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Systematic Review

Polysomnographic Parameters in Schizoaffective Disorder: A Systematic Review and Meta-Analysis

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Abstract

Background: Schizoaffective disorder (SZA) is a severe psychiatric condition characterized by overlapping affective and psychotic features; however, its sleep architecture remains poorly characterized. This systematic review and meta-analysis compared polysomnographic findings in drug-free patients with SZA with those of healthy controls (HC), patients with schizophrenia (SCZ), and patients with major depressive disorder (MDD). **Methods:** An extensive database search identified 40 studies. Nine case-control studies including 79 patients with SZA, 88 patients with SCZ, 79 HC, and 131 patients with MDD were included in the meta-analyses. Total sleep time, sleep efficiency, sleep latency, wake after sleep onset, and rapid-eye-movement (REM) and non-REM (NREM) sleep variables were analyzed. The primary outcome measure was the standardized mean difference (SMD). Data were analyzed using a random-effects model. Publication bias was assessed using Egger's regression test and funnel plot asymmetry. **Results:** Compared with HC, patients with SZA showed reduced total sleep time, increased sleep latency and wakefulness after sleep onset, reduced REM sleep duration, shortened REM latency, and reduced stage 4 sleep duration and percentage. Patients with SZA differed from those with MDD only in exhibiting increased sleep latency, whereas no significant differences were observed between patients with SZA and those with SCZ. **Conclusions:** Polysomnographic abnormalities in SZA demonstrate a general pattern of sleep disruption compared with HC, without clear differentiation from SCZ or MDD. Overall, current evidence does not support sleep architecture as a reliable biomarker for distinguishing SZA from related psychotic or affective disorders. These findings should be considered exploratory, given the small sample sizes, limited number of available studies, and substantial heterogeneity across studies. Further research is needed to determine whether specific sleep measures may better distinguish SZA from other psychiatric conditions.

Keywords: REM; NREM; sleep; schizoaffective disorder; polysomnography; electroencephalography; meta-analysis

Main Point

1. Sleep parameters do not differentiate schizoaffective disorder (SZA) from major depressive disorder (MDD) and schizophrenia (SCZ).

2. SZA is associated with impaired sleep continuity compared with healthy controls (HC).

3. Delta sleep reduction appears across SZA, SCZ, and MDD compared with HC.

4. Polysomnographic evidence in SZA is limited, with small and heterogeneous samples.

1. Introduction

1.1 Schizoaffective Disorder

Schizoaffective disorder (SZA) is a chronic condition which, according to current DSM-5 criteria, can be diagnosed when a mood disorder (depression, mania or both) is present for the majority of the total active and residual course of schizophrenia (SCZ), from the onset of psychotic symptoms up until the current diagnosis [1,2,3]. SZA is estimated to have a lifetime prevalence of 0.3%–1.1% [1,4,5]. Age of onset of SZA is 25–35, intermediate between that of SCZ and mood disorders [6,7,8], although it might be broader [9]. Women are twice as likely to be diagnosed with SZA than men, as for mood disorders [7,8,10,11,12,13]. Mixed states in SZA have been reported to be as frequent as mixed states in bipolar disorder (BD) and probably linked to a worse outcome [14]. Lifetime suicide risk in SZA is estimated to be 5%, although the presence of depressive symptoms might increase it [8,15]. SZA is mostly regarded as having a more favorable course than that of patients with SCZ but worse than that of patients with BD [8,14,16,17].

The historical perspective proposed from the end of the nineteenth century onward by Kraepelin [18] suggested that SCZ and BD were the two main diagnostic categories, with the psychoses associated with the former category having a poorer outcome than those associated with mood disorders [19]. The dichotomy proposed by Kraepelin, however, did not acknowledge those cases in which patients experience psychotic symptoms but also have periods of concomitant mood disorders. The term "schizoaffective psychosis" was first used by Jacob Kasanin in 1933 [20]; therefore the "schizoaffective subtype" of "schizophrenic reaction" is present in DSM since its first 1952 edition [2]. SZA started to be regarded as a separate diagnostic entity in DSM-III, while successive editions added subtypes (de-

pressed, bipolar, mixed) and from DSM-5 recognized SZA as a lifetime diagnosis [2]. International Classification of Diseases (ICD)-11 differs from DSM by dropping the longitudinal approach to the diagnosis of SZA, considering it difficult to ascertain the accurate temporal relationship between psychotic and mood episodes, and proposing the coexistence yet independence of the two classes of symptoms as a main criterion [3].

SZA has been generally regarded as having poor diagnostic reliability [1,2,3,4,5,6,13,21], making SZA a potentially misdiagnosed condition [2,22,23,24]. The question of whether SZA is an actual separate clinical entity or a subtype of SCZ or a depressive disorder has been frequently discussed in literature, contributing to the controversial nosography of SZA [6,7,8,21,22,25,26,27,28,29,30,31,32].

Several studies assessing clinical and biological features have been conducted to characterize SZA. Cognitive [33,34,35] and gray matter abnormalities [36,37,38,39] have been found in SZA, often resembling more those in SCZ than those in BD [8,34], or being intermediate between SCZ and BD [40]. SZA patients do not show a different ventricle-to-brain ratio compared to SCZ or BD [25,41]. Recent studies on fMRI [42], functional connectivity [43] and immune system [44,45] found that SZA, SCZ and BD share substantial biological abnormalities while also exhibiting partially distinct profiles.

Heritability of SZA seems to be like that of SCZ and BD [46]. Some studies found that SZA is genetically linked to both SCZ and BD and might constitute an intermediate form of these two conditions [47,48,49], with evidence that genes involved in glutamatergic abnormalities might play a key role in the onset of SZA, SCZ and BD [50]. In a recent study on Swedish population, SZA has been found to carry high genetic risk for both SCZ and BD while being clearly separable from psychotic BD, suggesting that SZA might not be, from a genetic perspective, a subtype of SZ, BD or MD [51]. As already suggested in early studies [25], SZA might be an intermediate condition in a putative polygenic continuum model of psychoses in which patients with major psychoses share genetic influences [52,53,54].

SZA is mainly treated with antipsychotics as SCZ [1,24,31,55], with paliperidone being the only FDA specifically approved medication for SZA [56,57]. Patients with SZA, nonetheless, receive additional prescription of benzodiazepines, antidepressants and mood stabilizers [1,17,24] and with a higher frequency compared to SCZ [17]. Electroconvulsive therapy (ECT) is also effective in treating treatment-resistant SZA [8,24].

1.2 Sleep Studies of SZA

Insomnia [58,59,60], obstructive sleep apnea (or at risk for it) [59,61,62] and circadian rhythm disorders [59,63] are sleep disturbances reported in SZA. Insomnia has been found to be associated with obesity [58] and suicidal ideation and risk in SZA patients [64]. Sleep disturbances were also associated with more severe negative symptoms and lower functioning [60]. A study that used a sleep spindles detection method reported different spindle phenotypes between SZA and SCZ; moreover, both slow and fast sleep spindles density were increased in those patients with a history of manic or hypomanic symptoms [65]. A recent study reported reduced thalamic nuclei volumes in SZA compared with SCZ [66], a potentially relevant finding given the central involvement of thalamo-cortical circuits in sleep spindles generation [67]. Notably, spindle deficits have already been consistently documented in SCZ [68,69].

The sleep of patients with SZA was first investigated in early descriptive studies, reporting abnormalities in REM percentage (%REM) and in slow-wave sleep (SWS) [70]. Another study reported normal REM latency in SZA but increased REM density (REMD) in depressed SZA patients compared to manic BD patients, manic SZA patients and SCZ [71]. Several other studies pooled SZA patients in samples together with SCZ patients, limiting the possibility to observe differences within the sample in sleep parameters.

Nonetheless, sleep architecture in samples composed entirely of SZA patients was investigated in case-control studies comparing patients with healthy controls (HC). The earliest study reported increased sleep onset latency (SOL) and wake after sleep onset (WASO) in SZA, with stage 4 duration (ST4) and percentage (%ST4) and delta sleep time (DELTA) deficits [72]. Subsequent studies supported these findings by also reporting reduced total sleep time (TST) and REM time (REMT) and shortened REM latency (REML) in SZA [73,74,75].

Other studies investigated differences between the sleep architecture of SZA and that of SCZ or affective disorder patients. Reich et al. [76] reported increased SOL, decreased sleep efficiency (SE) and decreased DELTA in SZA compared to SCZ, with SZA also showing shortened REML and increased REMT and REMD. Subsequent studies reported increased ST4 [72,73], %ST4 and %REM in SCZ compared to SZA [73].

An early study found decreased WASO and increased REMT and DELTA in SZA patients compared to those with psychotic depression [77], although a later report by the same authors found no differences between SZA and psychotic depression [78].

Furthermore no differences between SZA, SCZ and MDD were reported by successive studies [73,74,75].

Considering the previous heterogeneous and controversial results, the present study aimed to provide a qualitative and quantitative analysis of PSG findings in SZA.

