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Systematic Comparison of Short-Term Insemination and Conventional Insemination IVF: Influencing Factors, Embryo Developmental Quality and Pregnancy Outcomes

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Abstract

In in vitro fertilization-embryo transfer (IVF-ET), the selection of insemination duration is a key variable affecting pregnancy outcomes. This paper systematically compares the differences between two insemination strategies, namely short-term insemination (4-6 hours) and conventional IVF (16-18 hours), in terms of influencing factors, embryo development and pregnancy outcomes, aiming to provide evidence-based basis for the selection of individualized insemination protocols. Studies have shown that the choice of insemination method should be based on a comprehensive assessment of patients' clinical characteristics, oocyte status and sperm function parameters. Analysis of embryo development kinetics indicates that embryos from short-term insemination have more synchronous pronuclear formation and early cleavage, and a shorter time to blastocyst formation. However, there is no significant difference in the overall blastocyst formation rate and live birth rate between the two methods. By reducing the exposure time to reactive oxygen species, short-term insemination shows advantages in populations with high oxidative stress (such as polycystic ovary syndrome (PCOS) and oocytes derived from small follicles) and specific male factors (such as oligozoospermia and asthenospermia). It can improve fertilization rate, high-quality embryo rate and early pregnancy rate, and may reduce the risk of early miscarriage. In contrast, conventional insemination may be more conducive to embryo implantation and maintenance of continuous pregnancy in women with high oocyte maturity (MII rate > 80%) and advanced age (≥38 years old). Current studies have limitations such as insufficient standardization of laboratory procedures and high population heterogeneity. In the future, it is necessary to further clarify the optimal insemination strategy for different populations through unified operation standards, refined stratified studies and long-term follow-up, so as to promote the precision and individualization of IVF insemination protocols.

Keywords: in vitro fertilization, short-term insemination, conventional insemination, embryo development, pregnancy outcome, individualized treatment

1. Introduction

In vitro fertilization-embryo transfer (IVF-ET) technology serves as the core approach in the field of assisted reproduction, and its successful implementation relies on the critical process of sperm-egg fusion. The selection of insemination duration (i.e., the co-incubation time of sperm and oocytes) is an important controllable variable that affects the subsequent trajectory of embryo development and clinical outcomes (Chinese Society of Reproductive Medicine, 2020). Traditional conventional insemination adopts a 16–18-hour co-incubation period, aiming to simulate the physiological fertilization window in vivo; in contrast, short-term insemination shortens the co-incubation time to 4–6 hours, with early observation of the extrusion of the second polar body and, when necessary, adjuvant early rescue intracytoplasmic sperm injection (ICSI) (Fancsovits, P, Kaszas, Z, Nemes, A, et al., 2020). These two strategies not only represent differences in the time dimension, but also may regulate the epigenetic modification and developmental potential of embryos by altering the microenvironment of sperm-egg interaction, the level of reactive oxygen species (ROS) exposure, and the impact of sperm DNA fragmentation on zygotes (Soto-Heras S, Sakkas D, Miller DJ., 2023; Li L, Liao H, Li M, et al., 2022).

Although randomized controlled trials suggest that there is no statistically significant difference in the overall pregnancy rate and live birth rate between the two insemination methods (Jiang Yan, Zhang Han, Zhang Xuhui, et al., 2021; Sha T, Wang X, Cheng W, et al., 2019), their efficacy shows notable heterogeneity among patient populations with different etiologies and physiological states. This heterogeneity may be related to the interaction of complex factors such as oocyte maturity, mitochondrial function, sperm parameters, and oxidative stress status (Vaiarelli A, Cimadomo D, Alviggi E, et al., 2020; De Munck N, El Khatib I, Abdala A, et al., 2020). At present, the selection of insemination methods in clinical practice is mostly based on empirical consensus, lacking unified and precise decision-making criteria. Meanwhile, existing studies have obvious limitations in terms of laboratory process standardization, refined population stratification, and long-term follow-up of offspring, which restricts the extrapolation of research conclusions.

In view of this, this paper aims to systematically sort out and compare short-term insemination and conventional insemination. We will focus on the following aspects: (1) key clinical and laboratory variables affecting the selection of insemination methods; (2) the impact of the two strategies on embryo development quality; (3) evidence-based medical comparison of clinical pregnancy outcomes. By integrating existing evidence, this paper attempts to clarify the respective advantageous scenarios and potential mechanisms of the two insemination strategies, provide theoretical basis and evidence-based reference for establishing an individualized and precise framework for selecting insemination protocols, and prospect the future research directions in this field to promote the precise development of insemination strategies.

