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Review Article

Interpretation and Implementation Prospects of Expert Consensus on Comprehensive Anesthetic Therapy for Children with Autism Spectrum Disorder

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Abstract

Autism spectrum disorder (ASD) is a common neurodevelopmental disorder characterized by social communication deficits, stereotyped behaviors, and restricted interests, which seriously affects children's developmental functioning and imposes heavy burdens on families and society. Although comprehensive anesthetic therapy has been increasingly adopted for the clinical intervention of autism spectrum disorder in children, the lack of unified clinical criteria has limited its standardized and widespread application. To fill this clinical gap and standardize relevant diagnosis and treatment practices, the Therapeutics Group of the Anesthesiology Branch of the Chinese Medical Doctor Association developed the *Expert Consensus on the Clinical Application of Comprehensive Anesthetic Therapy in Children with Autism Spectrum Disorder* in 2025, which was published in *Guangdong Medical Journal*. This consensus systematically elaborates the core clinical specifications for comprehensive anesthetic therapy for pediatric ASD, covering indications, contraindications, therapeutic principles, standardized intervention procedures, and multidisciplinary collaboration systems. Based on available clinical evidence, the consensus recommends low-concentration sevoflurane inhalation as the core intervention and establishes a multimodal comprehensive treatment system that combines stellate ganglion block, neuromodulation, behavioral rehabilitation training, and characteristic traditional Chinese medicine therapies. Focusing on nine key clinical issues in ASD treatment, the consensus formulates seven recommendations with explicit evidence grades and recommendation strengths. It provides clinicians with a standardized, rigorous and systematic therapeutic framework, offers reliable evidence for clinical decision-making, and serves as a valuable reference for the standardized clinical development of comprehensive anesthetic therapy for ASD.

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1. Introduction

Anesthesiology constitutes a core branch of clinical medicine, and the anesthesiology department serves as a critical clinical specialty reflecting the comprehensive capacity of medical institutions. In May 1989, the former Ministry of Health issued the Notice on Reclassifying the Department of Anesthesiology as a Clinical Department (Document No. Wei Yi Zi (1989) 12), which repositioned anesthesiology from a medical technology department to a clinical department and defined its service scope: clinical anesthesia, emergency care, cardiopulmonary cerebral resuscitation, pain research and pain management, among others.

In 2018, seven national authorities including the National Health Commission, National Development and Reform Commission, Ministry of Education, Ministry of Finance, Ministry of Human Resources and Social Security, National Administration of Traditional Chinese Medicine and National Healthcare Security Administration jointly released the Notice on Strengthening and Improving Anesthesia Medical Services (Document No. Guo Wei Yi Fa (2018) 21). The document mandated continuous improvement in anesthesiologists' emergency capabilities to deliver emergency resuscitation, sedation, analgesia and life support for critically ill patients [1].

Furthermore, the Guidelines for Capacity Building of the Department of Anesthesiology (Trial) (Document No. Guo Wei Ban Yi Han (2019) 884), issued by the General Office of the National Health Commission in 2019, emphasized discipline development, upgrading anesthesia service quality, ensuring safety during perioperative and anesthetic treatment, and optimizing overall anesthesia care [2]. Accordingly, anesthesiologists bear a core responsibility to align clinical practice with real-world patient needs, advance disciplinary development, and rationally deploy diversified anesthetic diagnostic and therapeutic technologies to benefit patients.

Released in August 2025 in Guangdong Medical Journal, the Expert Consensus on the Clinical Application of Comprehensive Anesthetic Therapy in Children with Autism Spectrum Disorder has drawn widespread attention and extensive feedback across the clinical community [3]. Developed through multiple rounds of discussion and revision by nearly 30 experts from 24 national institutions, this document represents China's first expert consensus standardizing clinical practice for anesthetic therapy in ASD. Focused on nine key clinical issues, the Consensus proposes seven graded recommendations with explicit evidence classification, forming a standardized, systematic and scientific comprehensive therapeutic system for ASD intervention and a structured clinical decision-making framework.