In addition to quantitative synthesis, the systematic review includes studies that could not be subjected to meta-analysis due to insufficient or incompatible data but providing a more comprehensive characterization of the available evidence. As a novel contribution, the study further enables

Table 1. Drug-free SZA vs HC studies included in the meta-analysis.

Study	N. (SZA)/N. (HC)	Age (SZA/HC)	Males % (SZA/HC)	Diagnosis (SZA/HC)	Treatment	Diagnostic manual
Benson et al., 1980 [72]	9/19	NR/NR	NR/NR	Schizoaffective disorder/Healthy	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	8/13	33/29.7	100/100	Schizoaffective disorder/Healthy	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	9/19	33.4/30.2	100/100	Schizoaffective disorder/Healthy	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone et al., 1987 [74]	8/18	33.8/30.3	100/100	Schizoaffective disorder/Healthy	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone & Benson, 1995 [75]	8/10	34.5/32.3	100/100	Schizoaffective disorder/Healthy	Drug-free (2 days)	Research Diagnostic Criteria

"NR": data not reported in the original study. SZA, schizoaffective disorder; HC, healthy control.

Table 2. Drug-free SZA vs drug-free MDD studies included in the meta-analysis.

Study	N. (SZA)/N. (MDD)	Age (SZA/MDD)	Males % (SZA/MDD)	Diagnosis (SZA/MDD)	Treatment	Diagnostic manual
Kupfer & Foster, 1975 [77]	6/9	38.8/58.2	50/NR	Schizoaffective disorder/Psychotic depression	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Kupfer & Foster, 1975 [77]	6/25	38.8/41.1	50/NR	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Kupfer et al., 1979 [78]	12/29	44.4/48.1	42/31	Schizoaffective disorder/Psychotic depression	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson et al., 1980 [72]	9/6	NR/NR	NR/NR	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Coble et al., 1981 [79]	5/17	34.8/40.1	60/35	Schizoaffective disorder/Psychotic and nonpsychotic depression	Drug-free (2 weeks)	Research Diagnostic Criteria
Benson et al., 1983 [80]	2/5	NR/NR	100/100	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	8/10	33/40.3	100/100	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	9/7	33.4/37.7	100/100	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone et al., 1987 [74]	8/12	33.8/41.33	100/100	Schizoaffective disorder/MDD	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone & Benson, 1995 [75]	8/11	34.5/37.2	100/100	Schizoaffective disorder/MDD	Drug-free (2 days)	Research Diagnostic Criteria

"NR": data not reported in the original study. MDD, major depressive disorder.

Table 3. Drug-free SZA vs drug-free SCZ studies included in the meta-analysis.

Study	N. (SZA)/N. (SCZ)	Age (SZA/SCZ)	Males % (SZA/SCZ)	Diagnosis (SZA/SCZ)	Treatment	Diagnostic manual
Reich et al., 1975 [76]	3/14	38.8/20.8	NR/57	Schizoaffective disorder/Schizophrenia (acute)	Drug-free (≥2 weeks)	DSM-II
Reich et al., 1975 [76]	3/9	38.8/19	NR/11	Schizoaffective disorder/Schizophrenia (latent)	Drug-free (≥2 weeks)	DSM-II
Benson et al., 1980 [72]	9/9	NR/NR	NR/NR	Schizoaffective disorder/Schizophrenia	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson et al., 1983 [80]	2/7	NR/NR	100/100	Schizoaffective disorder/Schizophrenia	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	8/11	33/27	100/100	Schizoaffective disorder/Schizophrenia	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Benson & Zarcone, 1985 [73]	9/8	33.4/26.6	100/100	Schizoaffective disorder/Schizophrenia	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone et al., 1987 [74]	8/12	33.8/26.2	100/100	Schizoaffective disorder/Schizophrenia	Drug-free (≥2 weeks)	Research Diagnostic Criteria
Zarcone & Benson, 1995 [75]	8/18	34.5/33.1	100/100	Schizoaffective disorder/Schizophrenia	Drug-free (2 days)	Research Diagnostic Criteria

"NR": data not reported in the original study. SCZ, schizophrenia.

an exploratory comparative assessment of sleep architecture alterations shared across major psychiatric conditions to clarify the degree of similarity of SZA sleep with that of SCZ or MDD. TST, SOL, SE, WASO, REMT, %REM, REML, REMD, stage 1, 2, 3 sleep time (ST1, ST2, ST3) and percentage (%ST1, %ST2, %ST3), ST4, %ST4, DELTA and %DELTA in drug-free SZA patients were analyzed and, where available, compared with case-control data of HC, MDD and SCZ patients.

This study is structured as follows: first, the methods used for the systematic review and meta-analysis are described, including study selection, polysomnographic variables, and statistical procedures. The results section then presents the meta-analytic findings. Finally, the discussion addresses the interpretation of the findings in relation to previous literature, the main limitations of the study, potential sources of heterogeneity, and implications for future research.

2. Methods

Major databases were screened querying PubMed, Web of Science and PsycINFO from inception to 2025. Several combinations of keywords were implemented to identify all the studies of interest: "(sleep or sleep*) AND schizo*", "PSG or polysomnogra*", "EEG OR electroencephalogra*", "REM OR REMS OR rapid-eye-movement OR rapid-eye-movements", "paradox OR paradox*", "print OR print*", "D-phase OR dream OR dream*", "night OR night*", "monit*", "architect*". In addition, keywords regarding molecules and brand names were included to identify studies investigating the effect of psychotropic drugs on sleep architecture, such as: "atypical", "typical" and "antipsych*", "paliperidone", "risperidone", "Invega", "Risperdal" and so on. Although drug-related keywords were included in the search strategy to maximise sensitivity and capture PSG outcomes reported within pharmacological studies, no eligible studies investigating drug effects on sleep in SZA were ultimately identified or included in the final dataset.

The search returned 7515 studies, of which 3345 from PubMed, 4105 from WoS and 65 from PsycINFO. Of these, 4120 studies were found to be duplicates present on multiple databases. The eligibility of the remaining 3395 studies was assessed, with 3202 studies eventually excluded due to not providing any polysomnography data. 13 studies were excluded due to providing patient samples already presented in a previous study by the same author or co-author. 144 studies were excluded due to not having any SZA patients in their sample. 36 studies were evaluated as eligible and entirely retrieved. 40 studies were ultimately included in the study after being assessed as eligible: 36 studies were retrieved from database screening and 4 other studies were identified through manual search and retrieved. The meta-analysis included 9 studies, while the systematic review included all the other 31 studies. The eligibility assessment of each study was carried out after a full-text review of the articles by the authors (DM, GF and GB), all agreeing on the final decision for each study.

The meta-analysis investigated sleep architecture differences between the following groups: drug-free SZA and HC (Table 1, Ref. [72,73,74,75]), drug-free SZA and drug-free MDD (Table 2, Ref. [72,73,74,75,77,78,79,80]), drug-free SZA and drug-free SCZ (Table 3, Ref. [72,73,74,75,76,80]). Case-control studies that were eligible for the systematic review only (and excluded from the meta-analysis) are reported in Table 4 (Ref. [65,81,82,83,84,85,86,87,88,89,90,91,92,93,94]) with the

Table 4. Case-control studies included in the systematic review only.

Study (excluded)	N. (SZA)/N. (CTRL)	Age (SZA/CTRL)	Males % (SZA/CTRL)	Diagnosis (SZA/CTRL)	Treatment	Reason of exclusion	Diagnostic manual
Kupfer et al., 1971 [81]	4	36.48	25	1 Schizophrenia 1 Schizoaffective disorder 2 Depressive neurosis	Drug-free (≥2 weeks) → Chlorpromazine	Mixed sample	Not reported
Gillin et al., 1977 [82]	10	25	60	4 Schizoaffective disorder 2 Acute schizophrenia 1 Chronic schizophrenia 1 Schizoid personality disorder 2 Bipolar disorder	Drug-free (≥2 weeks) → Pimozide	Mixed sample	DSM-II
Gillin et al., 1978 [83]	7	23	43	3 Chronic schizophrenia 1 Acute schizophrenia 2 Schizoaffective disorder 1 Schizoid personality disorder + OCD	Drug-free (≥1 month) → Pimozide	Mixed sample	Research Diagnostic Criteria
Keshavan et al., 1996 [84]	16	29.9	50	11 Schizophrenia 5 Schizoaffective disorder	Drug-free (≥2 weeks) → Drug-free (31%) Neuroleptics (69%) + Antidepressants + Mood stabilizers	Mixed medication status/sample	DSM-III-R
Keshavan et al., 1996 [84]	15	29.7	NR	Schizophrenia 5 Schizoaffective disorder	Drug-free (≥2 weeks) → Haloperidol (67%) Fluphenazine (13%) Trifluoperazine (6.7%) Clozapine (6.7%) Risperidone (6.7%) + Anticholinergics (47%)	Mixed sample	DSM-III-R
Benson et al., 1996 [85]	14/15	33.6/30.5	100/100	11 Schizophrenia (presumably chronic) 3 Schizoaffective disorder/Healthy	Drug-free (2 days)	Mixed sample	Research Diagnostic Criteria
Nishino et al., 1998 [86]	14/14	33.3/34.4	100/100	12 Schizophrenia 2 Schizoaffective disorder/Healthy	Drug-free (2 days)	Mixed sample	Research Diagnostic Criteria
Keshavan et al., 1998 [87]	30/30	30.9/30.9	57/57	19 Schizophrenia 8 Schizoaffective disorder 3 Schizophreniform disorder/Healthy	Drug-free (Average 97.5 weeks; Median 40 weeks)	Mixed sample	DSM-III-R
Rotenberg et al., 2000 [88]	20/10	45.8/43.3	65/60	19 Schizophrenia 1 Schizoaffective disorder/Healthy	Drug-free (≥2 weeks)	Mixed sample	DSM-IV

Table 4. Continued.