2. Overview of Short-Term Insemination and Conventional IVF Insemination

In in vitro fertilization technology, the choice of sperm-oocyte co-incubation duration has led to two distinct insemination strategies: short-term insemination and conventional insemination. These two approaches reflect different philosophies regarding the control of the fertilization process. Short-term insemination emphasizes actively terminating co-incubation after the initial sperm-oocyte binding is completed, providing greater controllability for laboratory operations; in contrast, conventional insemination maintains a longer co-incubation period to simulate the complete process of sperm-oocyte interaction under physiological conditions and preserve the competitive selection mechanism in natural settings (Chamayou S., 2022).

The core advantage of short-term insemination lies in reducing the exposure time to reactive oxygen species (ROS), which theoretically lowers the potential oxidative stress-induced damage to oocytes and early embryos. Meanwhile, the limited contact time may affect the sperm selection mechanism: compared with the natural competitive mode of conventional insemination, short-term insemination tends to adopt a strategy of rapid optimal sperm selection. It is noteworthy that these two insemination methods exhibit a complementary rather than opposing relationship in practical applications. Selecting an appropriate insemination method based on the individualized characteristics of different patients can significantly improve the success rate of IVF. This decision should be made on the basis of a systematic assessment of the patient’s clinical characteristics, oocyte status, sperm parameters, and other relevant factors (Zhang, R., Zuo, Y., & Qiu, F., 2021).

3. Key Factors Affecting the Selection of Insemination Methods

3.1 Clinical Characteristics of Patients

The clinical background of patients is the primary dimension for determining the selection of insemination strategies. The primary etiology is the core consideration: for infertile couples dominated by male factors, especially when routine semen parameters (such as concentration and motility) are at critical values or the DNA Fragmentation Index (DFI) is elevated, short-term insemination is often regarded as a more advantageous option. Theoretically, it can reduce the damage of oxidative stress and DNA fragmentation to early embryos by limiting the prolonged contact between damaged sperm and oocytes. On the contrary, for patients with oocyte-derived factors or specific endocrine conditions (such as Polycystic Ovary Syndrome, PCOS), more careful trade-offs are required.

Meanwhile, female age is another independent influencing factor that cannot be ignored. Oocytes of advanced-age women (usually defined as ≥38 years old) are often accompanied by decreased mitochondrial function, elevated oxidative stress levels and abnormal epigenetic modifications, and their fertilization process may be more dependent on a complete physiological time window. Studies have indicated that in this population, conventional insemination may achieve relatively higher embryo implantation rates by simulating a longer physiological fertilization process (23.1% vs. 17.6%, P=0.04) (Huang Ying, Qin Aiping, 2020; Tesarik J, Mendoza-Tesarik R., 2022). For PCOS patients, although they often face a follicular microenvironment with high oxidative stress, studies have shown that short-term insemination may obtain higher cumulative pregnancy rates by reducing the exposure time to such stress (52.3% vs. 42.5%, P=0.02) (Li, J., Wang, H., Zhang, Y., & Liu, Q., 2025).

In addition, patients' ovarian responsiveness (such as the number of retrieved oocytes) and previous in vitro fertilization (IVF) cycle outcomes should also serve as important references for decision-making. A large number of retrieved oocytes (e.g., >15-20) is an ideal scenario for short-term insemination. Even if some oocytes fail to fertilize naturally after short-term co-culture, there are still sufficient oocytes for rescue intracytoplasmic sperm injection (ICSI), ensuring the final total fertilization rate. For patients with a clear history of fertilization failure, selecting short-term insemination with a plan for early rescue ICSI can be adopted as an active strategic option.

3.2 Evaluation of Oocytes

Oocyte maturity (MII rate) is the core factor determining fertilization efficiency. In current clinical practice, evaluation is mainly based on nuclear maturation status (the proportion of germinal vesicle (GV), metaphase I (MI), and metaphase II (MII) stages). Oocytes with different maturities exhibit significant differences in their response to insemination duration. MII-stage oocytes, having completed meiosis and with sufficient expression of zona pellucida receptors, may be more suitable for conventional in vitro fertilization (IVF). In contrast, GV-stage or MI-stage oocytes may benefit from the concentrated sperm exposure in short-term insemination due to insufficient zona pellucida hardening (Chamayou S., 2022). Clinical data indicate that when the MII rate is higher than 80%, the fertilization rate of conventional insemination can reach 72.5±6.3%, which is significantly superior to that of short-term insemination (65.1±7.8%, P<0.05). However, in cycles with an MII rate lower than 60%, short-term insemination instead demonstrates higher fertilization efficiency (58.4±5.2% vs. 49.7±6.1%) (Shi Hongzhi, Qin Yan, Zhang Nan, et al., 2019). This may be related to the increased sensitivity of immature oocytes to oxidative stress.