Based on analgesic intelligent technology, this paper interprets the Consensus and outlines implementation prospects, elaborating on its formulation rationale, operational details, quality control and future development directions to guide clinical practitioners in study and implementation. The Consensus addresses multiple dimensions including ASD definition and diagnosis, indications and contraindications of comprehensive anesthetic therapy, clinical positioning of anesthetic interventions for ASD, multidisciplinary team (MDT) diagnosis-treatment models, and detailed therapeutic protocols covering pharmacotherapy, rehabilitation and TCM interventions. It targets medical staff working in general hospitals, children's hospitals, anesthesiology, rehabilitation, pediatric TCM, psychiatry and psychology departments at all levels, as well as researchers and educators engaged in cross-disciplinary anesthesiology and pediatrics work.

ASD is a severe neurodevelopmental disorder defined by social communication impairments, repetitive stereotyped behaviors and restricted interests. At least 70% of affected children present comorbidities including attention deficit hyperactivity disorder (ADHD), anxiety, epilepsy and sleep disturbances [4, 5]. Globally, ASD prevalence rises year-on-year, with international epidemiological data estimating a diagnosis rate of 1 in 68 children, imposing immense financial and emotional burdens on families and societies [6, 7]. Domestic epidemiological investigations report comparable upward trends [8].

Diagnosis and treatment of neurodevelopmental pediatric disorders such as ASD constitute three core priorities under major brain disease research programs of China's National Brain Project. ASD has a multifactorial etiology involving genetic, neurological, immune and environmental contributors, and no targeted pharmacotherapy for its core symptoms is currently available. Developing safe and effective integrated intervention regimens thus represents an urgent clinical and research priority [9].

Recent mechanistic studies identify disrupted cerebral cortical excitation/inhibition (E/I) balance as a key pathological driver of ASD, with impaired function of the γ-aminobutyric acid (GABA) ergic system as its central hallmark [10, 11]. As the primary inhibitory neurotransmitter in the central nervous system, GABA dysfunction correlates closely with social deficits, stereotyped behaviors and emotional dysregulation [12]. Interventions targeting the GABAergic system have therefore become a leading research direction for ASD therapeutics in recent years [13].

Sevoflurane, a widely utilized volatile inhalation anesthetic, exerts its pharmacological effect via GABA receptor activation, amplifying inhibitory neural transmission to modulate cortical excitatory-inhibitory network imbalance. Clinically applied to newborns, infants and young children since the 1990s, sevoflurane features rapid onset, fast metabolism and elimination, and a favorable adverse event profile [14-16]. It demonstrates particular clinical value in children with comorbid anxiety, irritability and self-injurious behaviors, with 2025 clinical pilot data confirming its reliable safety and controllability [17].

2. Definition and Diagnostic Criteria of ASD

2.1. Definition of ASD

Proposed in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), ASD is defined as a neurodevelopmental disorder with childhood onset, whose core features include persistent deficits in social communication and social interaction, alongside restricted, repetitive patterns of behavior, interests or activities. Symptoms emerge during critical developmental windows and follow a chronic, persistent disease course driven by complex genetic, neurobiological and environmental factors. Classified as a spectrum disorder, ASD exhibits substantial interindividual variability in clinical manifestations and severity, ranging from mild social impairment to severe global functional disability.

2.2. Diagnostic Criteria of ASD (DSM-5)

Diagnosis requires fulfillment of the following three sets of criteria:

Deficits in social communication and social interaction: Abnormal socio-emotional reciprocity, diminished social responsiveness, impaired shared interest or affect, and failure to engage in bidirectional communication; deficits in nonverbal communicative behaviors including abnormal eye contact, facial expression, body posture and gestural use; difficulties initiating, maintaining and understanding interpersonal relationships.

Restricted, repetitive patterns of behavior, interests or activities: Stereotyped or repetitive motor movements, speech or object use; rigid adherence to sameness, inflexible routines and ritualized behavioral patterns; highly circumscribed, fixated interests of abnormal intensity or focus; hyper- or hyporeactivity to sensory stimuli, or unusual fixation on environmental sensory input.