Study (excluded)	N. (SZA)/N. (CTRL)	Age (SZA/CTRL)	Males % (SZA/CTRL)	Diagnosis (SZA/CTRL)	Treatment	Reason of exclusion	Diagnostic manual
Armitage et al., 2004 [89]	14	40.9	29	3 Schizoaffective disorder 11 Bipolar I disorder	Carbamazepine, BZD, mood stabilizers → + Clozapine	Mixed sample	DSM-IV
Kluge et al., 2014 [90]	15	32.8	47	Schizophrenia 1 Schizoaffective disorder	Drug-free (≥2 days) → Olanzapine	Mixed sample	DSM-IV
Kluge et al., 2014 [90]	15	36.7	33	Schizophrenia 2 Schizoaffective disorder 1 Schizophreniform disorder	Drug-free (≥2 days) → Clozapine	Mixed sample	DSM-IV
Göder et al., 2015 [91]	16/16	29.4/28.3	56/44	14 Chronic schizophrenia 2 Schizoaffective disorder/Healthy	Antipsychotics (2° Gen., 94%) Antipsychotics (1° Gen., 6%) + Antidepressants (13%) + BZD (6%) + Anticholinergics (6%) + Promethazine (6%)	Mixed sample	ICD-10
Kaskie et al., 2019 [92]	27/23	23.2/24.7	68/72	16 Schizophrenia 2 Schizoaffective disorder 4 Unspecified psychosis 3 MDD with psychotic features 2 Bipolar disorder/Healthy	Antipsychotics (2° Gen., 41%) Antipsychotics (3° Gen., 3.7%) + Antidepressants (83%) + Mood stabilizers (25%) + BZD (17%) 15 drug-naive	Mixed medication status/sample	DSM-IV
Gerstenberg et al., 2020 [93]	12/24	16.6/16.5	58/46	9 Schizophrenia 2 Schizoaffective Disorder 1 Brief Psychotic Disorder/Healthy	Antipsychotics (3° Gen., 58.3%) Antipsychotics (2°+3° Gen., 25.5%) Antipsychotics (2° Gen., 16.2%) + BZD (25%) + Anticholinergics (16.7%)	Mixed sample	DSM-IV
Petit et al., 2022 [65]	12/988	58.2/59.9	42/58	Schizoaffective disorder/Healthy	Medicated (25%) Drug-free (75%)	Mixed medication status	DSM-5
Denis et al., 2024 [94]	17/27	21/24	56/53	7 Schizophrenia 5 Schizoaffective disorder 4 Bipolar disorder 1 Unspecified psychosis/Healthy	Antipsychotics (2° Gen., 35%) Antipsychotics (3° Gen., 29%) Antipsychotics (1° Gen., 12%) + Mood stabilizers (47%) + Antidepressants (24%) + Anticholinergics (18%) + BZD (6%) 4 drug-free	Mixed medication status/sample	DSM-IV-TR

CTRL, Control group; DSM, Diagnostic and Statistical Manual of Mental Disorders; OCD, Obsessive-Compulsive Disorder; BZD, Benzodiazepines; ICD, International Classification of Diseases.
"NR": data not reported in the original study.

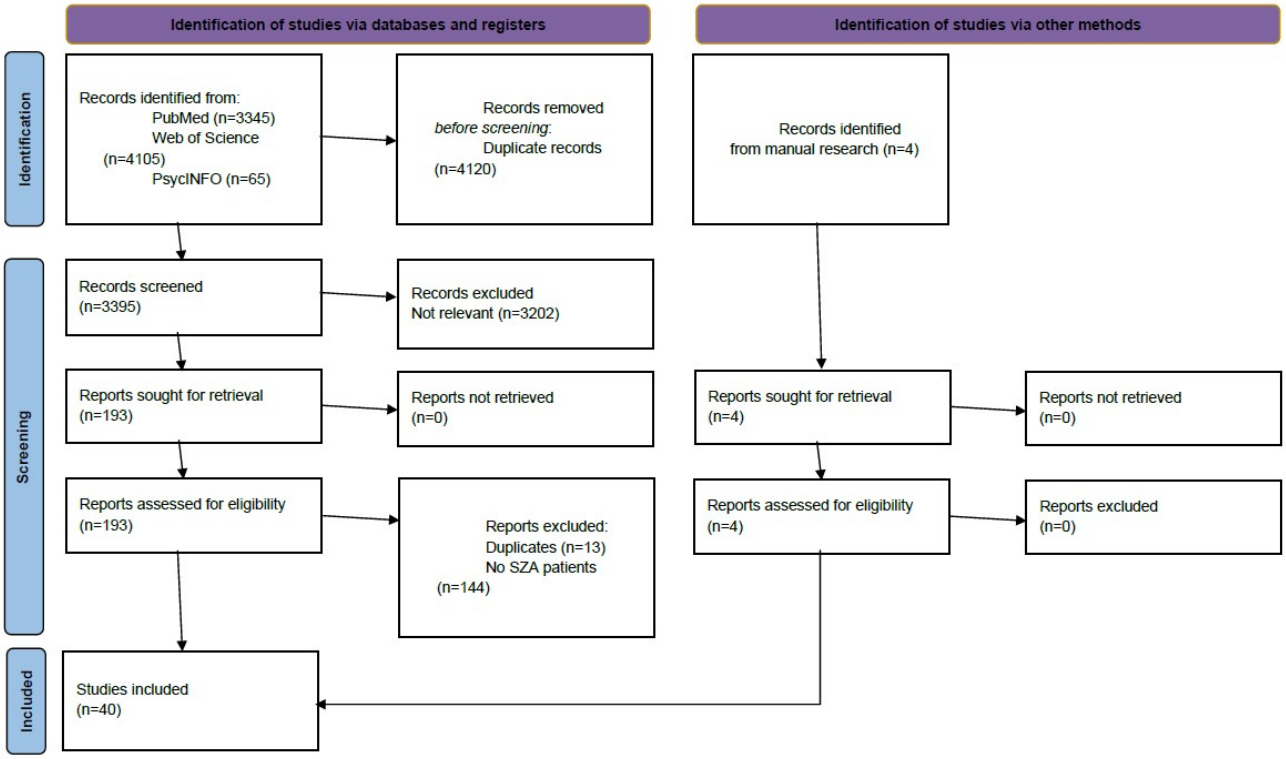

Fig. 1. PRISMA diagram.

reason for exclusion. Other non-case-control studies included in the systematic review only are reported in Table 5 (Ref. [70,71,95,96,97,98,99,100,101,102,103,104,105,106,107,108]). Fig. 1 presents the PRISMA (Preferred reporting items for systematic reviews and meta-analyses) diagram of the systematic review.

2.1 Eligibility Criteria

Studies were assessed as eligible for the meta-analysis based on the following inclusion criteria:

(1) Case-control studies including a sample of patients with SZA and a HC group.

(2) Case-control studies including a sample of patients with SZA and a MDD sample.

(3) Case-control studies including a sample of patients with SZA and a SCZ sample.

(4) Patient samples in a study had been drug-free for the same amount of time.

(5) Samples aged over 13 years.

(6) Studies in which diagnoses were established according to DSM and/or ICD criteria. Research diagnostic criteria (RDC) have been widely used to diagnose SZA and were therefore regarded as eligible.

(7) Studies in which sleep was assessed by polysomnography (PSG) and sleep stages were scored according to AASM or Rechtschaffen and Kales criteria. Studies using earlier scoring systems (e.g., Antrobus et al. [109], or Itil et al. [110]) were also included provided that the scoring methods were equivalent or largely comparable to those adopted in the later standard guidelines.

Exclusion from the meta-analysis was based on the following criteria:

(1) Studies with no control group.

(2) Studies with a control group different than SZA, SCZ, MDD or HC.

(3) Studies in which more than 5% of the total sample consisted of participants with diagnoses other than SZA (e.g., obsessive-compulsive disorder, bipolar disorder, or autism spectrum disorder).

(4) Studies in which the SZA sample included a subgroup with a different medication status from the majority of participants, exceeding 5% of the total sample (e.g., 90% drug-free and 10% receiving at least one antipsychotic).

(5) Studies including SZA patients with relevant comorbidities (e.g., narcolepsy or obstructive sleep apnea-hypopnea)

(6) Single-case studies.