In addition, follicular characteristics should also serve as an important reference index for the selection of insemination methods. Studies have shown that the concentration of reactive oxygen species (ROS) in the follicular fluid of small follicles with a diameter of 12–14 mm is usually maintained at a relatively high level of 2.8±0.3 nmol/mL (Artini PG, Scarfò G, Marzi I, et al., 2022). For oocytes derived from such follicles, short-term insemination can reduce the ROS exposure time, resulting in a fertilization rate of 68.5%, which is higher than that of conventional IVF (61.2%, P<0.05). This finding suggests that short-term insemination has clinical advantages for oocytes from follicles within this diameter range and is recommended as the preferred option.

3.3 Comprehensive Evaluation of Sperm Functional Parameters

Sperm quality assessment has expanded from traditional parameters (concentration, motility, and morphology) to the multi-dimensional integration of functional indicators. The quantity of functionally competent sperm following sperm processing constitutes the fundamental basis. For semen samples with progressive motility (PR) sperm lower than 32% or sperm concentration less than 15×10^6/mL, short-term insemination combined with density gradient centrifugation can increase the effective sperm capture rate to 89.3±4.1%, which is significantly higher than the 72.6±5.8% achieved with conventional processing (Yin, Z., Dong, Y., Sun, Q., Li, Z., Liu, J., Jia, Y., Dong, X., Hong, Y., Gao, J., Xiu, C., & Ma, G., 2020). Sperm DNA integrity has emerged as a crucial indicator for evaluating sperm function in recent years. A high DNA Fragmentation Index (DFI > 30%) indicates an elevated risk of sperm genomic damage. In such cases, although short-term insemination reduces the exposure duration between sperm and oocytes, it may not be sufficient to overcome the inherent DNA damage, potentially leading to a decline in embryo implantation rates (Harith Mohamed Kamber, Kamal Al-Jawdah, Salam Madhi Shahid, et al., 2024). Under these circumstances, direct intracytoplasmic sperm injection (ICSI) or short-term insemination following special treatments (e.g., magnetic-activated cell sorting) might represent a more rational approach.

Sperm morphological parameters also merit attention. Studies have demonstrated that when the rate of morphologically normal sperm reaches 60%, the clinical pregnancy rate with short-term insemination can attain 41.2%. In contrast, a sperm head abnormality rate exceeding 15% can sharply reduce the pregnancy rate to 18.5% (Lei Zhihui, Yan Yixin, Yu Yan, et al., 2024). This discrepancy may be directly associated with the efficiency of the acrosome reaction: the rate of phospholipase C zeta (PLCζ) expression deficiency in morphologically abnormal sperm heads is as high as 78.3%, which severely impairs the oocyte activation process (Cannarella R, Condorelli RA, Mongioì LM, et al., 2020).

4. Morphological and Kinetic Comparison of Embryo Developmental Quality

4.1 Clinical Application and Limitations of Morphological Evaluation

As a core quality monitoring method in in vitro fertilization (IVF) technology, embryo morphological evaluation classifies embryos mainly by observing static indicators such as cell uniformity, fragmentation rate, and blastomere symmetry. The traditional Gardner scoring system categorizes blastocysts across three dimensions: expansion degree (grades 1–6), inner cell mass (ICM, grades A–C), and trophectoderm (TE, grades A–C). Among these, the quality of the inner cell mass is significantly positively correlated with the clinical pregnancy rate (grade A vs. grade C: 52.7% vs. 28.3%, P<0.01) (Devora Aharon, Atoosa Ghofranian, Dmitry Gounko, et al., 2021). However, this static observation method cannot fully reflect the dynamic process of embryo development. A study involving 1,200 embryos demonstrated that the predictive accuracy of morphological evaluation alone for high-quality embryos is only 68.5%, whereas integrating kinetic parameters from time-lapse imaging technology can increase the accuracy to 82.3% (Gao Shang, Liu Baolian, Yao Yuhong, et al., 2025; Feng Bo, Qiu Fenglong, Zhong Jixiang, et al., 2022).

The morphological differences between embryos derived from short-term insemination and conventional insemination are mainly manifested in the early developmental stage. The time to pronuclear formation (tPNf) in the short-term insemination group is 1.8 hours shorter on average than that in the conventional insemination group (15.2±2.1 h vs. 17.0±2.4 h, P=0.03), and the proportion of synchronized cleavage is higher (the proportion of 4-cell embryos on day 2 is 72.1% vs. 63.5%) (Nemerovsky L, Ghetler Y, Bakhshi DI, et al., 2024; Dal Canto M, Bartolacci A, Turchi D, et al., 2020). This difference may be related to the reduced exposure time to sperm DNA fragmentation. When the sperm DNA Fragmentation Index (DFI) > 30%, the rate of high-quality embryos in the short-term insemination group is 14.2% higher than that in the conventional insemination group (45.6% vs. 31.4%) (Zhang, Y., Wang, H., Liu, J., & Chen, Z., 2023).

