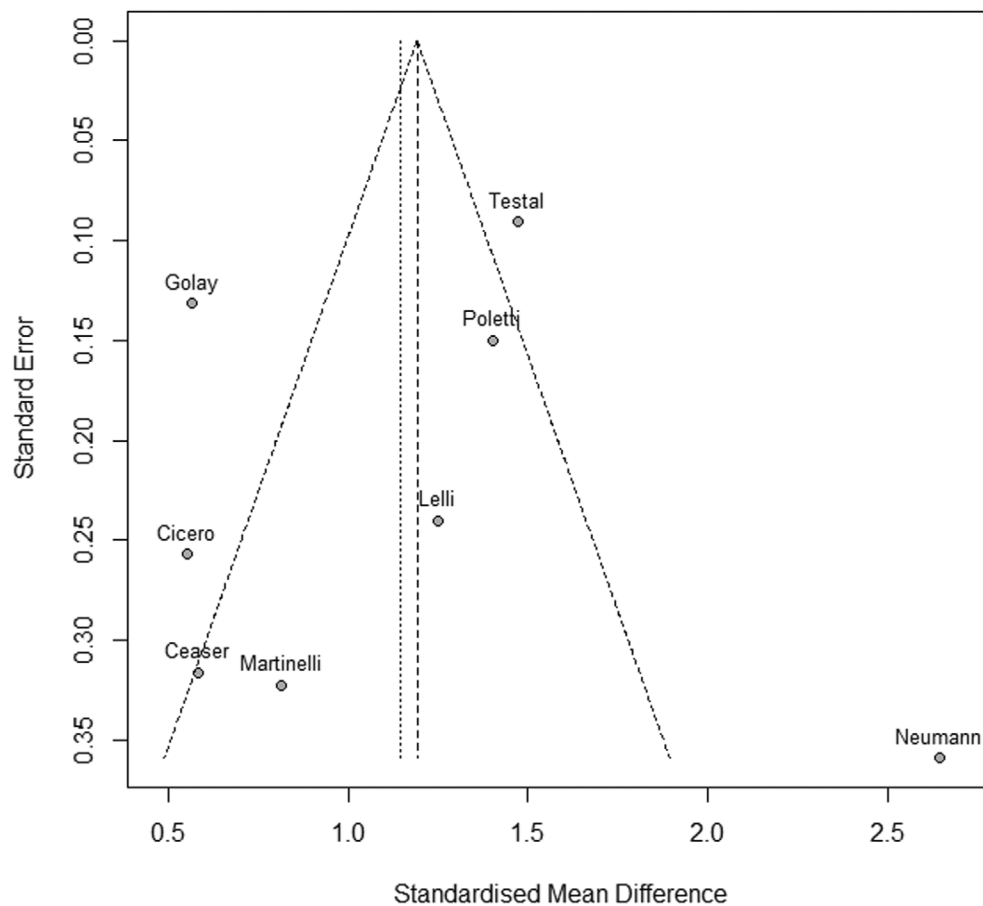


Fig. 3. Funnel plot (publication bias).

Table 2. Subscale differences between the psychosis and control sample

| | Enhanced Interpretation and Emotionality | Sharpening of Senses | Unveiling Experiences |
|-----------|--|----------------------|-----------------------|
| Overall | | | |
| Mean | 7.15 | 1.05 | 1.81 |
| SD | 3.82 | 1.32 | 1.92 |
| Psychosis | | | |
| Mean | 9.00 | 1.95 | 3.69 |
| SD | 3.64 | 1.44 | 2.28 |
| Controls | | | |
| Mean | 6.84* | 0.90* | 1.49* |
| SD | 3.77 | 1.24 | 1.66 |

*Significant difference between Psychosis and Control group, two-tailed t -test, $p < 0.0001$.

(Golay *et al.*, 2020). This difference is likely due to the increased sample size and heterogeneity (see below) in our study. While the factors “Enhanced Interpretation and Emotionality” and “Sharpening of Senses” remained almost unchanged, we propose the introduction of a new factor called “Unveiling Experiences” (UE). This construct potentially shares similarities with the previous “Heightened Cognition” subscale, such as feelings and thoughts of grandeur; however, upon inspection of the included items, several differences could be underlined. The UE subscale seems in fact to pertain more to dimensions of increased

permeability of self-world boundaries (Nelson, Thompson & Yung, 2012), feelings of mystic or religious enlightenment, and the concept of psychotic revelation or “apophenia” (Mishara, 2010). Moreover, LSD-induced mystical experiences and ego-dissolution have been associated with increased ASI scores (Wießner *et al.*, 2023), and ASI has been associated with alterations of the perception of “self” (Cicero, Docherty, Becker, Martin & Kerns, 2015). These findings suggest that mystical-like experiences and thoughts could be an integral feature of the psychosis process, even in early phases. This hypothesis is partially supported by a recent online survey’s data (Rosen, Park, Baxter, Tufano & Giersch, 2023), but in order to accurately test it, longitudinal studies would be needed.

Overall, the present factor analysis suggests that aberrant salience is associated with alterations in perception, emotional processing, and thought processes, even though the causal direction cannot be determined conclusively.

Heterogeneity

A relevant factor that has to be taken into account while reviewing our results is the high heterogeneity. This is potentially due to different male/female ratios and ethnicities between the two groups. An additional potential cause for the high heterogeneity is the variety of DSM diagnosis included in the “psychosis” group, comprising Bipolar Disorder with psychotic

Table 3. Factor loadings for the proposed three-factor model

| | 1 (“Enhanced Interpretation and Emotionality”) | 2 (“Unveiling Experiences”) | 3 (“Sharpening of Senses”) |
|-------|--|-----------------------------|----------------------------|
| ASI1 | 0.685 | 0.033 | -0.107 |
| ASI2 | 0.332 | 0.198 | 0.135 |
| ASI3 | -0.026 | -0.076 | 0.806 |
| ASI4 | 0.115 | 0.177 | 0.206 |
| ASI5 | 0.741 | -0.166 | -0.034 |
| ASI6 | 0.338 | 0.197 | 0.167 |
| ASI7 | 0.094 | 0.622 | -0.185 |
| ASI8 | 0.337 | 0.121 | -0.031 |
| ASI9 | 0.578 | -0.159 | -0.032 |
| ASI10 | 0.491 | 0.2 | -0.146 |
| ASI11 | 0.312 | 0.275 | 0.085 |
| ASI12 | -0.025 | -0.106 | 0.826 |
| ASI13 | -0.162 | 0.818 | -0.104 |
| ASI14 | 0.146 | 0.433 | 0.024 |
| ASI15 | 0.528 | -0.069 | 0.021 |
| ASI16 | 0.644 | -0.042 | 0.04 |
| ASI17 | 0.136 | 0.346 | 0.244 |
| ASI18 | -0.036 | -0.068 | 0.753 |
| ASI19 | -0.205 | 0.839 | -0.047 |
| ASI20 | 0.525 | 0.041 | -0.087 |
| ASI21 | 0.211 | 0.287 | 0.133 |
| ASI22 | -0.132 | 0.105 | 0.778 |
| ASI23 | -0.13 | 0.585 | 0.105 |
| ASI24 | -0.029 | 0.552 | 0.043 |
| ASI25 | 0.286 | 0.265 | 0.06 |
| ASI26 | 0.347 | 0.205 | 0.113 |
| ASI27 | 0.634 | -0.166 | 0.069 |
| ASI28 | 0.202 | 0.217 | 0.261 |
| ASI29 | 0.762 | -0.038 | -0.023 |

Note: Bold values signal the item’s highest factor loading.

Table 4. Correlation coefficients between the three-factor model’s components

| Component | 1 | 2 | 3 |
|-----------|-------|-------|-------|
| 1 | 1.00 | 0.554 | 0.520 |
| 2 | 0.554 | 1.00 | 0.588 |
| 3 | 0.520 | 0.588 | 1.00 |

1: “Enhanced Interpretation and Emotionality.”

2: “Unveiling Experiences.”

3: “Sharpening of Senses.”

features, Major Depression with psychotic features, Schizophrenia, and Schizoaffective Disorder. All of these diagnoses imply psychotic symptoms, and according to aberrant salience psychopathological theory they all share the same core (salience processing alteration) (Chun *et al.*, 2019; Kapur, 2003; Miyata, 2019); despite this, it is not unreasonable to consider that psychosis might have slightly different characteristics among these groups, especially on a wide statistical level. As an example, a patient diagnosed as affected by “Bipolar Disorder, type 1” according to the DSM is more likely than a patient diagnosed with “Schizophrenia” to suffer from delusions of grandeur, while the former might be more likely to experience persecutory delusions (Bebbington & Freeman, 2017; Picardi, Fonzi, Pallagrosi, Gigantesco & Biondi, 2018). However,

depending on which combinations of dimensional psychopathology are most prominent, these phenotypic differences may be expressed under the categories of a salience dysregulation syndrome with affective expression, with developmental expression, or not otherwise specified (Van Os, 2009).

Screening value

The optimal cutoff value estimated from specificity and sensitivity through the Youden Index was 13.5, which is close to the original cutoff of the ASI (Cicero *et al.*, 2010). However, since psychosis is a rare event in the population (prevalence around 1% [Moreno-Küstner, Martín & Pastor, 2018]), PPV and NPV are better measures for ASI’s usefulness for screening rather than specificity and sensitivity. In order to increase the PPV, higher ASI scores would be required, leading to a higher rate of false negatives; thus, as a good compromise, a PPV equal to or larger than 5% could be deemed appropriate to determine a cutoff point and warrant a psychiatric evaluation (as is common practice in oncology screening [Maxim, Niebo & Utell, 2014; Shapley, Mansell, Jordan & Jordan, 2010]). When applied to a general population (prevalence approximately equal to 1% and, as stated earlier, PPV approximately equal to 5%), the proposed cutoff is 21.50. At this value, NPV is equal to 99%. Applying ASI to preselected specific populations, though, could yield more fruitful results.

According to the aforementioned previous meta-analysis (Fusar-Poli *et al.*, 2015), the prevalence of psychosis among selected populations and the correlative estimated PPV of common psychosis screening tests (CAARMS, BSABS, BSIP, SIPS [Miller *et al.*, 2003; Riecher-Rössler *et al.*, 2008; Schultze-Lutter, Ruhrmann, Berning, Maier & Klosterkötter, 2010; Yung *et al.*, 2005]) is approximately the following: young adults at familial risk for psychosis: 12%, PPV 19.88%; users of high potency cannabis: 24%, PPV 36.49%. The prevalence data are also confirmed by other literature (Faridi, Pawliuk, King, Joobar & Malla, 2009; Moreno-Küstner *et al.*, 2018; Myles, Myles & Large, 2016; Semple, McIntosh & Lawrie, 2005; Sullivan *et al.*, 2020).

Assuming equal prevalence and requiring equal or larger PPVs, it is possible to calculate cutoff values for ASI whose performance is similar to that of the other mentioned tests. Thus, we propose a series of cutoff points warranting deeper evaluations according to the specific populations and stratified by desired PPVs and NPVs (Table 5).

For what concerns unselected young adults under 24 years old, prisoners, postpartum women, and refugees (prevalence of psychosis 3–4%) we proposed two cutoffs that differ in predictive power: 11.5 (PPV 5%) and 19.5 (PPV 10%). Regarding young adults at familial risk (prevalence of psychosis 12%) we proposed a cutoff of 12.5 (PPV 20%). Lastly, for what concerns users of high potency cannabis (prevalence of psychosis 24%) we proposed a cutoff of 11.5 (PPV 30%); in other words, one out of three heavy cannabis smokers presenting with an ASI total score higher than 11.5 may have psychotic symptoms.

Across all of the cutoffs, NPV remains high (>87% in all cases). ASI’s advantage, when compared with tests such as the

Table 5. Proposed cutoff of Aberrant Saliency Inventory (ASI) for different populations, with associated positive predictive values (PPVs) and negative predictive values (NPVs)

| Population | Prevalence of psychosis | PPV | NPV | Cutoff |
|---|-------------------------|-----|-----|--------|
| General population | 1% | 5% | 99% | 21.5 |
| Unselected young adults under 24 years old; prisoners; postpartum women; refugees | 4% | 7% | 98% | 11.5 |
| Unselected young adults under 24 years old; prisoners; postpartum women; refugees | 4% | 14% | 97% | 19.5 |
| Young adults at familial risk for psychosis | 12% | 20% | 93% | 12.5 |
| Users of high potency cannabis | 24% | 30% | 87% | 11.5 |

CAARMS, is its brevity; moreover, ASI is an entirely self-administered test. These characteristics are particularly interesting in regard to a potential online administration of the scale, leading to a cheap but effective screening of large groups among the general population.

Literature on the subject of online screening of psychiatric conditions, particularly psychosis, is growing (McDonald *et al.*, 2019; Savill, Nguyen, Shim & Loewy, 2022). Despite the acknowledgement of challenges and issues with this kind of screening procedure in terms of privacy and accuracy (Hassem & Laher, 2022), the benefit of low-cost, risk-free mass screening for serious conditions such as psychosis should not be overlooked. As a comparison, several practices among oncological screening are widely regarded as cost-effective such as colonoscopy for colon cancer. Its prevalence among the population, 2%, is comparable to that of psychosis (Mattiuzzi, Sanchis-Gomar & Lippi, 2019), while schizophrenia's burden alone in terms of DALYs surpasses that of colon cancer worldwide (He *et al.*, 2020; Safiri *et al.*, 2019). Colonoscopy, on average, costs more than \$2,000 (Fisher, Princic, Miller-Wilson, Wilson & Limburg, 2022), while a brief psychometric test is cheap and mostly discomfort-free. It is thus possible to argue that psychosis mass screening, possibly through ASI, is at least as worthwhile as colon cancer's. A potentially interesting setting for screening could be a general practitioner's evaluation.

Limitations

Despite the growing number of items on the topic, the amount of data available is still relatively limited. In addition, our research focused on published data, which could potentially introduce a publication bias. To account for this, we conducted a publication bias analysis that showed no evidence of bias, thereby validating our results. Moreover, the sample was imbalanced concerning gender distribution (see Results) and mostly focused on Europeans and African Americans, while the Asian sample and other ethnicities were almost absent (see Results). Finally, since past research has shown that ASI scores might be positively influenced by young age (Rodríguez-Testal *et al.*, 2022), we limited our sample to adults only; thus, we cannot make any inference on previous stages of the psychosis process.

Regarding the IPD meta-analysis, some of the aforementioned limitations persist, such as the limited number of studies and their imbalance in sample size: Most of the IPD sample was extracted from two studies (Golay *et al.*, 2020; Rodríguez-Testal *et al.*, 2022). Moreover, ASI cutoffs must always be taken with caution, since the PPVs, especially in the general population, are quite low (Zimmerman, 2022). As such, the ASI should be treated as a screening tool rather than a diagnostic one.

Future perspectives

The concept of saliency, as well as its relevance in the research and psychosis-predicting models fields, evolved in the past few years: For instance, in line with this evolution, more complex tools evaluating neurophenomenological aspects have been developed, such as the semi-structured interview EASE (Examination of Anomalous Self-Experience) (Pamas *et al.*, 2005) and the self-report questionnaire IPASE (Inventory of Psychotic-Like Anomalous Self-Experiences) (Nelson *et al.*, 2019), which appear to be related to aberrant saliency (Nelson *et al.*, 2020). These new instruments are built on the basic-self-disorder or ipseity-disturbance model of psychosis in schizophrenia, which postulates an abnormality of basic or minimal self-awareness, i.e., the first-person quality of experience (Sass, Borda, Madeira, Pienkos & Nelson, 2018). Unlike this model, aberrant saliency seems to be able to explain and predict psychosis as a transdiagnostic dimension, not specific for schizophrenia, and appears to be more relevant to anomalous world experiences rather than to self-experience (Nelson *et al.*, 2020), although these are overlapping constructs (Sass, Pienkos & Fuchs, 2017). Future research is needed to explore the relationship between ASI cutoff score and the EAWE (Examination of Anomalous World Experience) (Sass *et al.*, 2017), as well between ASI and the ESSS (Embodied Sense of Self Scale) (Patti *et al.*, 2022), in order to appreciate pre-cognitive embodied features such as self-recognition, self-consistence, and self-awareness and their role in saliency disturbances. Integrating the information derived from these more accurate instruments might yield even more promising results in the quest for accurately determining psychosis vulnerability (Nelson *et al.*, 2020), even if the amount of available data is still limited.

CONCLUSIONS AND CLINICAL IMPLICATIONS

In conclusion, ASI showed satisfactory qualities in differentiating psychotic subjects from non-psychotic controls. In spite of some limitations, the outcomes bear a good degree of reliability, by virtue of the strict eligibility criteria, which contributed to reduce the error threshold and to select the most representative and meaningful studies in which ASI was administered to psychotic and non-psychotic populations. A new factor structure is proposed, including the novel subscale "Unveiling Experiences." Moreover, our study suggests the use of different cutoffs depending on the specific population of interest, in order to maximize ASI's screening potential. Thus, we advise the use of ASI as a routine transdiagnostic tool for psychosis screening in general practice, given its brevity and its self-administered form:

Subjects with ASI total scores higher than the proposed cutoffs would therefore benefit from a psychiatric evaluation, which may detect individuals worthy of an early intervention. Further research on this topic is needed in order to increase sample sizes for future meta-analyses on the subject.

AUTHOR CONTRIBUTIONS

G.P.M. conceived the study, with the coordination offered by A.B., A.F., and A.P. for the study design. G.P.M. and O.B.B. designed the search algorithm, and O.B.B., G.P.M., I.F., and V.P. collected the data and performed the screening process. All authors contributed to the interpretation of the studies and to the synthesis of results. G.P.M. plotted the main figures and managed the statistical analysis. The first draft was written by G.P.M., V.P., O.B.B., and I.F., under the supervision of A.B., A.F., A.P., G.S., V.R., and D.C.C.; the final manuscript was approved by all the authors.

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CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

The database of the studies, with the extracted data items, can be shared upon reasonable request to the corresponding author.

ETHICS APPROVAL STATEMENT

The authors declare that ethical approval was not needed for this study.

PUBLIC SIGNIFICANCE STATEMENTS

This study confirms that the Aberrant Salience Inventory (ASI), a brief self-reported psychometric questionnaire that measures alterations of salience processes, is capable of differentiating between psychotic and non-psychotic individuals. Factor analysis was performed, detecting novel subscales. Additionally, it provides different cutoffs in order to maximize the predictive power of ASI in screening for psychosis among different populations of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Supporting Information.

Appendix S2. Supporting Information.

Appendix S3. Supporting Information.

Appendix S4. Supporting Information.

Appendix S5. Supporting Information.

Appendix S6. Supporting Information.

Appendix S7. Supporting Information.

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