(7) Studies reporting sleep alterations in SCZ patients without providing clearly extractable sleep data.

The excluded studies were retained in the systematic review.

As specified, studies were excluded if the SZA sample was not sufficiently homogeneous with respect to diagnostic composition or medication status. A conservative threshold (>5% of the sample) was applied [111] to min-

Table 5. Non-case-control studies included in the systematic review only.

Study	N. SZA/Sex/(Age)	Diagnosis	Medication status	Diagnostic manual
Hauri et al., 1973 [70]	2F (28.5)	Schizoaffective disorder	Drug-free (≥1 week)	Not reported
Gillin et al., 1981 [95]	3M, 3F (31)	4 Chronic schizophrenia 2 Schizoaffective disorder	Drug-free (≥1 week)	Research Diagnostic Criteria
Glassman et al., 1986 [96]	1M (39)	Schizoaffective disorder	Lithium carbonate, chlorpromazine, triazolam, benztropine	DSM-III
Lahmeyer et al., 1988 [71]	2F (29)	Schizoaffective disorder	Drug-free (2 weeks)	Research Diagnostic Criteria
Keshavan et al., 1991 [97]	7M, 5F (31.2)	8 Schizophrenia 3 Schizoaffective disorder 1 Schizotypal disorder	Drug-free (≥2 weeks) 2 drug-naive	Research Diagnostic Criteria
Keshavan et al., 1992 [98]	14M, 5F (30.5)	17 Schizophrenia 2 Schizoaffective disorder	Drug-free (≥2 weeks) 6 drug-naive	Research Diagnostic Criteria
Douglass et al., 1993 [99]	6NR (NR)	Schizoaffective disorder Schizophrenia	Drug-free (≥2 weeks)	DSM-III-R
Douglass et al., 1993 [99]	3NR (NR)	Schizophrenia Schizoaffective disorder + narcolepsy	Drug-free (≥2 weeks)	DSM-III-R
Keshavan et al., 1994 [100]	8M, 11F (30.6)	13 Schizophrenia 6 Schizoaffective disorder (suicidal behavior)	Drug-free (≥2 weeks)	DSM-III-R
Keshavan et al., 1994 [100]	12M, 8F (32.3)	16 Schizophrenia 4 Schizoaffective disorder (no suicidal behavior)	Drug-free (≥2 weeks)	DSM-III-R
Keshavan et al., 1995 [101]	10M, 10F (30)	8 Schizoaffective disorder 12 Schizophrenia	Drug-free (≥4 weeks) 12 drug-naive	DSM-III-R
Yamashita et al., 1999 [103]	1F (34)	Schizoaffective disorder (with haloperidol-induced akathisia)	Haloperidol + Chlorpromazine + Biperiden + BZD + Mood stabilizer → BZD + Mood stabilizer	DSM-IV
Wetter et al., 2002 [104]	1F (31)	Schizoaffective disorder (with risperidone-induced restless leg syndrome)	Risperidone + Mood stabilizers → Quetiapine + Mood stabilizers	NR
Baandrup et al., 2016 [102]	5M, 5F (49)	6 Schizophrenia 2 Schizoaffective disorder 2 Bipolar disorder	Antipsychotics + BZD + Antidepressants + Mood stabilizers + Anticholinergics	ICD-10
Weinhold et al., 2022 [105]	9M, 9F (40.7)	11 Schizophrenia 7 Schizoaffective disorder	Atypical antipsychotics + Antidepressants + Mood stabilizers	ICD-10
			Study summary (no clear sleep data)	
Itil et al., 1970 [108]	1NR (NR)	Schizoaffective disorder	Drug-free (≥4 weeks)	Not reported
Itil et al., 1970 [108]	1NR (NR)	Schizoaffective disorder (lobotomized)	Drug-free (≥4 weeks)	Not reported

Table 5. Continued.

Study	N. SZA/Sex/(Age)	Diagnosis	Medication status	Diagnostic manual
Giedke et al., 1992 [106]	12M, 18F (48)	4 Schizoaffective disorder 26 MDD	All patients on neuroleptics, antidepressants and BZD Sleep deprivation significantly improved depressed mood	Research Diagnostic Criteria
Keshavan et al., 1992 [107]	11M, 5F (31.65)	10 Schizophrenia 4 Schizoaffective disorder 1 Atypical psychosis 1 Psychotic affective disorder	Reduced NREM sleep REM activity increased, REML reduced (drug-free ≥2 days) Neuroleptic treatment did not improve sleep	DSM-III-R

"NR": data not reported in the original study.

imize potential confounding arising from the inclusion of participants with different primary diagnoses and from psychotropic medication exposure, both of which may significantly influence sleep architecture and PSG parameters. The 5% cut-off is inherently arbitrary and is acknowledged as a methodological limitation of the present work.

The quality of each study included in either the systematic review or the meta-analysis was assessed using the Newcastle-Ottawa Scale. Item-level scores for each included study are provided as supplementary material.

2.2 Data Extraction

The following data were extracted from each study: sample size, mean age, percentage of male participants, diagnosis, medication status, and mean and SD of sleep variables, including TST, SOL, SE, WASO, REMT, %REM, REML, REMD, ST1, ST2, ST3, ST4, %ST1, %ST2, %ST3, %ST4, DELTA, and %DELTA. In some studies, SDs for sleep variables were not reported. In these cases, SDs were estimated as follows. For each meta-analysis (e.g., REMT, SZA vs HC), a weighted average SD was computed based on the sample size of the included studies. This weighted SD was then assigned to studies within the same meta-analysis that did not report SDs. This approach has been considered acceptable for handling missing variance data [112] and represents the only imputation procedure applied in this study. In a limited number of studies, some sleep variables were not directly reported but could be derived from other available parameters (e.g., REMT = TST × %REM / 100). All instances of data derivation and imputation were reported in the **Supplementary Material**, where the meta-analytic and systematic review data are presented in extended form.

Eight of the nine studies included in the meta-analysis used the RDC for diagnosing SZA, while only one study applied DSM-II criteria. The diagnostic system used in each study, including those excluded from meta-analysis, is reported in Tables 1,2,3,4.

In several included studies, demographic variables such as age or sex were not reported. This is indicated in Tables 1,2,3,4 with a "NR" denoting unavailable data.

Some studies were reported multiple times in the corresponding tables for they included multiple independent patient samples or diagnostic subgroups that constituted separate datasets to the analyses. Therefore, repeated citations do not represent duplicate inclusion of the same sample, but distinct patient samples analyzed separately within the original study.

2.3 Statistical Analysis

Jamovi 2.6.44 (Windows x64 desktop version, Sydney, Australia) was used to perform the meta-analyses. R 4.6.0 (Windows x64 desktop version, Auckland, New Zealand), together with the metaPower 0.2.2 package (Houston, Texas), was used to compute statistical power for each meta-analysis. A minimum of three datasets from independent studies was required for each parameter to conduct a meta-analysis. Analyses were performed using standardized mean differences as the effect size metric.

A random-effects model was fitted to the data. Between-study heterogeneity (τ^2) was estimated using the restricted maximum-likelihood estimator. In addition to τ^2, the Q-test for heterogeneity and the I^2 statistic are reported. When any heterogeneity was detected ($\tau^2 > 0$, irrespective of the Q-test outcome), a prediction interval for the true effect sizes was also calculated. Studentized residuals and Cook's distances were used to identify potential outliers and influential studies within each model. Studies with studentized residuals exceeding the $100 \times (1 - 0.05/(2k))$th percentile of a standard normal distribution were considered potential outliers, corresponding to a Bonferroni-adjusted two-sided $\alpha = 0.05$ for k studies. Studies with Cook's distances greater than the median plus six times the interquartile range were considered influential. Publication bias and small-study effects were assessed using rank correlation test and regression test, with the standard error of the observed effect sizes as predictor of asymmetry.