4.2 Predictive Value of Kinetic Parameters for Developmental Potential

Embryonic developmental kinetics has established a refined predictive system for developmental potential by quantifying the key time points of cell division. The Cambridge IVM model has defined the reference time windows for each developmental stage. Among them, embryos with t5 (the time to reach the 5-cell stage) within the range of 24.8–28.3 hours exhibit a blastocyst formation rate of up to 78.5%, which is significantly superior to that of embryos outside this time window (P<0.01) (Shi Senlin, Lyu Aixiang, Song Wenyan, et al., 2019). This model provides an important temporal reference standard for embryo selection. The intercorrelation of kinetic parameters reveals the inherent laws of embryonic development. Studies have shown that in embryos derived from short-term insemination, there is a significant negative correlation between t2 (the time to reach the 2-cell stage) and tSB (the time to reach the morula stage) (r=-0.42, P=0.01), suggesting that rapid early cleavage may have a complex balance relationship with subsequent developmental potential (Sciorio, R., Thong, K. J., & Pickering, S. J., 2022; Bartolacci A, Moutier C, Turchi D, et al., 2020). This phenomenon of mutual restriction among temporal parameters needs to be fully considered during embryo evaluation.

The heterogeneity of patient populations significantly affects the kinetic characteristics of embryonic development. In patients with polycystic ovary syndrome (PCOS), the proportion of embryos with delayed tPNf (time to pronuclear formation) in the short-term insemination group is 37% lower than that in the conventional insemination group (18.9% vs 30.1%), whereas there is no statistically significant difference in the blastocyst formation rate between the two insemination methods (62.4% vs 58.7%) (Liu, Y., Zhang, X., Wang, L., & Li, J., 2025). In contrast, for advanced-age patients (≥38 years old), the coefficient of variation of kinetic parameters increases significantly, with the standard deviation of t2 reaching 3.2 hours (compared with 1.7 hours in the young group). In this population, the continuous embryo development rate (from day 3 to day 5) of conventional insemination is superior to that of short-term insemination (41.3% vs 35.8%) (Dal Canto M, Bartolacci A, Turchi D, et al., 2020; Chen, Q., Zhao, L., Wang, Y., et al., 2022).

4.3 Regulatory Effects of Culture Environment on Developmental Quality

As a core parameter of the culture environment, oxygen concentration exerts a systematic impact on the metabolic characteristics of embryos. Under hypoxic culture conditions (5% O_2), the reactive oxygen species (ROS) level of embryos derived from short-term insemination decreases by 42%, the mitochondrial membrane potential increases by 1.3-fold, and the total number of blastocyst cells rises by 19.5% (128±15 vs 107±12, P=0.02) (Tao Linlin, Li Guozhen, Yang Zhiwei, et al., 2020; Wang, F., Li, R., Zhang, H., et al., 2022). This finding provides an important basis for optimizing the culture environment.

The adaptability of the culture system is also a key factor affecting embryo developmental quality. Studies have confirmed that the sequential culture system exhibits better compatibility with short-term insemination—its high-quality embryo rate is 11.3% higher than that of the single culture system (58.2% vs 46.9%), and this difference becomes more pronounced when the sperm concentration is lower than 5×10^6/mL (Li Youzhu, Yan Xiaohong, Wu Rongfeng, et al., 2020; Pellegrini L, Gatti S, Navarro N, et al., 2024). This indicates that the selection of the culture system needs to be synergistically optimized with the insemination strategy.

5. Evidence-Based Medical Comparison of Clinical Pregnancy Outcomes

5.1 Comparison of Clinical Pregnancy Rate and Live Birth Rate

Randomized controlled trials (RCTs) provide high-level evidence to support the comparison of clinical efficacy between short-term insemination and conventional insemination. An RCT involving 320 patients with non-male-factor infertility showed that the clinical pregnancy rate in the short-term insemination group reached 52.6%, which was significantly higher than the 43.1% in the conventional insemination group (P=0.03). However, there was no statistically significant difference in the live birth rate between the two groups (41.8% vs. 38.5%, P=0.52) (Abbas AM, Hussein RS, Elsenity MA, et al., 2020). This result indicates that although short-term insemination may improve the conditions for early embryo implantation, its impact on the final live birth outcome remains to be verified.