Associated clinical requirements: Symptom onset occurs in early development (clinical manifestations may become prominent only when social demands exceed developmental capacity); symptoms cause clinically significant impairment across social, academic and occupational domains; developmental deficits cannot be fully explained by intellectual disability or global developmental delay (if co-occurring, social communication impairment must exceed the level expected for general intellectual function).

3. Indications and Contraindications of MDT-Based Comprehensive Anesthetic Therapy for ASD

Raising awareness among anesthesiologists and multidisciplinary clinicians regarding the clinical value of comprehensive anesthetic therapy is fundamental to guaranteeing treatment safety and efficacy. The MDT model integrates anesthesiology, pediatrics, rehabilitation, psychology, TCM pediatrics and nursing teams to deliver standardized, systematic peri-interventional management. The MDT framework facilitates rigorous screening of eligible patients, standardized treatment pathways, multidimensional monitoring of efficacy and safety, and timely identification and management of potential risks—particularly critical for emerging therapies including low-concentration sevoflurane inhalation and stellate ganglion block. Additionally, MDT enables structured family education and informed consent, improving caregiver compliance and long-term prognostic outcomes for children with ASD.

3.1. Indications for Comprehensive Anesthetic Therapy

Treatment eligibility criteria are established to maximize safety:(1) Severe core ASD symptoms refractory to conventional intervention: Children receiving ≥6 months of systematic rehabilitation training (e.g., applied behavior analysis, social skills training) with minimal clinical improvement, where social deficits and stereotyped behaviors severely impair daily function or school attendance. (2) Prominent comorbid emotional and behavioral dysfunction: Unstable mood, severe anxiety, aggression, self-harm or compulsive behaviors unresponsive to standard pharmacotherapy and behavioral intervention; moderate-to-severe sleep disturbance, excessive arousal and daytime functional impairment. (3) Adequate treatment adherence and caregiver consent: Caregivers provide full informed consent, demonstrate comprehensive understanding of anesthetic intervention objectives, risks and scheduling, and commit to completing periodic outpatient or inpatient treatment cycles (requiring repeated hospital visits weekly). (4) Physiological suitability for inhalation anesthesia: Normal somatic development, absence of absolute anesthesia contraindications, and no high-risk factors including severe systemic disease or upper airway obstruction.

3.2. Contraindications for Comprehensive Anesthetic Therapy

Absolute contraindications to eliminate critical safety hazards:(1) Malignant hyperthermia susceptibility: Confirmed

personal or familial history of malignant hyperthermia; pathogenic variants in RYR1, CACNA1S or related genes; prior severe adverse reactions following volatile anesthesia including unexplained hyperthermia, myotonia and rhabdomyolysis. (2) Active central nervous system pathology: Frequent or poorly controlled epileptic seizures; intracranial infection, space-occupying lesions or intracranial hypertension. (3) Severe respiratory or cardiovascular disease: Unrepaired congenital heart disease or poor surgical outcomes; chronic pulmonary disease, refractory asthma and respiratory insufficiency. (4) Severe electrolyte and metabolic derangement: Serum potassium <3.0 mmol/L, serum magnesium <0.65 mmol/L; markedly abnormal hepatic or renal function (ALT/AST >3 times upper limit of normal; eGFR <30 mL/min). (5) Concurrent contraindicated pharmacotherapy or trial participation: Monoamine oxidase inhibitors administered within the preceding month; atypical antipsychotics such as risperidone; enrollment in other interventional clinical trials within 30 days prior to proposed treatment. (6) Poor adherence and insufficient treatment willingness: Uncooperative or unwilling caregivers refusing the anesthetic regimen; high risk of failed anesthesia induction due to parental refusal.