3. Results

3.1 Study Characteristics

Nine studies, comprising 79 SZA patients, 88 SCZ patients, 79 HC and 131 MDD patients, were included in the

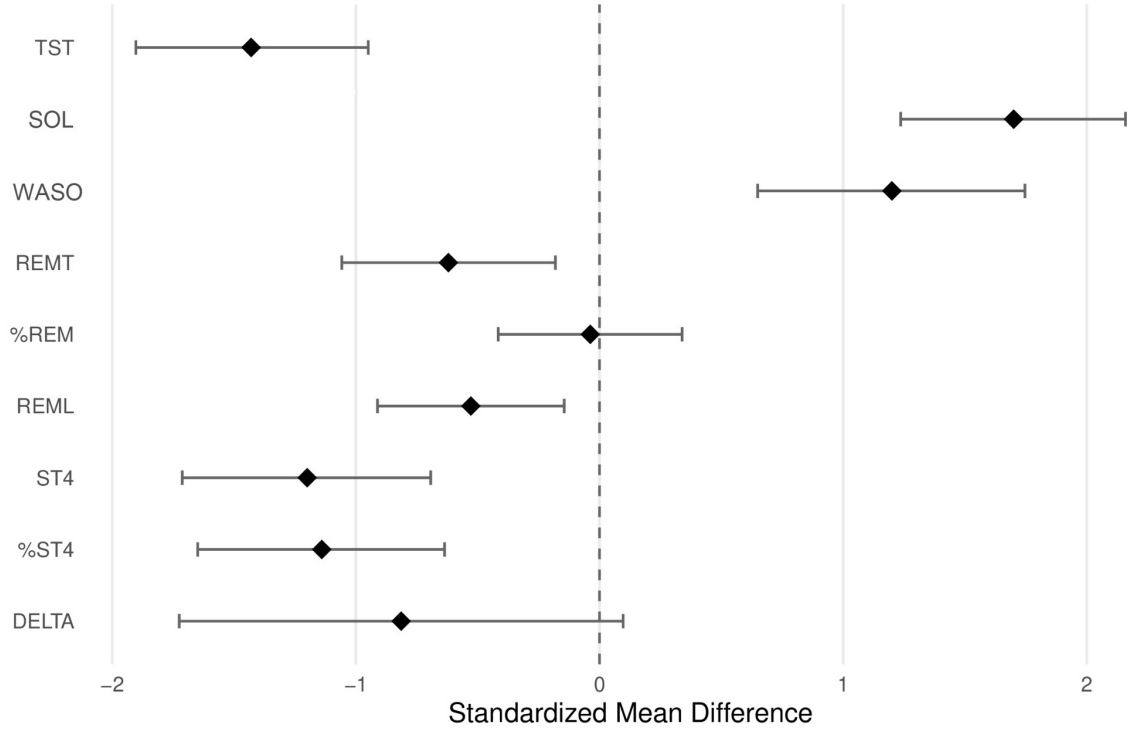

Fig. 2. Sleep parameters in drug-free SZA vs HC (forest plot).

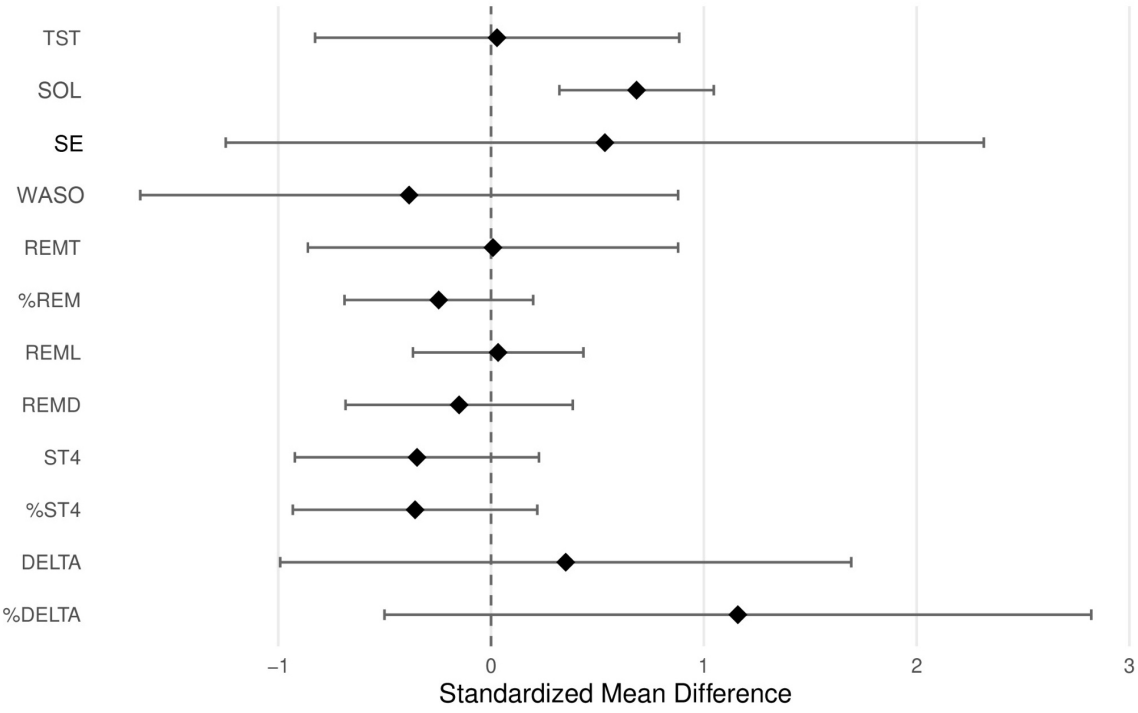

Fig. 3. Sleep parameters in drug-free SZA vs drug-free MDD (forest plot).

meta-analysis [72,73,74,75,76,77,78,79,80]. Some studies contributed with more than one dataset to each sleep parameter analysis.

Additional 31 studies, including 113 SZA patients, 263 SCZ patients, 1031 HC and 31 MDD patients, were included in the systematic review [65,70,71,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108].

Results are summarised in Table 6. Publication bias and funnel plot asymmetry, assessed using the rank correlation and regression tests, are reported in Table 7 (Ref. [72,74,75,76,77,80]), together with information on outliers

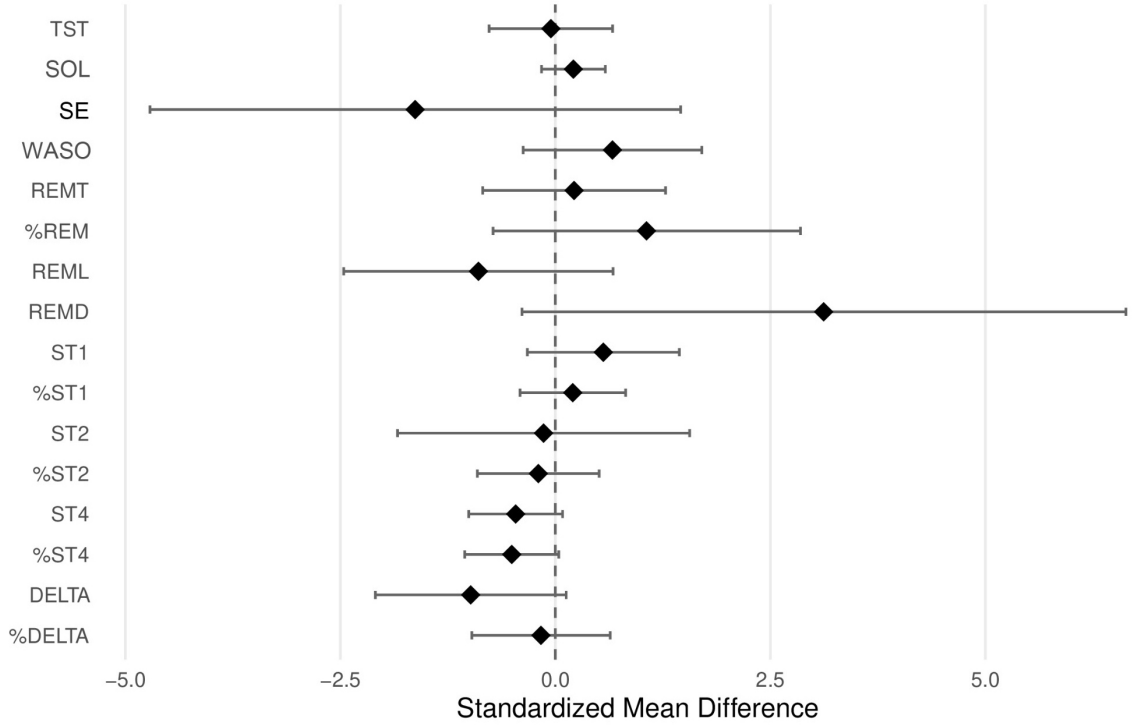

Fig. 4. Sleep parameters in drug-free SZA vs drug-free SCZ (forest plot).

and overly influential studies. Results from the meta-analyses comparing drug-free SZA with HC, drug-free MDD and drug-free SCZ are presented in forest plots in Figs. 2,3,4, respectively.

3.2 Total Sleep Time

Drug-free SZA showed reduced TST (SMD = –1.43; $p < 0.001$) compared to HC. TST of drug-free SZA was not different from that of drug-free MDD (SMD = 0.0286; $p = 0.948$) and drug-free SCZ (SMD = –0.0519; $p = 0.887$).

3.3 Sleep Latency

Drug-free SZA showed prolonged SOL compared to both HC (SMD = 1.70; $p < 0.001$) and drug-free MDD (SMD = 0.684; $p < 0.001$). SOL of drug-free SZA did not differ from that of drug-free SCZ (SMD = 0.210; $p = 0.266$).

3.4 Sleep Efficiency

Drug-free SZA SE did not differ from that of drug-free MDD (SMD = 0.535; $p = 0.556$) and drug-free SCZ (SMD = –1.63; $p = 0.301$). It was not possible to compare drug-free SZA and HC SE due to lack of data.

3.5 Wakefulness Time During Sleep

Drug-free SZA showed increased WASO compared to HC (SMD = 1.20; $p < 0.001$). WASO of drug-free SZA did not differ from that of drug-free MDD (SMD = –0.385; $p = 0.550$) and drug-free SCZ (SMD = 0.664; $p = 0.210$).

3.6 REM Time

Reduced REMT was found in drug-free SZA compared to HC (SMD = –0.620; $p = 0.006$). REMT of drug-free SZA did not differ from that of drug-free MDD (SMD = 0.009; $p = 0.984$) and drug-free SCZ (SMD = 0.218; $p = 0.688$).

3.7 REM Percentage

Drug-free SZA %REM did not differ from that of HC (SMD = –0.0382; $p = 0.843$), drug-free MDD (SMD = –0.246; $p = 0.277$) and drug-free SCZ (SMD = 1.06; $p = 0.244$).

3.8 REM Latency

Drug-free SZA showed shortened REML compared to HC (SMD = –0.528; $p = 0.007$). REML of drug-free SZA did not differ from that of drug-free MDD (SMD = 0.0335; $p = 0.870$) and drug-free SCZ (SMD = –0.894; $p = 0.263$).

3.9 REM Density

Drug-free SZA REMD did not differ from that of drug-free MDD (SMD = –0.150; $p = 0.582$) and drug-free SCZ (SMD = 3.12; $p = 0.081$). It was not possible to compare drug-free SZA and HC REMD due to lack of data.

3.10 Stage 1 Sleep Time

Drug-free SZA ST1 did not differ from that of drug-free SCZ (SMD = 0.558; $p = 0.216$). It was not possible to compare drug-free SZA ST1 to that of HC and drug-free MDD due to lack of data.

Table 6. Meta-analysis results.

	Meta-analysis				
SZA vs HC	N. of datasets	N. of subjects	Mean ± SD	RE Model	*p*-value
TST	4	33 vs 60	371.29 ± 72.7 vs 443.29 ± 28.72	–1.43 (–1.903 to –0.949)	***p* < 0.001**
SOL	5	42 vs 79	51.78 ± 39.47 vs 11 ± 8.09	1.70 (1.236 to 2.159)	***p* < 0.001**
WASO	3	25 vs 47	46.17 ± 42.34 vs 12.83 ± 10.94	1.20 (0.649 to 1.746)	***p* < 0.001**
REMT	4	33 vs 60	79.7 ± 29.22 vs 96.85 ± 20.05	–0.620 (–1.058 to –0.181)	***p* = 0.006**
%REM	5	42 vs 79	21.65 ± 5.98 vs 22.3 ± 5.02	–0.038 (–0.416 to 0.339)	$p = 0.843$
REML	5	42 vs 60	66.35 ± 28.33 vs 86.26 ± 34.76	–0.528 (–0.911 to –0.145)	***p* = 0.007**
ST4	3	26 vs 51	7.65 ± 16.17 vs 47.41 ± 37.00	–1.20 (–1.713 to –0.693)	***p* < 0.001**
%ST4	3	26 vs 51	1.88 ± 4.63 vs 10.53 ± 8.30	–1.14 (–1.649 to –0.636)	***p* < 0.001**
DELTA	3	25 vs 47	43.16 ± 32.25 vs 74.56 ± 30.90	–0.814 (–1.725 to 0.097)	$p = 0.080$
	Meta-analysis				
SZA vs MDD	N. of datasets	N. of subjects	Mean ± SD	RE Model	*p*-value
TST	7	53 vs 83	345.56 ± 67.65 vs 344.43 ± 58.48	0.028 (–0.827 to 0.884)	$p = 0.948$
SOL	7	56 vs 80	57.82 ± 43.48 vs 37.68 ± 33.80	0.684 (0.321 to 1.047)	***p* < 0.001**
SE	3	26 vs 49	68.52 ± 15.42 vs 67.19 ± 17.64	0.535 (–1.247 to 2.316)	$p = 0.556$
WASO	5	43 vs 67	40.08 ± 37.69 vs 42.41 ± 36.98	–0.385 (–1.649 to 0.879)	$p = 0.550$
REMT	7	53 vs 83	72.89 ± 25.6 vs 78.23 ± 35.85	0.009 (–0.861 to 0.879)	$p = 0.984$
%REM	8	62 vs 89	21.08 ± 5.65 vs 22.71 ± 6.71	–0.246 (–0.689 to 0.198)	$p = 0.277$
REML	10	67 vs 131	54.39 ± 25.57 vs 45.52 ± 22.90	0.033 (–0.367 to 0.434)	$p = 0.870$
REMD	3	20 vs 43	1.77 ± 0.71 vs 1.84 ± 0.95	–0.150 (–0.684 to 0.384)	$p = 0.582$
ST4	3	26 vs 23	7.65 ± 16.17 vs 14.78 ± 25.23	–0.348 (–0.922 to 0.225)	$p = 0.234$
%ST4	3	26 vs 23	1.88 ± 4.63 vs 3.60 ± 5.59	–0.357 (–0.932 to 0.217)	$p = 0.223$
DELTA	6	49 vs 92	26.74 ± 15.60 vs 21.26 ± 12.90	0.351 (–0.991 to 1.693)	$p = 0.609$
%DELTA	3	26 vs 49	5.42 ± 3.28 vs 2.22 ± 2.67	1.16 (–0.501 to 2.821)	$p = 0.171$
	Meta-analysis				
SZA vs SCZ	N. of datasets	N. of subjects	Mean ± SD	RE Model	*p*-value
TST	7	41 vs 79	368.62 ± 65.88 vs 369.82 ± 48.07	–0.052 (–0.770 to 0.666)	$p = 0.887$
SOL	6	44 vs 65	58.06 ± 36.12 vs 57.30 ± 36.78	0.210 (–0.160 to 0.581)	$p = 0.266$
SE	3	14 vs 41	71.80 ± 14.40 vs 78.63 ± 7.47	–1.63 (–4.714 to 1.458)	$p = 0.301$
WASO	5	31 vs 62	40.08 ± 32.34 vs 21.16 ± 14.97	0.664 (–0.375 to 1.703)	$p = 0.210$
REMT	7	41 vs 79	80.4 ± 25.6 vs 83.17 ± 18.53	0.218 (–0.845 to 1.281)	$p = 0.688$
%REM	8	50 vs 88	21.89 ± 5.36 vs 19.74 ± 2.86	1.06 (–0.724 to 2.850)	$p = 0.244$
REML	8	50 vs 88	62.27 ± 24.85 vs 67.15 ± 19.65	–0.894 (–2.461 to 0.672)	$p = 0.263$
REMD	3	8 vs 30	2.31 ± 0.20 vs 1.82 ± 0.10	3.12 (−0.388 to 6.635)	$p = 0.081$
ST1	3	14 vs 41	43.48 ± 8.9 vs 37.74 ± 4.69	0.558 (–0.326 to 1.441)	$p = 0.216$
%ST1	3	14 vs 41	12.63 ± 5.6 vs 10.76 ± 4.70	0.203 (–0.411 to 0.817)	$p = 0.516$
ST2	4	23 vs 50	194.74 ± 18.30 vs 201.45 ± 11.41	–0.137 (–1.836 to 1.561)	$p = 0.874$
%ST2	3	14 vs 41	56.02 ± 6.20 vs 58.83 ± 6.30	–0.198 (–0.907 to 0.510)	$p = 0.583$
ST4	3	26 vs 28	7.65 ± 16.17 vs 17.38 ± 26.08	–0.461 (–1.007 to 0.084)	$p = 0.097$
%ST4	3	26 vs 28	1.88 ± 4.63 vs 4.68 ± 6.55	–0.507 (–1.054 to 0.040)	$p = 0.069$
DELTA	5	31 vs 62	38.33 ± 20.36 vs 42.39 ± 15.50	–0.984 (–2.093 to 0.126)	$p = 0.082$
%DELTA	3	14 vs 41	9.91 ± 8.19 vs 10.25 ± 7.20	–0.167 (–0.972 to 0.638)	$p = 0.685$

Statistically significant meta-analysis *p*-values are shown in bold. TST, total sleep time; SOL, sleep onset latency; WASO, wake after sleep onset; REMT, rapid-eye-movement time; ST1, Stage 1 sleep time; ST2, Stage 2 sleep time; ST4, Stage 4 sleep time; %ST1, Stage 1 sleep percentage; %ST2, Stage 2 sleep percentage; %ST4, Stage 4 sleep percentage; DELTA, Delta sleep time; %DELTA, Delta sleep percentage; SE, sleep efficiency; REML, rapid-eye-movement latency; REMD, rapid-eye-movement density; RE, random effect.

Table 7. Publication bias and funnel plot asymmetry (rank correlation and regression test) analysis.

	Heterogeneity			Publication Bias			Funnel plot asymmetry	
SZA vs HC	Q	I^2	*p*-value	Fail-Safe N (*p*-value)	Outlier	Overly influential	Rank correlation (*p*-value)	Regression test (*p*-value)
TST	2.797	0%	$p = 0.424$	48 ($p < 0.001$)	-	-	$p = 0.7500$	$p = 0.4260$
SOL	4.379	10.43%	$p = 0.357$	105 ($p < 0.001$)	-	Benson et al., 1980 [72]	$p = 0.0833$	$p = 0.1477$
WASO	2.262	6.62%	$p = 0.323$	19 ($p < 0.001$)	-	-	$p = 1.0000$	$p = 0.8293$
REMT	1.495	0%	$p = 0.683$	8 ($p = 0.002$)	-	-	$p = 0.3333$	$p = 0.2678$
%REM	1.722	0%	$p = 0.787$	0 ($p = 0.399$)	-	-	$p = 0.4833$	$p = 0.3592$
REML	1.369	0%	$p = 0.849$	9 ($p = 0.003$)	-	-	$p = 0.8167$	$p = 0.8123$
ST4	0.166	0%	$p = 0.920$	21 ($p < 0.001$)	-	-	$p = 1.0000$	$p = 0.9619$
%ST4	0.429	0%	$p = 0.807$	19 ($p < 0.001$)	-	-	$p = 1.0000$	$p = 0.9100$
DELTA	6.107	67.66%	$p = 0.047$	8 ($p < 0.001$)	Zarcone et al., 1995 [75]	-	$p = 0.3333$	$p = 0.0874$
	Heterogeneity			Publication Bias			Funnel plot asymmetry	
SZA vs MDD	Q	I^2	*p*-value	Fail-Safe N (*p*-value)	Outlier	Overly influential	Rank correlation (*p*-value)	Regression test (*p*-value)
TST	21.237	80.04%	$p = 0.002$	0 ($p = 0.431$)	Kupfer & Foster, 1975 [77]	Kupfer & Foster, 1975 [77]	$p = 0.7726$	$p = 0.1983$
SOL	4.931	0%	$p = 0.553$	31 ($p < 0.001$)	-	-	$p = 1.0000$	$p = 0.4002$
SE	14.418	90.44%	$p < 0.001$	0 ($p = 0.093$)	Kupfer & Foster, 1975 [77]	-	$p = 1.0000$	$p = 0.2274$
WASO	19.199	88.48%	$p < 0.001$	0 ($p = 0.137$)	Kupfer & Foster, 1975 [77]	Kupfer & Foster, 1975 [77]	$p = 1.0000$	$p = 0.0239$*
REMT	20.393	80.67%	$p = 0.002$	0 ($p = 0.349$)	Kupfer & Foster, 1975 [77]	Kupfer & Foster, 1975 [77]	$p = 0.2389$	$p = 0.0652$
%REM	11.842	37.83%	$p = 0.106$	0 ($p = 0.092$)	Kupfer & Foster, 1975 [77]	-	$p = 0.2751$	$p = 0.3701$
REML	14.28	35.00%	$p = 0.113$	0 ($p = 0.439$)	-	-	$p = 1.0000$	$p = 0.8657$
REMD	0.152	0%	$p = 0.927$	0 ($p = 0.342$)	-	-	$p = 1.0000$	$p = 0.7320$
ST4	1.051	0%	$p = 0.591$	0 ($p = 0.110$)	-	-	$p = 1.0000$	$p = 0.4381$
%ST4	1.281	0%	$p = 0.527$	0 ($p = 0.104$)	-	-	$p = 1.0000$	$p = 0.4131$
DELTA	30.314	91.28%	$p < 0.001$	0 ($p = 0.184$)	Kupfer & Foster, 1975 [77]	-	$p = 0.7194$	$p = 0.0379$*
%DELTA	12.554	88.30%	$p = 0.002$	9 ($p < 0.001$)	Kupfer & Foster, 1975 [77]	-	$p = 0.3333$	$p = 0.0005$*
	Heterogeneity			Publication Bias			Funnel plot asymmetry	
SZA vs SCZ	Q	I^2	*p*-value	Fail-Safe N (*p*-value)	Outlier	Overly influential	Rank correlation (*p*-value)	Regression test (*p*-value)
TST	15.949	66.73%	$p = 0.014$	0 ($p = 0.378$)	Reich et al., 1975 [76]	-	$p = 1.0000$	$p = 0.6722$
SOL	20.661	0%	$p = 0.004$	5 ($p = 0.018$)	Reich et al., 1975 [76]	-	$p = 0.3988$	$p = 0.0003$*
SE	14.999	93.61%	$p < 0.001$	7 ($p = 0.002$)	Reich et al., 1975 [76]	-	$p = 1.0000$	$p = 0.0343$*
WASO	14.377	77.93%	$p = 0.006$	10 ($p = 0.003$)	Reich et al., 1975 [76]	-	$p = 0.4833$	$p = 0.8658$
REMT	24.28	84.39%	$p < 0.001$	0 ($p = 0.382$)	Reich et al., 1975 [76]	Reich et al., 1975 [76]	$p = 0.0690$	$p = 0.0005$*
%REM	61.892	94.47%	$p < 0.001$	13 ($p = 0.005$)	Zarcone et al., 1987 [74]	Zarcone et al., 1987 [74]	$p = 0.1789$	$p < 0.0001$*
REML	41.256	93.60%	$p < 0.001$	7 ($p = 0.014$)	Reich et al., 1975 [76]	Reich et al., 1975 [76]	$p = 0.3988$	$p < 0.0001$*
REMD	21.365	89.27%	$p < 0.001$	23 ($p < 0.001$)	Benson et al., 1983 [80]	-	$p = 1.0000$	$p = 0.0185$*
ST1	3.517	44.12%	$p = 0.172$	1 ($p = 0.043$)	-	-	$p = 0.3333$	$p = 0.0898$
%ST1	0.161	0%	$p = 0.923$	0 ($p = 0.289$)	-	-	$p = 0.3333$	$p = 0.7012$
ST2	26.218	88.52%	$p < 0.001$	0 ($p = 0.250$)	Zarcone et al., 1995 [75]	-	$p = 0.7500$	$p = 0.5116$
%ST2	2.372	19.39%	$p = 0.305$	0 ($p = 0.327$)	-	-	$p = 0.3333$	$p = 0.1563$
ST4	0.862	0%	$p = 0.650$	1 ($p = 0.049$)	-	-	$p = 1.0000$	$p = 0.9210$
%ST4	1.101	0%	$p = 0.577$	1 ($p = 0.034$)	-	-	$p = 1.0000$	$p = 0.7572$
DELTA	16.348	80.35%	$p = 0.003$	16 ($p < 0.001$)	-	-	$p = 0.0167$*	$p = 0.0001$*
%DELTA	2.916	35.41%	$p = 0.233$	0 ($p = 0.276$)	-	-	$p = 0.3333$	$p = 0.0878$

*Asymmetry found.

3.11 Stage 1 Sleep Percentage

Drug-free SZA %ST1 did not differ from that of drug-free SCZ (SMD = 0.203; $p = 0.516$). It was not possible to compare drug-free SZA %ST1 to that of HC and drug-free MDD due to lack of data.

3.12 Stage 2 Sleep Time

Drug-free SZA ST2 did not differ from that of drug-free SCZ (SMD = –0.137; $p = 0.874$). It was not possible to compare drug-free SZA ST2 to that of HC and drug-free MDD due to lack of data.

3.13 Stage 2 Sleep Percentage

Drug-free SZA %ST2 did not differ from that of drug-free SCZ (SMD = –0.198; $p = 0.583$). It was not possible to compare drug-free SZA %ST2 to that of HC and drug-free MDD due to lack of data.

3.14 Stage 3 Sleep Time

It was not possible to perform a meta-analysis for ST3 in any case-control due to lack of data.

3.15 Stage 3 Sleep Percentage

It was not possible to perform a meta-analysis for %ST3 in any case-control due to lack of data.

3.16 Stage 4 Sleep Time

Drug-free SZA showed reduced ST4 compared to HC (SMD = –1.20; $p < 0.001$). ST4 of drug-free SZA did not differ from that of drug-free MDD (SMD = –0.348; $p = 0.234$) and drug-free SCZ (SMD = –0.461; $p = 0.097$).

3.17 Stage 4 Sleep Percentage

Drug-free SZA showed reduced %ST4 compared to HC (SMD = –1.14; $p < 0.001$). %ST4 of drug-free SZA did not differ from that of drug-free MDD (SMD = –0.357; $p = 0.223$) and drug-free SCZ (SMD = –0.507; $p = 0.069$).

3.18 Delta Sleep Time

Drug-free SZA DELTA did not differ from that of HC (SMD = –0.814; $p = 0.080$), drug-free MDD (SMD = 0.351; $p = 0.609$) and drug-free SCZ (SMD = –0.984; $p = 0.082$).

3.19 Delta Sleep Percentage

Drug-free SZA %DELTA did not differ from that of drug-free MDD (SMD = 1.16; $p = 0.171$) and drug-free SCZ (SMD = –0.167; $p = 0.685$). It was not possible to compare drug-free SZA %DELTA to that of HC due to lack of data.

4. Discussion

4.1 Previous Studies

Literature on sleep including samples with only SZA patients is limited, with most of the studies including SZA patients together with SCZ patients; therefore, it is difficult to clearly understand which sleep disturbances and abnormalities occur in SZA and their prevalence, as it is difficult to understand whether SZA sleep resembles more that of SCZ or that of affective disorders. The present work is the only systematic review and meta-analysis to date regarding sleep in SZA. Very few literature reviews on SZA have been performed, with each of them suggesting the necessity of more studies focused on these patients' sleep [25,113]; however, case-control sleep studies providing clear, drug-free SZA patients sample can be found only in the 1975–1995 span.

In a previous meta-analysis on REM sleep in SCZ [111], the SZA case-control studies identified were excluded from the SCZ meta-analysis, and are now analyzed and discussed. The debate surrounding whether SZA exists as a separate nosography entity or not, as previously reported, might help understand the loss of interest towards this investigation.

Our meta-analysis results strengthen previous reports regarding sleep continuity fragmentation in SZA with decreased TST, increased SOL and WASO compared to HC. Sleep architecture analyses found decreased REMT and shortened REML, together with ST4 and %ST4 reduction. Nonetheless, in contrast with earlier reports, our meta-analysis did not find reduced DELTA (ST3+ST4) in SZA compared to HC.

We found significantly longer SOL in SZA compared to MDD, a result that was not consistently reported in previous studies. No differences were found between sleep parameters of SZA and SCZ.

According to our results and in line with more recent PSG studies [72,74,75], sleep variables do not allow to clearly characterize SZA patients from either SCZ or MDD patients. In the latest PSG study of SZA, although based on partially treated samples, Petit et al. [65] supported the idea that it might not be possible to differentiate SCZ, SZA, and BD patients by sleep parameters, as they found no PSG differences across these samples.

4.2 Clinical Implications

PSG parameters alone are not recommended for the differential diagnosis of SZA. The assessment of sleep disturbances as dimensional features (rather than categorical markers) is relevant for guiding adjunctive interventions targeting sleep quality.

Knowledge regarding the beneficial effect of drug treatment on the sleep of SZA patients is limited. Paliperidone, the only approved treatment for SZA in the United States, was reported to improve both subjective sleep quality [114] and sleep continuity [115].

4.3 Limitations and Future Perspectives

The majority of the meta-analyses performed in this study were based on datasets between three and ten, reflecting the limited availability of eligible studies. Meta-

analyses, such as %DELTA in SCZ vs HC or those concerning the first two stages of sleep in SCZ vs MDD, could not be performed due to insufficient data. Most meta-analyses included fewer than five studies, below what has been suggested as a practical lower boundary for obtaining more stable random-effects meta-analytic estimates [116]. Post-hoc analysis revealed that the statistical power of most of the meta-analyses was low (<0.8), especially in those comparing SZA to MDD and to SCZ, substantially increasing the risk of type II error.

These constraints result in a partial characterization of sleep abnormalities in SZA, as several potentially relevant parameters could not be adequately examined. Therefore, the present meta-analysis should be considered exploratory. In addition, several analyses showed substantial heterogeneity, further limiting the strength of quantitative inferences and supporting more hypothesis-generating interpretation rather than definitive conclusions.

A major contributor to between-study heterogeneity is the marked demographic imbalance across samples. Most of the included studies recruited predominantly male participants, with female SZA patients being underrepresented, despite schizoaffective disorder being reported to occur more frequently in females. In addition, most samples were concentrated within a narrow age range (approximately 30–40 years), limiting generalizability across the lifespan and potentially increasing sensitivity to modest between-study age differences.

Diagnostic classification represents another important source of heterogeneity. In the meta-analyses, 8 of 9 studies used Research Diagnostic Criteria (RDC), while one study used DSM-II criteria. Although relatively consistent within the meta-analytic subset, the broader set of studies included in the systematic review shows greater variability in diagnostic frameworks across DSM and ICD versions. This inconsistency in diagnostic operationalization likely increases conceptual heterogeneity and reduces comparability across studies in the qualitative synthesis.

Although most studies applied a minimum washout period of ≥2 weeks, one study [75] used a shorter ≥2 days period. Residual pharmacological effects on sleep architecture cannot be entirely excluded, as several psychotropic agents may exert prolonged effects beyond such washout periods. However, given that only a single study deviated from the ≥2 week standard, its influence on the overall estimates is likely limited, although its contribution to residual heterogeneity cannot be formally quantified in the present dataset.

A further limitation concerns clinical heterogeneity within the MDD samples. Several included studies did not consistently distinguish between psychotic and non-psychotic forms of unipolar depression, preventing stratified analyses. Given that psychotic features may be associated with distinct sleep architecture alterations, the lack of diagnostic separation may have contributed to residual heterogeneity and limited the precision with which sleep findings can be attributed to specific depressive subtypes. Our meta-analysis found increased SOL in SZA compared with MDD; initial insomnia has been reported to be more severe in psychotic than non-psychotic depression [117], suggesting that prolonged SOL may be more closely related to psychotic symptomatology. This interpretation is further supported by the absence of SOL differences between SZA and SCZ in our analyses.

It must also be noted that the approach used to handle missing SDs represents a potential source of bias and may have influenced both effect size precision and between-study variability. Specifically, imputing missing SDs using weighted averages derived from studies within the same meta-analysis assumes homogeneity of variance across studies. Although this procedure allowed the inclusion of studies that otherwise would have been excluded due to incomplete reporting, it may have artificially constrained within-study variance in some cases while inflating it in others. This could have distorted the true magnitude of heterogeneity. For this reason, results involving imputed SDs should be interpreted with caution.

Our study did not permit a thorough investigation of DELTA in SZA compared to HC, as it was not possible to perform a meta-analysis with adequate statistical power of REMD in SZA compared to that in SCZ. This limitation is relevant given that REMD has consistently been reported as elevated in mood disorders [118,119,120,121], while early PSG study reported REMD levels in SZA and MDD exceeding those observed in HC and non-affective psychoses [71,72,73,74,75,76,77].

Given these limitations, the observed null findings should not be interpreted as evidence of equivalence between the studied populations, but rather as reflecting the limited and underpowered evidence base. It is nonetheless plausible that sleep macroarchitecture measures derived from standard PSG are not diagnosis-specific and therefore do not clearly differentiate SZA from other psychiatric conditions.

In this context, emerging research on sleep microarchitecture (e.g., sleep spindles) appears more sensitive to subtle group differences and may help clarify distinctions across conditions that can be conceptualized as lying along a psychosis-affective spectrum rather than representing discrete entities. Future research should also prioritize larger drug-free or minimally treated SZA cohorts to reduce the confounding effects of psychotropic medications on sleep architecture. Nonetheless, the effects of pharmacological treatment on sleep parameters, together with its clinical efficacy in SZA, should also be investigated. Longitudinal designs following patients across different illness phases and diagnostic transitions, especially given the high diagnostic shift in this population [122], may also help clarify the temporal stability and diagnostic specificity of PSG abnormalities. In addition, the relevance of REMD warrants further

investigation, given its proposed utility as a clinical marker and its potential role in differentiating diagnostic subgroups [111,120,123,124].

Multimodal studies integrating PSG and electrophysiological measures with neuroimaging, as well as modern non-invasive digital sleep assessment tools such as actigraphy [125,126] and digital phenotyping [127,128] could improve understanding of the neurobiological mechanisms underlying sleep alterations across psychotic and affective disorders.

5. Conclusions

This systematic review and meta-analysis found that SZA is characterized by sleep disruption, including reduced TST, increased SOL and WASO, shortened REML, and reduced SWS compared to HC. However, these alterations do not allow to differentiate SZA from either SCZ or MDD, as most PSG parameters overlap across these conditions. Limited statistical power due to insufficient available data highlights the need for further studies with larger minimally treated samples to clarify the potential diagnostic specificity of sleep parameters in SZA.

Abbreviations

BD, Bipolar disorder; DELTA, Delta sleep time; %DELTA, Delta sleep percentage; EEG, Electroencephalography; HC, Healthy control; MDD, Major depressive disorder; NREM, Non-REM sleep; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; PSG, Polysomnography; RDC, Research diagnostic criteria; REM, Rapid-eye-movement; REMD, Rapid-eye-movement density; REML, Rapid-eye-movement latency; REMT, Rapid-eye-movement time; %REM, Rapid-eye-movement percentage; SCZ, Schizophrenia; SD, Standard deviation; SE, Sleep efficiency; SOL, Sleep onset latency; ST1, Stage 1 sleep time; ST2, Stage 2 sleep time; ST4, Stage 4 sleep time; %ST1, Stage 1 sleep percentage; %ST2, Stage 2 sleep percentage; %ST4, Stage 4 sleep percentage; SWS, Slow-wave sleep; SZA, Schizoaffective disorder; TST, Total sleep time; WASO, Wake after sleep onset; WoS, Web of Science.

Availability of Data and Materials

Data fully provided in **Supplementary Material**.

Author Contributions

Conceptualization, data curation, formal analysis, investigation, methodology, software, writing (original draft) (DM). Conceptualization, methodology, project administration, supervision, validation, visualization, writing (review & editing) (GF). Conceptualization, methodology, project administration, supervision, validation, visualization, writing (review & editing) (GB). All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/AP52900.

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