In the population with male-factor infertility, the selection of insemination strategies presents more complex effect characteristics. Clinical trials targeting patients with oligoasthenospermia have demonstrated that when the progressive motility (PR) rate ranges from 10% to 20%, the live birth rate of short-term insemination can reach 36.4%, which is 7.2 percentage points higher than that of conventional insemination (P=0.04) (Zhang Qingjian, Song Ge, Jiang Ronghua, et al., 2023; Liu Manman, Xu Shilian, Zhang Hebo, et al., 2024). This difference may be related to the time-dependent accumulation of oxidative damage to sperm DNA. Nevertheless, it is noteworthy that in patients with severe oligoasthenoteratospermia (PR<5%), the live birth rates of both insemination methods are lower than 25%, suggesting that early switching to the intracytoplasmic sperm injection (ICSI) strategy should be considered in such cases (Persson S, Elenis E, Turkmen S, et al., 2019; Kang K, Kim BY, Park JW, et al., 2019).

The application of time-lapse imaging technology has provided a new perspective for in-depth understanding of the relationship between insemination strategies and embryo developmental potential. Studies have shown that the blastulation time (tBL) of embryos from short-term insemination is 95.5±6.1 hours on average, which is 3.2 hours shorter than that of the conventional insemination group (P<0.01). Moreover, the clinical pregnancy rate of embryos with tBL<96 hours is significantly increased by 14.8% (P=0.02) (Jiang Yan, Zhang Han, Zhang Xuhui, et al., 2021; Persson S, Elenis E, Turkmen S, et al., 2019). This finding supports that short-term insemination may optimize the synchrony of embryo development, but more large-sample studies are needed to verify its long-term impact on live birth rates (González-Ortega C, Piña-Aguilar RE, Cancino-Villarreal P, et al., 2019; Kamath, M. S., Sunkara, S. K., Pundir, J., et al., 2019).

5.2 Comparison of Sustained Pregnancy Maintenance Capacity

Research data indicate that short-term insemination may reduce the risk of early miscarriage. A retrospective analysis involving 1,024 pregnancy cases showed that the early miscarriage rate (before 12 weeks of gestation) in the short-term insemination group was 8.3%, which was significantly lower than the 12.1% observed in the conventional insemination group (odds ratio [OR] = 0.67, 95% confidence interval [CI] 0.48–0.93) (Wang, J., Li, X., Zhang, Y., et al., 2020). In the population of patients with polycystic ovary syndrome (PCOS), this difference was even more pronounced: the miscarriage risk in the short-term insemination group was 42% lower than that in the conventional group (10.2% vs. 17.6%, P=0.03) (Xia Leizhen, Wu Qiongfang, Zhao Yan, et al., 2022; Pan Ye, Feng Haiying, Liu Qingqing, et al., 2019). This may be attributed to the fact that short-term insemination mitigates the interference of a hyperoxic environment with the epigenetic regulation of embryos.

However, the capacity for sustained pregnancy maintenance is influenced by multiple factors and exhibits distinct characteristic patterns. In the population of patients aged ≥35 years, the late pregnancy loss rate (after 20 weeks of gestation) in the conventional insemination group was 5.1%, lower than the 7.8% in the short-term insemination group (P=0.08) (Shen Jinhua, Zhou Yaqian, Yang Yide, et al., 2020; Kolte AM, Westergaard D, Lidegaard O, et al., 2020). This trend may be associated with the decline in oocyte quality among advanced-age women and their heightened sensitivity to changes in the culture environment. The impact of sperm DNA integrity on pregnancy maintenance capacity cannot be overlooked. When the sperm DNA Fragmentation Index (DFI) exceeds 30%, the risk of late miscarriage in the short-term insemination group increases by 2.3-fold (95% CI 1.2–4.5) (Zhang Qingjian, Song Ge, Zhong Xiaoying, et al., 2020; Devora Aharon, Dmitry Gounko, Tamar Alkon, et al., 2021). This finding suggests that the integrity status of sperm genetic material should be fully considered when formulating individualized insemination strategies.

5.3 Differential Effects in Special Patient Populations: PCOS, Advanced-Age Women and Severe Male-Factor Infertility

Patients with polycystic ovary syndrome (PCOS) exhibit unique responses to short-term insemination. A meta-analysis showed that the cumulative pregnancy rate of short-term insemination in PCOS patients can reach 58.3%, which is 11.5 percentage points higher than that of conventional insemination (P=0.01), with a 23% reduction in the incidence of ovarian hyperstimulation syndrome (OHSS) (Tang K, Wu L, Luo Y, et al., 2021). This advantage may be attributed to the mitigation of oxidative stress-induced embryonic damage in a hyperandrogenic environment by short-term insemination. The efficacy evaluation in advanced-age women (≥38 years old) presents an opposite trend. Conventional insemination yields slightly better embryo implantation rates (22.4% vs. 18.1%) and live birth rates (28.6% vs. 23.3%) than short-term insemination in this population (Erica Johnstone, Meredith Humphreys, C Matthew Peterson, et al., 2019). This may be associated with the decreased mitochondrial function of oocytes in advanced-age women, which requires a longer duration to complete the fertilization process. The selection of insemination strategies for patients with severe male-factor infertility needs to be particularly prudent. In patients with non-obstructive azoospermia, the live birth rate of short-term insemination is only 16%, showing no significant difference from that of conventional intracytoplasmic sperm injection (ICSI) (Kang K, Kim BY, Park JW, et al., 2019). This suggests that direct ICSI, rather than short-term insemination, should be prioritized for such patients.

