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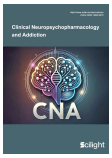

Opinion

Can Substance-Induced Psychoses (SIP) Shed Light on the Paradigm of Schizophrenia?

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Abstract: Substance-induced psychoses (SIP) may offer a useful vantage point for exploring mechanisms underlying psychotic disorders and for examining the phenomenological specificities of schizophrenia. Clinical observations suggest that a clinically relevant subset of patients does not fully recover after an episode of substance-induced psychosis, raising the hypothesis of more persistent psychotic trajectories that may differ from both acute SIP and primary psychotic disorders (PPD). In this context, the proposal of Substance-Related Exogenous Psychosis (SREP) situates exogenous psychoses as conditions related to, yet not fully overlapping with, schizophrenia. Drawing on the tradition of classical psychopathology, from Bonhoeffer's exogenous model to the concept of lysergic psychoma, and integrating it with recent research on self-disorders, the hypothesis emerges that substance-induced psychoses may function as heuristic phenomenological models useful for exploring the genesis of psychotic phenomena. Examination of ipseity through the EASE interview suggest similarities between SIP and PPD, but also significant differences: SIP are characterized by more superficial and transient alterations of the self, whereas schizophrenia involves deeper and structurally embedded disturbances. From this perspective, the phenomenological comparison of schizophrenia, SIP, and SREP may help delineate with greater precision which dimensions of self-experience are compromised across these psychotic conditions. This conceptual framework is intended as a hypothesis-generating perspective, which may guide future longitudinal studies integrating phenomenology and substance-related mechanisms to refine the boundaries between acute SIP, persistent SIP/SREP trajectories, and schizophrenia spectrum disorders.

Keywords: substance-induced psychosis (SIP); schizophrenia; ipseity; self-disorders; anomalous self-experience (EASE); phenomenological psychopathology

1. Introduction

An increasingly relevant line of investigation developed in recent years concerns the clinical [1,2], psychopathological [3], and therapeutic [4,5] characterization of substance-induced psychoses (SIP) [1]. Episodes of psychotic symptoms induced by substances are frequent, particularly in relation to specific classes of drugs such as stimulants [6], psychedelics [7], and novel psychoactive substances (NPS) [8].

Recently, several studies have attempted to elucidate their clinical and psychopathological manifestations, as well as to distinguish them from primary psychotic disorders (PPD) [2–8]. Caton et al. [1] conducted a study aimed at identifying significant demographic, familial, and clinical differences between SIP and PPD. Individuals classified as SIP, who were subsequently monitored over variable follow-up periods, exhibited a higher frequency of visual hallucinations, a greater prevalence of suicidal ideation in the previous year, more frequent episodes of

violent behavior, and a higher likelihood of having a family history of substance misuse. Moreover, the SIP group demonstrated higher levels of insight [1].

Although available data remain limited, a notable finding is the substantial proportion of individuals who do not fully recover after episodes of substance-induced psychosis, raising questions about the potential relationship between prolonged and high-dose substance use and the development of persistent or full-blown psychosis [8,9]. The restrictive definition of SIP does not account for these enduring psychotic conditions, which present clinical differences from primary psychotic disorders (PPD). For this reason, some authors have proposed a distinct clinical entity termed Substance-Related Exogenous Psychosis (SREP) [10]. SREP, introduced as a novel diagnostic category, includes both transient and persistent forms of substance-induced psychosis (i.e., psychosis arising after substance use). It is conceptualized as a disorder within the schizophrenia spectrum, characterized by specific features that clearly differentiate it from Schizophrenia/PPD in clinical presentation, epidemiology, etiological mechanisms, and response to treatment [10].

From a clinical and phenomenological perspective, it may be useful to outline provisional boundaries between acute substance-induced psychosis (Substance-Induced Psychosis, SIP), persistent substance-induced psychotic conditions, Substance-Related Exogenous Psychosis (SREP), and schizophrenia spectrum disorders. Acute SIP are typically characterized by a close temporal relationship with substance intoxication or withdrawal, prominent perceptual disturbances, relatively preserved insight, and a tendency toward full or near-full remission following abstinence and symptomatic treatment [7]. Persistent SIP, by contrast, refer to psychotic manifestations that extend beyond the expected period of intoxication or withdrawal, raising questions about longer-lasting substance-related effects or an underlying vulnerability [1,3,7]. It is within this context that SREP has been proposed as a phenomenological–clinical construct encompassing recurrent or persistent exogenous psychotic conditions in which psychotic symptoms remain temporally and clinically linked to substance exposure, yet display a degree of stabilization and autonomy over time [10]. Although SREP may share certain features with schizophrenia spectrum disorders, it is distinguished by differences in longitudinal trajectory, depth of self-disorders, and treatment response, with less pronounced and less structurally embedded disturbances of ipseity compared to schizophrenia. Schizophrenia spectrum disorders, conversely, are characterized by enduring and pervasive basic self-disorders, progressive phenomenological reorganization, and relative independence from exogenous triggering factors [3,10].