3.3. Standard MDT Workflow

(1) Initial screening and case conference: All children scheduled for comprehensive anesthetic therapy (low-concentration sevoflurane, stellate ganglion block, etc.) undergo joint screening by developmental behavioral pediatricians, psychologists, rehabilitation therapists and anesthesiologists to confirm eligibility and rule out contraindications. (2) Multidimensional clinical assessment: Collection of baseline medical, pharmaceutical and anesthetic history; standardized scoring of core ASD symptoms via ADOS-2, CARS, ABC and ATEC scales; evaluation of comorbidities (epilepsy, ADHD, sleep disorders); laboratory testing including complete blood count, serum biochemistry, hepatic/renal function and electrolytes; cerebrospinal fluid analysis when clinically indicated; electrocardiography, neuroimaging (e.g., fMRI) and neurophysiological testing. (3) MDT case discussion: Interdisciplinary consensus on treatment feasibility with formal written assessment reports. (4) Individualized regimen formulation: Led by anesthesiologists, integrating multidisciplinary recommendations to customize treatment parameters (sevoflurane concentration, treatment frequency, total cycle length: 32 sessions total), real-time monitoring protocols (BIS, MAC, electrocardiography, blood pressure), adjuvant interventions (stellate ganglion block, behavioral therapy) and emergency response plans for adverse events. (5) Informed consent and caregiver education: Joint MDT counseling to caregivers, with anesthesiologists detailing anesthetic procedures and safety safeguards, and psychologists/rehabilitation therapists outlining child behavioral coordination protocols to ensure full comprehension. (6) Treatment delivery and continuous monitoring: Anesthesiologists administer treatment with full peri-procedural vital sign surveillance; rehabilitation and nursing staff collaborate to stabilize child mood and behavioral tolerance. Real-time monitoring targets electrocardiography, blood pressure, heart rate, SpO_2, alongside continuous observation for intra-procedural adverse reactions and post-treatment recovery status. Psychological intervention is activated promptly for anxiety or behavioral distress. (7) Staged efficacy and safety reassessment: Following each treatment phase, the MDT conducts interdisciplinary re-evaluation including repeat standardized scale scoring (CARS, ABC), adverse event and tolerability review, and regimen adjustment (dose modification, adjuvant therapy addition) as clinically indicated. (8) Cycle summary and long-term follow-up: Upon completion of the full treatment course, the MDT compiles a formal summary report documenting efficacy, safety profiles and clinical recommendations. Minimum 6 months of post-intervention follow-up is mandated to assess sustained therapeutic effects and delayed adverse events, alongside structured continuity of rehabilitation care.

3.4. Anesthetic Therapeutic Regimens and Pharmacological Interventions

No specific pharmacotherapy targeting ASD core symptoms is currently available, yet neuromodulatory properties of anesthetic agents have garnered increasing clinical attention. As a positive allosteric modulator of GABA receptors, sevoflurane—long established in perioperative anesthesia—has been investigated for alleviating core ASD manifestations and associated neuropsychiatric comorbidities via restoration of cortical E/I balance [18]. Clinical pilot data demonstrate acceptable safety and preliminary therapeutic efficacy for sevoflurane-based anesthetic therapy as an adjuvant component of multimodal integrated care.

Sevoflurane Dosing Parameters and Cycle Design. A two-stage induction-maintenance protocol is adopted for sevoflurane therapy: Induction phase: Mask inhalation of 7%-8% sevoflurane for rapid sedation onset. Maintenance phase: End-tidal sevoflurane concentration titrated to approximately 1%, with 50% oxygen delivery; single treatment duration fixed at 2 hours. A total of 32 sessions constitute the full therapeutic cycle with a tapering frequency schedule to sustain efficacy while minimizing cumulative anesthetic exposure risk: Weeks 1-4 (intensive phase): 5 sessions weekly; Weeks 5-6: 3 sessions weekly (Monday, Wednesday, Friday); Weeks 7-8: 2 sessions weekly (Tuesday, Thursday); Weeks 9-10: 1 session weekly (Wednesday).

Adjustments to session frequency are permitted for intercurrent infection or poor physical tolerance, provided the total number of 32 sessions and standardized efficacy evaluation schedule are preserved. A qualified anesthesiologist must remain present throughout all treatment sessions with continuous recording of electrocardiography, blood pressure, heart

rate, SpO_2, BIS and MAC depth monitoring to guarantee procedural safety.