6. Limitations and Shortcomings of the Research

Current comparative studies on short-term insemination and conventional insemination exhibit significant differences in laboratory operations, such as inconsistent sperm washing methods and criteria for determining insemination timing, which render direct comparisons of research findings difficult (Wu Xiyan, Huang Ling, Peng Xinhua, et al., 2021). A systematic review encompassing 32 studies showed that the fertilization rate in the short-term insemination group ranged from 28% to 82%, while that in the conventional insemination group ranged from 45% to 78%. This discrepancy is mainly attributable to the heterogeneity of laboratory procedures.

In addition, the heterogeneity of patient populations further undermines the reliability of the conclusions. The proportion of advanced-age patients (≥38 years old) varied from 12% to 45% across different studies, and there were also inconsistencies in the inclusion criteria for severe male-factor infertility (sperm concentration < 5×10^6/mL) (Chen, S., Zhang, L., Wang, Y., et al., 2023). Such sampling bias resulted in multi-center studies showing that the live birth rate of short-term insemination was 9.3% lower than that of conventional insemination in the advanced-age group ($P=0.04$), but 11.7% higher in the male-factor infertility group ($P=0.02$) (Li Caixia, Deng Yun, Gao Wenyi, et al., 2022). In the future, it will be necessary to unify operational standards through international consensus and adopt a stratified random design to control confounding factors.

7. Conclusion

As two important insemination strategies in in vitro fertilization (IVF), the selection of short-term insemination and conventional insemination should be based on individualized and precise assessment. Through a systematic literature review, this paper demonstrates that although there is no significant difference in the overall live birth rate between the two insemination methods, their therapeutic effects vary among populations with different clinical characteristics. By limiting the sperm-oocyte co-incubation duration and reducing exposure to reactive oxygen species (ROS), short-term insemination shows advantages in scenarios such as male-factor infertility, polycystic ovary syndrome (PCOS) patients, and follicular microenvironments with high oxidative stress. It helps improve fertilization efficiency, optimize the synchrony of early embryonic development, and may reduce the risk of early pregnancy loss. In contrast, conventional insemination, by simulating a more complete physiological fertilization window, exhibits better capacity for sustained embryonic development and pregnancy maintenance potential in populations such as those with high oocyte maturity and advanced-age women.

Analysis of embryonic developmental kinetics indicates that embryos derived from short-term insemination have shorter pronuclear formation and blastocyst formation times, suggesting a more compact developmental process. Current research is still constrained by challenges such as insufficient standardization of laboratory procedures and population heterogeneity. Future studies need to unify operational standards, deepen mechanism exploration, and conduct long-term follow-up research, so as to establish a more comprehensive and generalizable individualized insemination decision-making system, and ultimately promote the continuous improvement of assisted reproductive outcomes.

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Hepatitis A and Hepatitis E Viruses Can Develop Acute Viral Hepatitis: Prevention Is the Best Policy

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Abstract

Acute viral hepatitis is caused by hepatitis A virus (HAV) and hepatitis E virus (HEV) that is a great health problem worldwide. Both of the viruses are non-enveloped ribonucleic acid (RNA) and cause a self-limiting viral infection that is transmitted by fecal-oral route, primarily through the consumption of contaminated food and water. Both of the viruses can develop mono-infection or co-infection that is a common cause of viral hepatitis in developing countries. Some common symptoms of both diseases are fever, headache, malaise, nausea, vomiting, diarrhea, anorexia, abdominal pain, dark urine, and jaundice. The HAV is more common cause of acute hepatitis in children, and HEV is responsible for the majority of epidemic and sporadic hepatitis in adults. This study is planned to discuss the transmission and management of HAV and HEV infections to reduce morbidity and mortality for the welfare of the patients.

Keywords: HAV and HEV, co-infection, acute viral hepatitis

1. Introduction

Hepatitis A virus (HAV) and hepatitis E virus (HEV) are responsible for sporadic and epidemic forms of acute viral hepatitis (AVH) worldwide (Shinde et al., 2020). Acute liver failure and acute viral hepatitis are serious illnesses caused by the HAV and HEV. About 1.5 million clinical cases of HAV are recorded per year with about 7,134 deaths. There are globally about 20 million HEV infections each year, over which 3 million cases are symptomatic with about 56,600 deaths per year; and about 20-30% mortality among pregnant women particularly in the third trimester (WHO, 2020).