These distinctions are intended as heuristic and hypothesis-generating rather than as operational diagnostic criteria, and are meant to provide a clinical map to guide future longitudinal and phenomenological investigations.

From a historical perspective, several authors have addressed the issue of substance-induced psychoses. Karl Bonhoeffer was among the first, developing the concept of the *exogenous reaction*, which he regarded as a relatively uniform response triggered by an external noxious agent, including toxic, infectious, traumatic, or degenerative factors [11]. Bonhoeffer's exogenous (hexogen) model emerged in dialectical opposition to Bleuler's endogenous model, coinciding with Bleuler's initial adoption of the term "schizophrenia," which embodied the notion of a pathological process characterized by progression, deterioration, and cognitive decline—elements strongly influenced by Kraepelin's work [12]. In contrast to Bleuler, Bonhoeffer emphasized disturbances of consciousness as the core feature, encompassing a continuum ranging from confusion to dream-like experiences, and progressing to delirium and stupor [11].

At the same time, the concept of *lysergic psychoma*, coined by Cargnello and Callieri in 1963, has its conceptual origins in Hellpach's definition and, more substantially, in the exogenous model developed by Karl Bonhoeffer (1897) [13,14]. This construct can be delineated as a psychopathological syndrome [15,16], characterized by the perception of an alien presence within one's own cognitive processes. In classical phenomenological terms, the notion of psychoma was used to convey the experience of a quasi-autonomous pathological process progressively infiltrating the field of consciousness. The metaphor of an "alien" or metastasis-like presence does not imply a foreign entity, but rather captures the subjective sense of an intrusive and expanding alteration that undermines the unity, transparency, and critical control of self-experience, gradually eroding the integrity of the experiencing subject [17,18].

Karl Bonhoeffer included lysergic psychoma among the models of exogenous psychoses, conditions in which an external noxious agent can directly influence the emergence of a fully developed psychosis. His objective was to identify the fundamental basis of a functional disturbance -an exogenous complex capable of interacting with an endogenous predisposition and ultimately giving rise to a complete psychotic syndrome. Bonhoeffer first described this phenomenon while working with alcohol-dependent patients in Breslau under Wernicke's supervision [14]. Clinically, it presents with distinct alterations in the domains of thought, mood, and sensory perception—most notably auditory and visual hallucinations, disturbances in bodily experience, and anomalies in spatial and temporal processing [19].

The construct of lysergic psychoma represents a key framework for understanding substance-induced phenomena more broadly, extending beyond lysergic hallucinogens alone. In 1927, Kurt Beringer, a student of Bonhoeffer, further expanded the concept in relation to mescaline and other lysergic substances in Heidelberg [20].

In Italy, Giovanni Enrico Morselli, in 1932, personally ingested mescaline and documented its effects in several essays, providing an in-depth account of the exogenous model of psychoma as a toxic phenomenon [21]. Morselli also described the clinical effects induced by LSD in a group of volunteers, including himself, noting a prolonged syndrome characterized by visual hallucinations, delusional perceptions, and paranoid thinking [21]. This experience was compared to schizophrenia, with altered perception identified as the primary point of convergence [21–23].

Underlying these studies was the notion that exogenous psychoses constituted "synthetic" models of psychosis [18]: conditions in which, once the toxic effect of the substance had dissipated and a restitutio ad integrum was achieved, the psychotic picture appeared in a more "reduced" and structurally simplified form. Owing to this sharper phenomenological delimitation, such forms were considered more amenable to investigation, and their analysis was regarded as a useful means of contributing to the understanding of the pathogenetic mechanisms of endogenous psychoses.

2. Discussion

Reinterpreted in light of contemporary knowledge, the aforementioned approach now represents a promising avenue for current research aimed at clarifying the phenomenological dynamics of psychosis.

Today, it is well established that in schizophrenia the core abnormality pertains to disturbances at the pre-reflective level of selfhood, known as ipseity [24]. This self-disorder—also referred to as an ipseity disturbance or basic self-disturbance (BSD)—is expressed through a constellation of mutually implicative anomalous self-experiences (ASE). These include a diminished sense of presence and existence, hyperreflexivity, a reduced sense of agency and ownership over experiences and actions, feelings of unreality, and profound disturbances of "common sense" [24,25]. As psychosis emerges, these self-disorders gradually become more articulated and thematized, eventually culminating in delusions, hallucinations, and passivity phenomena [24,26–28]. A semi-structured instrument, the Examination of Anomalous Self-Experience (EASE), was specifically developed to comprehensively assess these self-disorders. Using the EASE and related measures, several studies have demonstrated that ASE cluster within the schizophrenia spectrum, including schizotypal and prodromal conditions [26–36].

Building on the assumption that primary psychoses and SIP share a common underlying neurobiological vulnerability—albeit quantitatively more pronounced in schizophrenia [37]—our hypothesis is that a comparison of self-related domains across patients with schizophrenia, substance-induced psychosis, and SREP may reveal which dimensions are impaired in schizophrenia and in chronic substance-induced psychoses, and which, conversely, remain preserved in acute substance-induced conditions. From this perspective, substance-induced psychoses may meaningfully contribute to clarifying the specific dimension of selfhood that differentiates schizophrenia from SREP and SIP, thereby identifying the core phenomenological domain of a disorder that continues to represent one of the most complex and debated issues in contemporary psychiatry.

In this context, an initial study by De Risio & Mosca [34] pursued this direction. The study compared ASEs between PPD and SIP using the EASE interview, recruiting a total of 54 clinically stable patients, 27 with schizophrenia spectrum disorders (SSD) and 27 with SIP. While total EASE scores did not differ significantly between groups, Domain 4 (Demarcation/Transitivism) was markedly higher in the SIP group. In contrast, Domain 2 (Self-awareness and Presence) tended to be higher in the PPD group, and Domain 5 (Existential Reorientation) showed a similar trend, in line with classical phenomenological models of schizophrenia. These findings suggest that, in schizophrenia (PPD), self-disturbances reflect deep, structural alterations of ipseity, whereas in SIP the anomalies may be more superficial, transient, and linked to pharmacodynamic effects (e.g., perceptual instability, derealization, ego-diffusion). This indicates that SIP and PPD share certain phenomenological patterns, but likely arise from different underlying mechanisms. While the present framework emphasizes qualitative differences in the depth and structural embedding of self-disturbances across substance-induced psychoses and schizophrenia, alternative interpretations deserve consideration. One possibility is that substance-induced psychotic episodes may act as unmasking events, revealing an underlying vulnerability that would otherwise remain latent. From this perspective, some cases currently classified as SIP or SREP might represent early or atypical expressions of schizophrenia spectrum disorders.

A second hypothesis is that repeated intoxications and recurrent psychotic episodes may exert sensitization effects, progressively impacting self-experience and leading to more persistent or stabilized psychotic configurations over time. Finally, diagnostic overlap and misclassification remain possible, particularly in early

phases of psychosis, when longitudinal information is limited. Acknowledging these competing interpretations underscores the need for prospective, longitudinal, and phenomenologically informed studies capable of disentangling pharmacodynamic effects, vulnerability-related mechanisms, and disorder-specific trajectories.

3. Conclusions

This opinion paper proposes a conceptual and phenomenological framework aimed at reinterpreting substance-induced psychoses as heuristic models for exploring psychotic psychopathology. Rather than advancing a definitive nosological classification, the present contribution is intended as hypothesis-generating, highlighting qualitative differences in the depth and structural embedding of self-disturbances across acute SIP, SREP trajectories, and schizophrenia spectrum disorders.

Within this framework, the comparative assessment of anomalous self-experiences using instruments such as the Examination of Anomalous Self-Experience (EASE) emerges as a particularly valuable approach. Phenomenological profiling based on self-disorders may help clarify which dimensions of ipseity disruption are shared across psychotic conditions and which are more specific to schizophrenia, thereby refining the clinical and psychopathological boundaries between exogenous and endogenous psychoses.

Finally, these considerations underscore the need for longitudinal and multimodal research designs integrating phenomenological, clinical, and substance-related variables. Future studies tracking the temporal evolution of self-disturbances may be crucial to disentangling pharmacodynamic effects, vulnerability-related mechanisms, and disorder-specific trajectories, and to further testing the conceptual distinctions outlined in this paper.

4. Prospective

Future research should aim to refine the phenomenological distinctions between schizophrenia, substance-induced psychoses, and Substance-Related Exogenous Psychosis (SREP), integrating longitudinal designs and multimodal assessment tools. Particular attention should be devoted to tracking the temporal evolution of self-disturbances and their interaction with neurobiological vulnerability and substance-related mechanisms. Expanding this line of inquiry may contribute to a more precise nosological framework and support the development of targeted interventions capable of addressing the specific depth and structure of ipseity disruption across diverse psychotic conditions.

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A.M. and F.M.F.: conceptualization; A.M.: methodology, writing, original draft preparation; F.M.F: visualization, supervision; validation. Both authors have read and agreed to the published version of the manuscript.

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During the preparation of this manuscript, the authors used ChatGPT 5.2 for language editing.

References

1. Caton, C.L.; Drake, R.E.; Hasin, D.S.; et al. Differences between early-phase primary psychotic disorders with concurrent substance use and substance-induced psychoses. *Arch. Gen. Psychiatry* **2005**, *62*, 137–145.
2. Chiappini, S.; Mosca, A.; Semeraro, F.; et al. Navigating the challenges of substance use and psychopathology in depression, bipolar disorder, and schizophrenia. *Compr. Psychiatry* **2025**, *142*, 152616. https://doi.org/10.1016/j.comppsych.2025.152616.
3. Ricci, V.; Aragona, M.; Maina, G.; et al. Phenomenology of hallucinations in endogenous and substance-related exogenous psychoses. *Psychopathology* **2025**, *30*, 1–21. https://doi.org/10.1159/000547087.
4. Martinotti, G.; Chiappini, S.; Mosca, A.; et al. Atypical Antipsychotic Drugs in Dual Disorders: Current Evidence for Clinical Practice. *Curr. Pharm. Des.* **2022**, *28*, 2241–2259. https://doi.org/10.2174/1381612828666220623092853.
5. Mosca, A.; Chiappini, S.; Miuli, A.; et al. Clinical Management of Synthetic-Cannabinoid-Induced Psychosis: A Systematic Review of Treatment Strategies and Outcomes. *Brain Sci.* **2025**, *15*, 1006. https://doi.org/10.3390/brainsci15091006.
6. Kalayasiri, R.; Verachai, V.; Gelernter, J.; et al. Clinical features of methamphetamine-induced paranoia and preliminary genetic association with DBH-1021C→T in a Thai treatment cohort. *Addiction* **2014**, *109*, 965–976.
7. Sabé, M.; Sulstarova, A.; Glangetas, A.; et al. Reconsidering evidence for psychedelic-induced psychosis: An overview of reviews, a systematic review, and meta-analysis of human studies. *Mol. Psychiatry* **2025**, *30*, 1223–1255. https://doi.org/10.1038/s41380-024-02800-5.
8. Mosca, A.; Mancusi, G.; Chiappini, S.; et al. Novel psychoactive substances (NPS) as a risk factor for psychosis: A systematic review of the literature. *Neurosci. Biobehav. Rev.* **2025**, *179*, 106431. https://doi.org/10.1016/j.neubiorev.2025.106431.
9. Papanti, D.; Schifano, F.; Botteon, G.; et al. "Spiceophrenia": A systematic overview of "spice"-related psychopathological issues and a case report. *Hum. Psychopharmacol. Clin. Exp.* **2013**, *28*, 379–389. https://doi.org/10.1002/hup.2312.
10. Martinotti, G.; De Risio, L.; Vannini, C.; et al. Substance-related exogenous psychosis: A postmodern syndrome. *CNS Spectr*. **2021**, *26*, 84–91.
11. Bonhoeffer, K. *Der Geisteszustand des Alkoholdeliranten*; Maretzke & Märtin: Trzebnica, Poland, 1897.
12. Bleuler, E. Die Prognose der Dementia praecox (Schizophreniegruppe). *Allg. Z. Psychiat.* **1908**, *65*, 436–464.
13. Bonhoeffer, K. Zur Frage der Klassifikation der sympomatischen Psychosen. *Berl. Klin. Wochenschr.* **1908**, *45*, 2257–2260.
14. Bonhoeffer, K. Klinische und anatomische Beitrage zur Kenntnis der Alkoholdelirien. *Mschr. Psychiat. Neurol*. **1897**, *1*, 6–41.
15. Angrist, B.M.; Gershon, S. The phenomenology of experimentally induced am- phetamine psychosis—Preliminary observations. *Biol. Psychiatry* **1970**, *2*, 95–107.
16. Mathias, S.; Lubman, D.I.; Hides, L. Substance-induced psychosis: A diagnostic conundrum. *J. Clin. Psychiatry* **2008**, *69*, 358–367.
17. De Giacomo, U.; Morselli, G. E.; Cargnello, D.; et al. *Le Psicosi Sperimentali*; Feltrinelli: Milano, Italy, 1962
18. Di Petta, G.; Tittarelli, D. *Le Psicosi Sintetiche. Il Contributo Della Psicopatologia Fenomenologica Italiana Alle Psicosi Indotte da Sostanze*; Feltrinelli: Milano, Italy, 2016.
19. Ricci, V.; Maina, G.; Di Petta, G.; Martinotti, G. The Resurgence of Exogenous Psychosis: A Phenomenological Examination of Substance-Induced Psychopathology. *J. Nerv. Ment. Dis.* **2024**, *212*, 457–459. https://doi.org/10.1097/NMD.0000000000001800.
20. Beringer, K. *Der Meskalinrausch. Seine Geschichte und Erscheinungsweise*; Springer-Verlag Berlin Heidelberg GmbH, Berlin, Germany, 1927.
21. Morselli, G.E. Expérience mescalinique et vécu schizophrénique. *L'Evolution Psychiatr.* **1959**, 275.
22. Morselli, G.E. Neuropsychiatry & Experimental Psychiatry. In Proceedings of the Comunicazione al II Congresso Internazionale, Londra, UK, 29 July–2 August 1935.
23. Morselli, G.E. Mescalina e schizofrenia. *Riv. Psicol.* **1945**, 3.
24. Sass, L.A.; Parnas, J. Schizophrenia, consciousness, and the self. *Schizophr. Bull.* **2003**, *29*, 427–444.
25. Sass, L.A. Self-disturbance and schizophrenia: Structure, specificity, pathogenesis (current issues, new directions). *Schizophr. Res.* **2014**, *152*, 5–11.
26. Nelson, B.; Parnas, J.; Sass, L.A. Disturbance of minimal self (ipseity) in schizophrenia: Clarification and current status. *Schizophr. Bull.* **2014**, *40*, 479–482.
27. Sass, L.; Parnas, J.; Zahavi, D. Phenomenological psychopathology and schizophrenia: Contemporary approaches and misunderstandings. *Philos. Psychiatry Psychol.* **2011**, *18*, 1–23.
28. Sass, L.A. *Self-Disturbance in Schizophrenia: Hyperreflexivity and Diminished Self-Affection*; Cambridge University Press: Cambridge, UK, 2003. pp. 242–271.
29. Parnas, J.; Jansson, L.; Sass, L.A.; et al. Self-experience in the prodromal phases of schizophrenia: A pilot study of first-admissions. *Neurol. Psychiatry Brain Res.* **1998**, *6*, 97–106.
30. Moller, P.; Husby, R. The initial prodrome in schizophrenia: Searching for naturalistic core dimensions of experience and behavior. *Schizophr. Bull.* **2000**, *26*, 217–232.

31. Nordgaard, J.; Handest, P.; Vollmer-Larsen, A.; et al. Temporal persistence of anomalous self-experience: A 5years follow-up. *Schizophr. Res.* **2017**, *179*, 36–40.
32. Nordgaard, J.; Nilsson, L.S.; Saebye, D.; et al. Self-disorders in schizophrenia-spectrum disorders: A 5-year follow-up study. *Eur. Arch. Psychiatry Clin. Neurosci.* **2018**, *268*, 713–718.
33. Parnas, J.; Handest, P.; Jansson, L.; et al. Anomalous subjective experience among first-admitted schizophrenia spectrum patients: Empirical investigation. *Psychopathology* **2005**, *38*, 259–267.
34. Parnas, J.; Handest, P.; Saebye, D.; et al. Anomalies of subjective experience in schizophrenia and psychotic bipolar illness. *Acta Psychiatr. Scand.* **2003**, *108*, 126–133.
35. Hur, J.W.; Kwon, J.S.; Lee, T.Y.; et al. The crisis of minimal self-awareness in schizophrenia: A meta-analytic review. *Schizophr. Res.* **2014**, *152*, 58–64.
36. Stoychev, K.; Veleva, I.; Mineva-Dimitrova, E.; et al. Symptom severity and cognitive performance in patients with substance induced psychotic disorder and schizophrenia: A cross-sectional comparative study. *Schizophr. Res. Cogn.* **2025**, *42*, 100388. https://doi.org/10.1016/j.scog.2025.100388.
37. De Risio, L.; Mosca, A.; Pasino, A.; et al. Anomalous self-experience in substance-induced and primary psychotic disorders: A cross-sectional comparative study using the EASE interview. *Ann. Gen. Psychiatry* **2025**, *24*, 72. https://doi.org/10.1186/s12991-025-00608-3.