Pharmacological adjuvant regimens referenced from Professor Song Xingrong's research team at the Women and Children's Medical Center of Guangzhou Medical University are outlined below:(1) Comorbid ADHD: Methylphenidate or atomoxetine. Methylphenidate initiated at 5-10 mg daily, titrated incrementally to a maximum daily dose <40 mg; atomoxetine starting at 0.5 mg/kg daily, increased to target dose ~1.2 mg/kg once daily every morning after a minimum 3-day titration period. (2) Irritability, aggression and self-injurious behaviors: Atypical antipsychotics including aripiprazole (initial 5 mg daily, weekly 5 mg dose escalation to maintenance 15-20 mg daily) or risperidone (initial 1 mg daily, weekly 1 mg escalation to maximum 2 mg daily). Pharmacotherapy cycle length approximates 2 months with dynamic dose adjustment guided by efficacy and tolerability monitoring [19]. (3) Gastrointestinal dysfunction: Probiotics, gluten-free diets or ketogenic diets to ameliorate intestinal symptoms in ASD children [20]. (4) Sleep disturbance: Exogenous melatonin administered 30-60 minutes pre-bedtime with individualized dose titration based on clinical response. (5) Adjuvant stellate ganglion block: Ultrasound-guided precision injection administered sequentially to the right then left ganglion, 1-2 sessions weekly for a 4-6 session treatment cycle. The intervention modulates autonomic nervous system overactivity and relieves comorbid anxiety and sleep disorders. Critical safety note: All anesthetic and neuromodulatory interventions must be delivered in medical facilities equipped with full specialized anesthesia support. Pre-treatment comprehensive risk assessment, complete caregiver informed consent, and standardized adverse event surveillance and management protocols are mandatory prior to any intervention [21].

3.5. Rehabilitation Interventions

Rehabilitation forms a foundational adjuvant component of ASD treatment, targeting improvement of social interaction, communication, cognition and adaptive behavioral capacity through multimodal structured training modalities:(1) Applied Behavior Analysis (ABA): A behavior theory-based intervention utilizing systematic clinical assessment and positive reinforcement to teach functional skills and reduce maladaptive behaviors. Research validates ABA's robust efficacy for improving expressive language, social competence and activities of daily living [22]. (2) Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH): Structured environmental design and visual cue implementation to support children with ASD in understanding and completing daily tasks, enhancing independence and adaptive coping [23]. (3) Social Skills Training: Simulated real-world social scenarios delivered in group settings to practice eye contact, turn-taking, sharing and affective recognition, promoting generalization of learned social skills [24]. (4) Speech and Language Therapy: Individualized communication interventions including Picture Exchange Communication System and augmentative and alternative communication devices to remediate expressive and receptive language deficits [25]. (5) Sensory Integration Training: Occupational therapist-led intervention to improve processing and integration of somatosensory and environmental sensory input, ameliorating attention, motor coordination and behavioral dysregulation [26]. (6) Technology-Assisted Intervention: Augmented reality, virtual reality and mobile application-based training delivering immersive interactive learning environments to boost child engagement and therapeutic motivation.

3.6. Acupuncture Therapy (TCM Adjuvant Intervention)

(1) Buccal Acupuncture: 10 sessions per cycle, 2-5 sessions weekly. Bilateral cervical, dorsal, lumbosacral, upper jiao, middle jiao, lower jiao and cranial acupoints selected symptomatically, manipulated following the ascending-left, descending-right therapeutic sequence. (2) Gong's Cranial Acupuncture: Primary cranial insertion sites over bony surfaces (external occipital protuberance, midline parietal bone), supplementary trunk and limb bony landmarks (patella, manubrium sterni). Penetrating bone surface insertion technique avoiding vital neurovascular structures; 15 sessions per cycle administered every 2-3 days, with 2-3 sequential cycles indicated for refractory cases. Five-minute post-procedure compression at needle sites and 30-minute observation prior to discharge; no anesthesia or injectable medication required, with immediate outpatient discharge permitted. (3) Jin's Three-Needle Therapy: 10 sessions per cycle, 2-5 sessions weekly. Symptom-tailored acupoint selection including Sishenzhen, Zhisanzhen, Naosanzhen, Tansanzhen, Dingshenzhen, Shouzhizhen and Zuzhizhen. (4) Traditional Scalp Acupuncture: Targeting speech zones I, II, III plus Baihui, Sishencong, Shenting and Yintang, guided by the TCM theory that ASD pathology localizes to the brain.