In 1973, 27nm HAV-like particles were visualized in stool samples obtained during acute phase of illness after inoculation of MS-1 strain in volunteers Stephen Feinstone, Albert Kapikian, and Robert Purcell (Feinstone et al., 1973). The HAV was first isolated in 1979 (Khuroo & Sofi, 2020). The HEV was discovered in 1983 by Russian virologist Mikhail Surenovich Balayan investigating an outbreak of unexplained hepatitis using immunoelectron microscopy among Soviet soldiers serving in Afghanistan. In 1989, the viral genome was successfully sequenced and this pathogen was formally designated as HEV (Izopet & Kamar, N. et al., 2014).

The HAV and HEV are responsible for acute viral hepatitis and more than 300 million people worldwide suffer from viral hepatitis annually (Kotwal et al., 2014). The HEV prevalence is highest in the East and South Asia, and the HAV prevalence is worldwide, especially in Africa, Asia, Europe, and North and South America. The HAV and HEV affect more men than women both in developed and developing countries (Kamar et al., 2014).

2. Literature Review

In any research, the literature review section is an introductory unit of research that helps the novice researchers to understand the subject, and it serves as an indicator of the subject that has been carried out before (Creswell, 2007). Ravindra V. Shinde and his coauthors have found that both the HAV and HEV are primarily transmitted via the fecal-oral course. In their study they have wanted to determine the seroprevalence of HAV and HEV, and rate of co-infection in patients attending rural tertiary care center (Shinde et al., 2020). Bodhrun Naher and her coworkers have wanted to learn about the seroprevalence of HAV and HEV infections, and their co-infections in acute viral hepatitis (AVH) cases of the hospitals of Bangladesh. In their study they have found that seroprevalence of HAV was 13.75%, HEV 5.75%, and co-infection of HAV and HEV 5.25% (Naher et al., 2023).

Stanley M. Lemon and Christopher M. Walker have studied and compared HAV and HEV biology in humans and animals to enhance the understanding of host-pathogen balance in the liver, and may contribute ultimately to the control of other infectious diseases of the liver (Lemon & Walker, 2019). Ankita Sharma and her coworkers have wanted to determine the seroprevalence of acute viral hepatitis (AVH) in developing countries for HAV and HEV. They have found that the prevalence of HAV is significantly higher than that of HEV; and HAV is more predominant in males compared to females (Sharma et al., 2024). Parul Patel and her coauthors have shown that acute viral hepatitis (AVH) due to HAV and HEV infection is a major public health problem in developing countries and is an important cause of morbidity and mortality (Patel et al., 2019).

Jinwal Meena and her coworkers have expressed that HAV and HEV are enterically transmitted viruses responsible for causing acute viral hepatitis that pose a heavy burden on the healthcare system of developing nations (Meena et al., 2021). Sarita Rawat and her coworkers have studied to determine prevalence of HAV and HEV in patients presenting with acute viral hepatitis and the co-infection of these viruses in patients (Rawat et al., 2019). Meghna S. Palewar and her coauthors have emphasized on the importance of screening all hepatitis viral markers for early diagnosis and curtailment of outbreaks and epidemics by the public health sector reducing morbidity and mortality (Palewar et al., 2022).

3. Research Methodology of the Study

The research design is the plan of the researchers to develop research area that is underpinned by philosophy, methodology and method (Tie et al., 2019). Methodology is a guideline for performing good research. It examines the purposes, problems, and questions of research (Kothari, 2008). Research methodology is a strategy for planning, arranging, designing and conducting fruitful research confidently to obtain a successful result (Legesse, 2014). To prepare this article, I have used secondary data sources that are collected from published and unpublished data sources (Mohajan, 2017, 2018, 2020). I have studied books of famous authors, handbooks, and theses. I have also collected valuable information from websites and internets (Mohajan, 2024a-e).

4. Objective of the Study

Main objective of this article is to discuss the aspects of HAV and HEV for the reduction of their fatality (Mohajan, 2024g-i). Both of these viruses can damage the liver and are associated with significant morbidity and mortality. These are responsible for acute viral hepatitis. Sometimes the infection with the viruses may be chronic hepatitis, liver cirrhosis, and liver failure (Mohajan, 2024k-p). Other minor objectives of the study are as follows (Mohajan, 2024f, j):

1) to focus on the characteristics of HAV and HAV,
2) to highlight on their symptoms and transmission, and
3) to stress on their prevention and treatment strategies.

5. Hepatitis A Virus (HAV)

Hepatitis A virus (HAV) infection is the most common form of acute viral hepatitis in the world that can damage the liver. It is tissue or cell specific and attacks only the liver. It is highly endemic in developing nations due to overcrowding and poor sanitation (Ambrosch et al., 2004). It never progresses into chronicity, but it can cause debilitating symptoms and acute liver failure, which is associated with high mortality (Squires et al., 2006).

5.1 Virology HAV

The HAV is a small, non-enveloped, 27-32nm ribonucleic acid (RNA) virus in the genus Hepatovirus of the family Picornaviridae (Enkirch et al., 2019). There are six HAV genotypes based on examining a 168-nucleotide fragment of the VP1-2A region. Only genotypes I, II and III infect humans and genotypes IV to VI cannot infect humans (Smith & Simmonds, 2018). Genotypes I, II, and III are further divided into subtypes A and B (Cella et al., 2018). The HAV usually affects infants and young children in developing countries, and causes an asymptomatic and self-limiting infection (Agarwal et al., 2017).

5.2 Symptoms and Transmission of HAV

The incubation period of HAV is from 15 to 50 days, with an average of 25 to 30 days. It is asymptomatic and self-limiting infections, leading to lifelong immunity (Franco et al., 2012). The symptoms of HAV are extreme fatigue, nausea, vomiting, malaise, dark urine, anorexia, jaundice, and abdominal pain along with elevated liver enzymes (Sarangi et al., 2019). The source of infection resides in contaminated food and water, and the transmission takes place by the oral pathway through the "fecal-oral" system (Heymann, 2008). Sharing of forks, spoons, knives, and other utensils that have virus on them can spread the HAV. The disease is not spread by kissing, sneezing or saliva (WHO, 2012).

5.3 Prevention and Treatment of Hepatitis A

Prevention strategy of HAV is not costly and difficult. A person must wash hands carefully and thoroughly with soap and warm running water after using the toilet or changing diapers (Chen et al., 2010). The HAV vaccine is very safe and effective. It is made through the killing (inactivated) HAV by formaldehyde (Keeffe, 2006). The HAV vaccine is introduced in 1995 in the USA by American microbiologist Maurice Ralph Hilleman (1919-2005) and his team that saves millions of lives every year (CDC, 2018). No specific treatment of HAV is available, complete rest following infection is important for recovery. It is generally mild and self-limiting with a typical recovery in two weeks. Treatment of the HAV is palliative and supportive care (Gerardi & Zimmerman, 2005).

6. Hepatitis E Virus (HEV)

The HEV is the most common cause of acute viral hepatitis globally that is responsible for the major liver infection (Pilot et al., 1987). The prevalence of HEV is in animal species with zoonotic potential in humans (Yugo & Meng, 2013). Infection with the HEV may be related to acute illness, chronic hepatitis, liver cirrhosis, and liver failure (Guerra et al., 2017).

6.1 Virology HEV

The HEV is a small, non-enveloped, single-stranded, positive-sense ribonucleic acid (RNA) virus in the genus Orthohepevirus of the family Hepeviridae. The genome is of 7.2 kb and 27-34nm in diameter that is highly unstable due to the lack of a lipid membrane (Mayr et al., 2018). The HEV can be clustered genetically into 8 genotypes (GTs); HEV1-8 that recognize with distinct differences in geographic distribution (Sridhar et al., 2017).

6.2 Symptoms and Transmission of HEV

Usually, HEV infected people have no symptoms. Some symptoms of hepatitis E are jaundice, fever, tiredness, loss of appetite, malaise, anorexia, nausea, vomiting, abdominal pain, joint pain, hepatomegaly, pruritus dark urine, pale stools, and arthralgia (Mirazo et al., 2014). The HEV is transmitted by fecal-oral route, primarily through the consumption of contaminated food and water (Kumar et al., 2017).

6.3 Vaccination and Treatment of Hepatitis E

The HEV infections are usually self-limiting and asymptomatic in immunocompetent individuals (Mohajan, 2024j). Prevention is the most effective policy to protect HEV (Wedemeyer et al., 2012). No effective and specific treatments against HEV infection have been developed yet, and also there is no HEV vaccine available, and treatment is palliative and supportive (Mirazo et al., 2014). Current therapeutics used to treat HEV infection are the nucleoside analog ribavirin and pegylated interferon-α (PEG IFN-α) (Kamar et al., 2014). A Chinese vaccine has been demonstrated to be protective against HEV in the general population and seems to be safe in pregnancy; however, its safety and efficacy is not determined (Wu et al., 2020).

7. Conclusions

From this study, I have observed that viral hepatitis is a major public health problem in the worldwide. The HAV and HEV usually spread through the direct contact with an infected person, and a higher prevalence of HEV as compared with HAV infection. These can be transmitted through fecal contamination of food and water. Improvements in socioeconomic condition, personal hygiene, and sanitation can reduce the fatality of the diseases. Moreover, both of the diseases can be treated with medications, therapies, and nutrition supports. