Narco Analysis Agents:Truth Serum's properties for Psychotherapeutic Activity

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Abstract— **This paper presents a comprehensive medical analysis evaluating the evolution of historical forensic "truth serums" into targeted tools in modern psychiatric healing and neurobiology. The study systematically analyzes the pharmacokinetic and multi-receptor pharmacodynamic profiles of thiopental sodium, scopolamine hydrobromide, and propofol. At controlled concentrations, these agents induce central nervous system (CNS) disinhibition by suppressing high-level cortical executive functions, facilitating cathartic abreaction in chronic Post-Traumatic Stress Disorder (PTSD) and showing rapid-acting antidepressant efficacy. However, a critical neurobiological paradox is established regarding acute trauma management: the administration of propofol during the immediate aftermath of trauma may pathologically consolidate subcortical fear memory traces in the amygdala, potentially increasing the subsequent incidence of postoperative PTSD (10). This paper outlines clinical profiles and safety considerations regarding the use of these agents in psychiatric care.**

Index Terms—**Acute trauma, Amygdala, CNS disinhibition, Narcoanalysis, Post-Traumatic Stress Disorder, Propofol, Scopolamine, Thiopental sodium.**

I. INTRODUCTION

The therapeutic utilization of central nervous system (CNS) disinhibiting agents resides at the critical boundary of clinical psychiatry, molecular anesthesia, and neurobiology (1). Historically defined as chemical agents capable of compelling an individual to reveal repressed or consciously withheld information, substances such as thiopental sodium, sodium amytal, and scopolamine hydrobromide are, in a strict scientific sense, misnomers (1). They do not invariably elicit objective truth; instead, the primary pharmacological phenomenon they induce is cortical disinhibition via the depression of high-level prefrontal networks (2). By lowering the cognitive and volitional barriers required to suppress or manipulate memory structures, these agents behave as facilitators of emotional release, heightened talkativeness, and increased suggestibility (2).

The somatic paradigm of utilizing sub-anesthetic drug infusions dates back to World War I, where British psychologist Charles S. Myers introduced the term "shell shock" in 1915 to characterize acute combat-related psychological casualties (4). By 1930, William Bleckwenn pioneered the use of intravenous barbiturate infusions to treat catatonic mutism, demonstrating that sub-anesthetic doses could temporarily release patients from catatonia to talk, eat, and interact normally (5). This framework was adapted during World War II by American psychiatrists Roy Grinker and John Spiegel into "narcosynthesis" a therapeutic technique detailed in their landmark 1945 treatise, Men Under Stress (4). Faced with an epidemic of "operational fatigue," clinicians utilized intravenous thiopental sodium to bypass conscious defenses, inducing a light hypnotic trance where soldiers underwent "cathartic abreaction"

the vivid recall and emotional re-living of repressed battle-related traumas (4, 5).

Conversely, the translation of these agents into forensic interrogation yielded highly inconsistent and legally fraught outcomes (1). Early forensic experiments by Robert House utilized a "twilight sleep" protocol combining morphine sulfate, scopolamine hydrobromide, and light chloroform inhalation (1). Subsequent forensic research established that while barbiturates significantly reduce the volitional will to resist questioning, they heavily impair high-level cognitive processing (1). Under their sedative influence, subjects enter a highly suggestible state, making them prone to fabricating elaborate lies or agreeing to leading questions, thereby rendering objective forensic truth highly elusive (1).

In modern psychiatric therapeutics, scopolamine and propofol are at the forefront of a paradigm shift in treating affective disorders (14). By acting on central muscarinic and GABAergic/NMDA pathways, these compounds can induce rapid, robust antidepressant and antianxiety effects within days or even hours bypassing the slow therapeutic timeline of traditional monoaminergic drugs (14, 15).

II. PHYSICOCHEMICAL AND PHARMACOKINETIC DYNAMICS OF THIOPENTAL SODIUM

Thiopental sodium is an ultra-short-acting, highly lipophilic thiobarbiturate derivative (6). Chemically, it is the sulfur analog of pentobarbital, where the oxygen atom at the (C_2) position of the barbituric acid ring is replaced by a sulfur atom (6). This minor structural modification dramatically increases its lipid solubility, allowing it to rapidly cross the blood-brain barrier (BBB) (2). Following a single intravenous bolus injection, thiopental reaches peak brain concentration within 30 to 45 seconds, with approximately 60% of the total administered dose concentrating in highly vascularized cerebral tissues almost immediately (6).

The rapid termination of thiopental's central hypnotic effect is not a result of hepatic metabolism, but rather a function of rapid pharmacokinetic redistribution (2). Within 5 to 10 minutes post-injection, the concentration of the drug in the brain drops below the threshold for hypnosis as it redistributes down its concentration gradient into moderately perfused tissues, primarily skeletal muscle, and eventually into poorly perfused adipose tissue (2). This rapid redistribution accounts for the quick awakening observed after a single induction dose (2).

However, when thiopental sodium is administered via continuous infusion or in large, repeated maintenance doses, its pharmacokinetic profile changes significantly (2). Thiopental possesses a long terminal elimination half-life, ranging from 5.5 to 26 hours, and is metabolized slowly in the liver by cytochrome P450 enzymes (2). At high cumulative doses, peripheral tissue compartments (muscle and fat) become saturated, causing the drug's elimination to transition from first-order to zero-order kinetics (2). This saturation leads to significant drug accumulation, resulting in highly prolonged recovery times and persistent sedative effects (2).

From a formulation perspective, thiopental sodium is prepared as a highly alkaline, sterile yellow powder that must be reconstituted with sterile water or physiological saline to a 2.5% solution (7). Due to its high pH (typically exceeding 10.5), thiopental is highly irritating to vascular intima and acts as a severe vesicant (2). Extravasation or accidental intra-arterial injection can cause severe chemical endarteritis, intense vasospasm, thrombosis, and subsequent tissue necrosis (2). Clinical administration, therefore, requires a patent intravenous line, often beginning with a small test dose to assess individual patient sensitivity (8).

For standard general anesthesia induction, the agent is administered slowly over 20 to 40 seconds (8). When used historically for continuous sedative maintenance in psychiatric narcoanalysis, it was delivered as a slow intravenous drip in concentrations of 0.2% or 0.4% (8). The use of sterile water as a diluent for these low concentrations is strictly contraindicated, as it leads to hypotonic hemolysis (8). Furthermore, standard clinical protocols mandate premedication with anticholinergic agents, such as atropine or scopolamine, to suppress vagal reflexes and inhibit excessive airway secretions stimulated by the barbiturate (8).

III. MOLECULAR PHARMACODYNAMICS OF THIOPENTAL-INDUCED NARCOANALYSIS

The central nervous system depressant and disinhibitory actions of thiopental sodium are primarily mediated via its interactions with the γ -

aminobutyric acid type A ($GABA_A$) receptor complex (2). The $GABA_A$ receptor is a ligand-gated pentameric chloride ion channel that serves as the major inhibitory neurotransmitter target in the mammalian brain (2). Thiopental binds to specific allosteric sites on the receptor, distinct from the binding site of endogenous GABA (2). At low, sub-anesthetic concentrations, thiopental acts as a positive allosteric modulator, enhancing the affinity of the receptor for GABA and significantly prolonging the duration of chloride channel opening in response to GABA binding (2). This action increases the influx of chloride ions into the postsynaptic neuron, causing membrane hyperpolarization and a widespread reduction in neuronal excitability (2). At higher, anesthetic concentrations, thiopental can directly gate the chloride channel even in the absence of GABA, leading to profound, generalized CNS depression (2).

Simultaneously, thiopental sodium exerts distinct metabolic and electrophysiological effects on the cerebral cortex (6). It decreases the cerebral metabolic rate of oxygen ($CMRO_2$) and decreases the cerebrovascular response to carbon dioxide (2). This reduction in metabolic demand induces cerebral vasoconstriction, which in turn decreases intracranial pressure (ICP) while maintaining cerebral perfusion pressure (2). This phenomenon, often called the "inverse steal" or "Robin Hood" effect, selectively diverts blood flow from healthy, vasoconstricted areas of the brain to ischemic regions where local acidosis has already caused maximal vasodilation (6).

At the cellular level, the transition from consciousness to drug-induced sedation develops in distinct neurochemical stages (3):

- Hypoxic Hyperactive Stage: During initial or low-dose administration, thiopental restricts cerebral energy metabolism, which selectively blocks energy-dependent pathways (9). Specifically, tonic activating cholinergic reactions in the cerebral cortex are suppressed, as acetylcholine-mediated excitation relies on active, energy-supported neurotransmitter synthesis and release (9). Conversely, glutamatergic excitation which is more resistant to immediate energy deprivation persists (9). This temporary neurochemical imbalance between depressed cholinergic arousal and sustained glutamatergic transmission generates a hyperactive, disinhibited state (9). Electrophysiologically, this stage is characterized by transient, high-amplitude epileptiform discharges on the electroencephalogram (EEG) and involuntary, unmotivated psychomotor movements (9).
- Narcotic Stage: As the dose of thiopental is increased, a transition to the narcotic stage occurs (9). At this level, both motor activity and conscious processing are suppressed, and the EEG shows a characteristic flattening of oscillations (9).
- Post-Narcotic State: Upon emergence from the narcotic stage, the brain enters a post-narcotic state associated with a slow recovery of ionic homeostasis (9). During this phase, there is a steady drop in the amplitude of cortical neuron spikes, which clinically manifests as prolonged lethargy, confusion, and a state of cognitive disinhibition (9).

It is during the transition between the hyperactive and narcotic stages (clinically aligned with Stage II of anesthesia, or the light hypnotic trance) that the state of talkativeness and emotional release is achieved (3). By selectively depressing cortical inhibitory circuits while leaving subcortical emotional centers partially active, thiopental allows patients to verbalize thoughts and feelings that are normally suppressed by the prefrontal cortex (3).

IV. MUSCARINIC ANTAGONISM AND THE RAPID ANTIDEPRESSANT ACTION OF SCOPOLAMINE

Scopolamine hydrobromide (hyoscine) is a naturally occurring tropane alkaloid extracted from plants of the Solanaceae family (11). Structurally, it is closely related to atropine but contains an additional epoxide oxygen bridge, which increases its lipid solubility and allows it to readily cross the blood-brain barrier (11). From a formulation perspective, scopolamine has been successfully developed as a transdermal patch system, delivering the drug at a controlled, steady rate over a 72-hour period (11). This delivery route bypasses first-pass hepatic metabolism, improves systemic bioavailability, and maintains stable plasma concentrations, thereby minimizing acute side effects (11).

The traditional view of scopolamine as a simple sedative and antiemetic was challenged by landmark clinical trials at the National Institute of Mental Health (NIMH) (14). These studies investigated the role of the

cholinergic neurotransmitter system in depression, leading to the discovery of scopolamine's rapid-acting antidepressant properties (14). The prevailing neurobiological hypothesis suggests that major depressive disorder (MDD) and bipolar disorder (BD) are characterized by an overactive cholinergic system, which disrupts downstream monoaminergic and glutamatergic signaling in the prefrontal cortex (15). By acting as a competitive antagonist of central muscarinic acetylcholine receptors particularly the (M_1) receptor subtype scopolamine blocks this pathological cholinergic hyperactivity, rapidly restoring normal mood and affect (11).

The clinical efficacy of scopolamine was evaluated in a series of double-blind, randomized, placebo-controlled crossover trials (13). Depressed outpatients meeting DSM-IV criteria for recurrent MDD or BD were randomized to receive a series of intravenous infusions of either a placebo saline solution or scopolamine hydrobromide, with each infusion separated by 3 to 5 days (13). The trial protocols excluded concurrent medications, requiring a washout period for prescription drugs, anticholinergic agents, and strong CYP3A4 inhibitors (within 14 days) or CYP3A4 inducers (within 21 days) (11). Muscarinic receptor occupancy in the brain was evaluated using positron emission tomography (PET) scans utilizing the specific radiotracer [^{11}C] EMO (also known as [^{11}C] LSN3172176) (11).

The clinical results demonstrated rapid, robust, and long-lasting antidepressant and antianxiety effects (13). Patients in the placebo-first (P/S) group showed no significant improvement during the placebo series but experienced rapid reductions in depression and anxiety ratings measured by the Montgomery-Asberg Depression Rating Scale (MADRS) and the Hamilton Anxiety Rating Scale (HARS) following the transition to scopolamine (13). This improvement was statistically significant at the first evaluation, which took place 3 to 4 days after the initial infusion, and often within hours of administration (14).

In the scopolamine-first (S/P) group, significant reductions in MADRS and HARS scores occurred rapidly and persisted throughout the subsequent three-week placebo phase, well beyond the expected pharmacokinetic clearance of the drug (13). At the study's conclusion, approximately 64% of patients achieved a full clinical response ($\geq$ 50%) reduction in MADRS score), and 50% entered complete clinical remission (13). This sustained efficacy suggests that transient muscarinic (M_1) blockade triggers downstream neuroplastic remodeling, including the modulation of AMPA and NMDA glutamate receptors, resulting in lasting synaptic changes (12).

The tolerability and adverse effect profiles of scopolamine were closely monitored during these trials, as summarized in Table I.

Table I: Adverse Effect Profile of Scopolamine Hydrobromide Infusion Cohorts

Observed Adverse Effect	Placebo Cohort (n=22)	Scopolamine Cohort (n=22)	Clinical Significance & Management
Drowsiness	13	17	Expected central antihistaminic/anticholinergic sedation; transient (17).
Dry Mouth	3	18	Classic peripheral muscarinic receptor blockade; self-limiting (11).
Blurred Vision	4	16	Mydriasis and cycloplegia; resolves within hours of infusion (17).
Lightheadedness	4	15	Related to transient autonomic shifts; managed with recumbency (17).
Dizziness	3	9	Transient vestibular alteration; resolves spontaneously (11).
Hypotension (No Intervention)	0	1	Minor decrease in systolic/diastolic blood pressure; clinically stable (18).
Nervousness	1	1	No significant drug-placebo variance (18).
Headache	0	1	Mild; resolved without pharmacological intervention (18).
Vertigo	0	1	Transient; resolved within the recovery window (18).

Importantly, scopolamine was well-tolerated, and no serious adverse events occurred (18). Cardiovascular parameters, including heart rate and blood pressure, decreased slightly following infusion compared to placebo, but no subject developed symptomatic hypotension or cardiovascular insufficiency (18).

None of the patients developed hypomania, and manic symptoms remained low throughout the study (18). While some patients reported transient cognitive confusion during active infusion, baseline cognitive performance remained stable, with no persistent deficits observed on computerized selective attention tasks (12).

V. FORMULATION, MULTI-RECEPTOR PHARMACODYNAMICS, AND AFFECTIVE THERAPEUTICS

Propofol (2,6-diisopropylphenol) is an alkylphenol derivative that has largely replaced thiopental sodium for the induction and maintenance of general anesthesia (2). Because propofol is highly insoluble in aqueous solutions, it is formulated as a lipid emulsion containing soybean oil, glycerol, and egg lecithin (20). This lipid formulation can cause pain and burning on injection, which can be minimized by utilizing larger veins or co-administering lidocaine (19). Propofol is highly lipophilic and has a large volume of distribution, resulting in a rapid onset of action (within 30 to 40 seconds) (2). Its recovery profile is also exceptionally fast and predictable due to rapid redistribution and high metabolic clearance (2).

Propofol possesses a unique, multi-receptor pharmacodynamic profile (21). It acts as a potent positive allosteric modulator of the $GABA_A$ receptor, binding to distinct transmembrane sites to enhance chloride currents (21). At higher doses, it can directly gate the channel in the absence of GABA (21). Additionally, propofol potentiates glycine receptor function and directly inhibits the N-methyl-D-aspartate (NMDA) subtype of glutamate receptors (21). This dual GABAergic-ant glutamatergic action resembles the molecular mechanisms of ketamine and electroconvulsive therapy (ECT), leading researchers to investigate propofol as a novel, rapid-acting treatment for treatment-resistant depression (TRD) (21).

To gather preliminary data on the safety, tolerability, and antidepressant efficacy of deep propofol anesthesia, researchers conducted an open-label clinical trial (NCT02935647) in patients with moderate-to-severe, medication-resistant depression (21). A total of 10 healthy participants (aged 18 to 55 years) with treatment-resistant depression each underwent a series of 10 propofol infusions administered 3 times per week (21). Dosing was titrated using real-time EEG feedback from a bispectral index (BIS) monitor to achieve deep anesthesia with a target burst-suppression ratio (SR ≥ 15) maintained for 15 minutes per session (21). The propofol dosing protocol was divided into two phases:

- Induction Phase: Propofol was initiated with an intravenous bolus. Lower induction doses were used during the initial sessions to ensure hemodynamic stability, and higher doses were introduced in subsequent treatments as tolerated (21).
- Maintenance Phase: Following induction, a continuous infusion was initiated, supplemented with repeated boluses as needed to maintain the target EEG burst-suppression state (21).

The clinical results demonstrated significant antidepressant efficacy and excellent tolerability (21). No serious adverse events occurred across the 99 administered treatments (21). Post-anesthetic recovery was smooth: patients typically woke up within 10 minutes without significant nausea, dysphoria, or cognitive deficits (21). Scores on the Montreal Cognitive Assessment (MoCA) remained completely stable throughout and after the treatment series (21).

In terms of efficacy, scores on the 24-item Hamilton Depression Rating Scale (HDRS-24) decreased, representing an average 58% improvement from baseline (21). Six of the 10 subjects met the clinical criteria for treatment response (≥ 50%) improvement), and 5 of these 6 responders maintained this improvement for at least 3 months during the post-treatment follow-up phase (21). Furthermore, self-rated depression improvements in the propofol group were comparable to those in a control group of 20 patients who underwent electroconvulsive therapy (ECT) (21). This suggests that deep propofol anesthesia can induce rapid, durable antidepressant effects similar to ECT but with a significantly lower risk of cognitive side effects (21).

The clinical utility of propofol varies significantly across different dosing regimens, as detailed in Table II.

Table II: Clinical Utility and Outcomes of Propofol Dosing Regimen

Dosing Regimen	Clinical Indication	Co-administered Agents	Clinical Outcomes & Therapeutic Efficacy
Deep Anesthesia (SR ≥ 15, 15 mins) (21)	Treatment-Resistant Depression (TRD) (21)	None (to ensure hemodynamic stability) (21)	Rapid, durable antidepressant efficacy (58% HDRS improvement); stable cognitive scores (MoCA) (21).
Subhypnotic Infusion (Continuous for 24 hours) (22)	Chemotherapy-Induced Nausea & Vomiting (CINV) (22)	Dexamethasone & Serotonin Antagonists (Ondansetron) (22)	80% to 90% of patients with refractory CINV achieved complete control of nausea and vomiting (22).
Balanced Sedation (Starter bolus + maintenance boluses) (23)	Diagnostic Colonoscopy (23)	Midazolam (23)	Moderate sedation achieved in 98% of cases; reduced propofol requirement; rapid recovery (23).
Pediatric Infusion (Varied rates) (24)	Deep Extubation (DE) in Dental Surgery (24)	Sevoflurane (24)	Significantly reduced emergence agitation (EA) and airway irritation without increasing complications (24).
Anaesthetic-Led Infusion (Mean dose: (1089 mg ±) (26)	Double Balloon Enteroscopy (DBE) (26)	None (administered outside operating theater) (26)	High tolerability (median distress score 0.2/10) and cost-effective delivery of complex diagnostic services (26).

VI. NEUROBIOLOGICAL RISK OF PROPOFOL IN ACUTE TRAUMA: THE CONSOLIDATION PARADOX

Despite the therapeutic efficacy of propofol and scopolamine in treating established psychiatric disorders, a critical neurobiological paradox exists: the early administration of certain sedative-hypnotic agents in the immediate aftermath of acute trauma can significantly worsen subsequent psychological outcomes, increasing the risk of developing PTSD (10). This clinical concern is highlighted by prospective clinical trials evaluating the impact of intraoperative anesthetic choice on the subsequent development of PTSD in emergency trauma patients (20).

In a landmark, prospective, randomized, double-blind controlled trial (ChiCTR2100050202), Zhong and colleagues evaluated 300 emergency surgery trauma patients aged 18 to 60 years (20). To prevent confounding, the trial established strict exclusion criteria, omitting patients with craniocerebral or spinal cord injuries, decompensated haemorrhagic shock, liver or renal dysfunction, a history of alcohol or drug abuse, or pre-existing neurological or psychiatric disorders (30). Patients were randomized to receive anesthesia maintenance with either a continuous infusion of propofol or the inhalational anesthetic sevoflurane (20). At 1 month postoperatively, the incidence and severity of PTSD were evaluated using the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (20).

The clinical outcomes revealed a significant divergence between the two cohorts (20):

- PTSD Incidence: The incidence of PTSD in the propofol group was nearly double that of the sevoflurane group (23.2% versus 12.2%, $p = 0.014$) (20).
- Injury-to-Admission Time: In the propofol cohort, the time from injury to hospital admission was negatively correlated with the subsequent CAPS-5 score ($r = -0.226$, $p < 0.001$) (28). This correlation indicates that earlier propofol administration following trauma led to more severe PTSD symptoms (28). No such correlation was found in the sevoflurane cohort ($r = 0.002$, $p = 0.612$) (28).
- Multivariate Regression: A logistic regression model confirmed that propofol use was an independent risk factor for the development of postoperative PTSD (OR = 2.236, 95% CI: 1.152 ~ 4.430, $p = 0.017$) (28). Other perioperative factors including age, gender, BMI, diabetes, and postoperative pain scores showed no significant correlation with PTSD, as detailed in Table III.

Table III: Multivariate Logistic Regression Analysis of Risk Factors for Postoperative PTSD

Potential Risk Factor Analyzed	Odds Ratio (OR)	95% Credibility Interval	Statistical Significance (P-value)
Anesthetics (Propofol Maintenance)	2.236	1.152 ~ 4.430	0.017 (28)
ICU Admission	0.409	0.162 ~ 0.934	0.058 (28)
Injury-to-Admission Time	0.968	0.934 ~ 1.012	0.083 (28)
Postoperative 48h Pain (VAS)	0.842	0.656 ~ 1.054	0.176 (28)
Gender (Male vs. Female)	0.711	0.342 ~ 1.214	0.359 (28)
Diabetes Mellitus	0.683	0.263 ~ 1.412	0.435 (28)
Postoperative 6h Pain (VAS)	0.914	0.714 ~ 1.112	0.473 (28)
Hypertension	1.336	0.450 ~ 2.114	0.602 (28)
Body Mass Index (BMI)	0.984	0.921 ~ 1.034	0.625 (28)
Postoperative 24h Pain (VAS)	0.966	0.777 ~ 1.142	0.759 (28)
Age	0.997	0.962 ~ 1.024	0.857 (28)
Delirium Occurrence	1.007	0.382 ~ 1.989	0.989 (28)

This consolidation paradox is rooted in the neurobiology of fear memory systems (10). The brain's fear response is coordinated by the amygdala, where the basolateral nucleus processes threat-related sensory inputs and projects to the hippocampus to form explicit memories, and to the central nucleus to execute autonomic fear behaviors (10). During acute traumatic stress, elevated levels of central noradrenaline and glucocorticoids trigger rapid consolidation of these emotional fear memories in the amygdala (10).

Crucially, unconscious fear memory systems in the amygdala are significantly less sensitive to standard anesthetic suppression than conscious explicit memory systems in the hippocampus (10). While propofol successfully induces general anaesthesia and suppresses conscious cortical awareness, it may fail to block the sub-cortical consolidation of fear memories in the amygdala (10). At low or sub-hypnotic doses, which are inevitably encountered during induction and emergence, propofol can paradoxically enhance fear learning, thereby strengthening and reinforcing the traumatic memory trace (10).

In contrast, sevoflurane has been shown to inhibit explicit memory for emotionally charged images by decreasing functional connectivity between the basolateral amygdala and the hippocampus (10). This decoupling of conscious memory from emotional processing reduces the risk of long-term trauma consolidation (10).

This divergence in clinical outcomes highlights a critical pharmacological warning: while sub-hypnotic pharmacological disinhibition is highly therapeutic for processing chronic, established PTSD in a controlled, supportive clinical setting, early anesthetic exposure to propofol during the acute phase of trauma is clinically contraindicated due to the risk of pathologically consolidating fear memories (5).

VII. CONCLUSION

The historical evolution of thiopental sodium, scopolamine, and propofol demonstrates a clear transition from their crude origins as forensic "truth serums" to highly targeted tools in modern psychiatric healing and neurobiology (5). Under controlled, sub-hypnotic sedation, a disinhibited state allows patients to verbalize and process deeply repressed traumatic memories without triggering severe autonomic hyperarousal, facilitating therapeutic abreaction in chronic PTSD (3). Furthermore, scopolamine and propofol are at the forefront of a paradigm shift in the treatment of affective disorders, inducing rapid, robust antidepressant and antianxiety effects within days or even hours bypassing the slow therapeutic timeline of traditional monoaminergic drugs (14).

However, the clinical application of these agents requires careful attention to the timing of administration (10). Although sub-hypnotic disinhibition is highly therapeutic for processing chronic, established traumas, the administration of propofol in the acute phase of trauma is clinically contraindicated (10). Because unconscious fear memory systems in the amygdala remain active during general anesthesia, early propofol administration can pathologically consolidate fear memories, doubling the risk of developing postoperative PTSD (10). To safely utilize these powerful compounds, clinical

protocols must differentiate between the chronic treatment of affective disorders and the acute management of trauma, ensuring that anesthetic selection is guided by both long-term psychiatric outcomes and immediate physiological needs (10).

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