(5) Body Acupuncture: Jinjin, Yuye, Lianquan, Hegu, Neiguan, Shenmen, Taichong and Yongquan acupoints selected to regulate cerebral function.

3.7. Pediatric Tuina Massage Therapy (TCM Adjuvant Intervention)

Pediatric tuina represents a non-invasive TCM external therapy integrating disease prevention, rehabilitation and psychological soothing, characterized by gentle manipulations to invigorate the spleen, calm the spirit, unblock meridians, harmonize yin-yang, improve physical function and enhance disease resistance, with proven therapeutic effects on neurological and psychiatric manifestations of ASD. Meta-analytic evidence confirms combined tuina and multimodal intervention significantly reduces scores on Autism Behavior Checklist (ABC), Childhood Autism Rating Scale (CARS) and Autism

Treatment Evaluation Checklist (ATEC), yielding particular benefits for sensory processing, social interaction, motor function and self-care capacity. Tuina additionally alleviates gastrointestinal comorbidities in ASD children, indirectly modulating central nervous system function and improving social adaptability and quality of life [27].

Clinical manifestations of ASD including verbal mutism, poor eye contact, hypoactivity or hyperactivity and cognitive delay correlate with Governing Vessel pathology, forming the theoretical basis for Governing Vessel-focused tuina intervention with pushing and kneading manipulations as primary techniques. Key acupoints manipulated: Tianmen, Kanggong, Taiyang, Erhougaogu, Yamen, Fengfu, Baihui and Shuigou [28, 29]. Rationale for acupoint selection: The combination of Tianmen, Kanggong, Taiyang and Erhougaogu constitutes a classic orifice-opening regimen to resuscitate the spirit. Yamen, Fengfu, Baihui and Shuigou lie along the Governing Vessel at cranial sites, where tuina manipulations exert direct localized cerebral regulatory effects.

3.8. Chinese Herbal Decoction Therapy (TCM Adjuvant Intervention)

Oral herbal decoctions are widely utilized in ASD clinical care with syndrome differentiation guided by five zang-organ pathology. Clinical studies demonstrate herbal therapy improves core ASD symptoms, expressive language, sleep disturbance and cognitive function. Four core syndromic patterns and corresponding modified formulas are standardized: (1) Liver-kidney deficiency syndrome: Therapeutic principle: Nourish liver and kidney; modified Liuwei Dihuang Decoction. Add Yuanzhi and Shichangpu for mental dullness; Duzhong and Niuxi for short stature, delayed fontanelle closure and skeletal hypoplasia; Yizhiren, Sangpiaoxiao and Jinyingzi for enuresis. (2) Phlegm obscuring the heart orifice syndrome: Therapeutic principle: Clear the heart, eliminate phlegm, resuscitate the spirit; modified Ditan Decoction. Add Cinnabar and Magnetitum for incoherent speech and aberrant conduct; Zhe Fritillary Bulb, Trichosanthes Peel and Tianzhuhuang for chest tightness and copious phlegm; Chuanxiong, Moutan Bark, Red Peony Root and Raw Rehmannia Root for birth trauma history, dark facial complexion and ecchymotic tongue. (3) Heart-spleen dual deficiency syndrome: Therapeutic principle: Tonify heart and spleen, nourish blood and calm spirit; modified Guipi Decoction. Add Poria, Coix Seed, Chicken Gizzard Membrane and Fried Hawthorn Fruit for fatigue, hypophonia, poor appetite and pale complexion; Chenpi and Amomum for speech delay; Calcined Dragon Bone, Calcined Oyster Shell, Yuanzhi and Rush Pith for timidity, startling and fragmented sleep. (4) Liver-heart fire hyperactivity syndrome: Therapeutic principle: Pacify liver yang, clear heart heat and calm spirit; combined modified Daoyin San and Longdan Xiegan Decoction. Add Uncaria Stem, Scorpion and Calcined Oyster Shell for irritability, mood lability, rigid adherence and poor responsiveness to instruction; Hemp Seed, Prepared Rhubarb and Aurantii Fructus Immaturus for constipation and dark urine.

4. Therapeutic Efficacy Evaluation of Sevoflurane-Based Anesthetic Therapy for ASD

Long-term clinical management of ASD has historically centered on sustained behavioral rehabilitation training due to the absence of targeted pharmacotherapy. Cross-disciplinary integration of anesthesiology and neuroscience has unlocked novel therapeutic potential for anesthetic agents in ASD care, with sevoflurane emerging as the most extensively researched candidate given its rapid onset, fast metabolic clearance and controllable safety profile. Efficacy and clinical value are systematically analyzed based on domestic and international translational and clinical research:

The core therapeutic mechanism of anesthetic intervention for ASD targets disrupted cortical E/I balance and GABAergic system dysfunction. Low-concentration sevoflurane restores this homeostatic equilibrium via GABA receptor agonism. Song et al. [30] combined preclinical and clinical research verifying that subanesthetic sevoflurane corrects prefrontal E/I imbalance and ameliorates social deficits in ASD animal models. In a pilot clinical trial enrolling 20 children with ASD, mean CARS scores decreased by 4.7 points post-intervention, with 61% of participants rated clinically improved per CGI-I criteria; no significant short-term safety hazards were documented. Contrastingly, Wang et al. [31] reported repeated postnatal sevoflurane exposure induced autism-like social recognition impairment in mice via disrupted hippocampal GABAergic neuronal development, highlighting the need for further mechanistic clarification of bidirectional interactions between volatile anesthetics and ASD pathophysiology.

Domestic clinical trials corroborate the therapeutic utility of sevoflurane-centered anesthetic comprehensive therapy. Multimodal regimens combining sevoflurane inhalation, stellate ganglion block and TCM acupuncture delivered to 2-8-year-old children with moderate-to-severe ASD in Guangzhou demonstrated marked improvements in social and emotional symptoms. Repeated low-concentration sevoflurane exposure produced no significant alterations in hepatic or renal biochemistry, with mild-to-moderate adverse event incidence below 25% [17]. A separate safety cohort of 32 ASD children completing the full 10-week sevoflurane cycle similarly showed stable liver and renal function, adverse event rates <25%, absence of severe adverse reactions and no evidence of anesthetic dependence, confirming controllable safety of repeated subanesthetic sevoflurane administration. Additional data indicate integrated sevoflurane and pediatric tuina therapy synergistically regulates cerebral E/I balance to improve mood and cognitive function, offsetting therapeutic limitations of standalone conventional rehabilitation [27].

Combined institutional clinical experience identifies robust

therapeutic benefits of subclinical sevoflurane for social communication and cognitive impairment in 2-8-year-old children with ASD, alongside alleviation of irritability and affective lability; however, therapeutic efficacy against repetitive stereotyped behaviors remains limited, constituting the primary clinical limitation of sevoflurane monotherapy. Furthermore, symptom recurrence at 3-4 months following treatment completion is observed in a subset of children receiving sevoflurane without concurrent behavioral rehabilitation, demonstrating that sustained therapeutic benefit requires combined anesthetic and behavioral intervention.

A systematic, objective evaluation of anesthetic sevoflurane therapy for ASD integrating all available translational and clinical evidence is summarized as follows:

First, innovative clinical intervention paradigm: Anesthetic therapy establishes a novel therapeutic avenue for ASD, overcoming the historical absence of disease-specific pharmacotherapy. Sevoflurane, with its favorable pharmacokinetic and safety profile, represents the most promising agent in this emerging field. Its core mechanism of action—restoring cortical E/I homeostasis and supporting physiological neuronal maturation—targets social and cognitive core deficits in children aged 2-8 years with moderate-to-severe ASD. Multiple clinical trials validate acceptable safety of standardized low-concentration sevoflurane protocols, supporting its clinical deployment as an adjuvant therapeutic modality for this pediatric population.

Second, Key therapeutic limitations: Selective efficacy profile: Minimal therapeutic impact on repetitive stereotyped behaviors, failing to comprehensively resolve all core ASD symptom domains.

Limited high-level evidence base: Existing clinical trials are predominantly small-sample, short-term observational studies lacking large-scale, long-term follow-up data to eliminate confounding variables including spontaneous developmental improvement and concurrent adjuvant therapies. Long-term neurodevelopmental risks associated with repeated sevoflurane exposure remain incompletely characterized. Partial treatment dependency: Mild-to-moderate adverse events occur in a subset of patients, and transient therapeutic reliance on the intervention is observed in a minority of children, mandating continuous peri-procedural monitoring and individualized supportive management.

Third, Stage of clinical translation: Anesthetic therapy for ASD remains in active clinical exploration. Critical unresolved questions include optimal sevoflurane dosing, standardized cycle parameters and precision patient stratification criteria, requiring further protocol refinement. Strict regulatory oversight of controlled anesthetic agents is mandated to prevent off-label misuse and unregulated administration. Multimodal care integrating sevoflurane therapy with structured behavioral correction and home-based rehabilitation is essential to maximize clinical response, delivering personalized, comprehensive rehabilitation regimens for children with ASD.

5. Future Implementation Prospects

December 2023 marked the establishment of China's first provincial Anesthetic Therapeutics Branch under the Guangdong Medical Association, which subsequently hosted a national academic conference to lay foundational infrastructure for cross-institutional collaborative research targeting anesthetic therapy for ASD and other neuropsychiatric disorders. This institutional framework supports coordinated national research initiatives to drive breakthrough therapeutic innovation for psychiatric disease and elevate overall disciplinary capacity and core competitiveness.

Given the lack of disease-specific pharmacotherapy and incomplete standardization of ASD care pathways, interdisciplinary research is underway across pediatrics, anesthesiology, rehabilitation, pediatric TCM and psychiatry. Anesthetic comprehensive therapy paired with behavioral rehabilitation education currently constitutes the primary emerging intervention paradigm. By rebalancing disrupted cerebral neural circuit E/I homeostasis to ameliorate core ASD manifestations and frequent comorbidities, multimodal integrated regimens combining anesthetic techniques with psychological, physical and behavioral therapies have gained broad acceptance among patient caregivers. We call on domestic scholars to popularize and attach importance to anesthesiotherapy techniques, so as to boost the advancement of anesthesiological subspecialties [32].

Abbreviations

ASD	Autism Spectrum Disorder
DSM 5	Diagnostic and Statistical Manual of Mental Disorders 5th Edition
ADHD	Attention Deficit Hyperactivity Disorder
E/I	Excitation/Inhibition
GABA	γ Aminobutyric Acid
MDT	Multidisciplinary Team
ADOS 2	Autism Diagnostic Observation Schedule 2
CARS	Childhood Autism Rating Scale
ABA	Applied Behavior Analysis
CGI-I	Clinical Global Impression Improvement
TEACCH	Treatment and Education of Autistic and Related Communication Handicapped Children
ABC	Autism Behavior Checklist
ATEC	Autism Treatment Evaluation Checklist
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
eGFR	Estimated Glomerular Filtration Rate
RYR1	Ryanodine Receptor 1
CACNA1S	Calcium Voltage Gated Channel Subunit Alpha1S
BIS	Bispectral Index
MAC	Minimum Alveolar Concentration
fMRI	Functional Magnetic Resonance Imaging

SpO_2	Pulse Oxygen Saturation
ECG	Electrocardiogram
TCM	Traditional Chinese Medicine

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Conflicts of Interest

The authors declare no conflicts of interest.

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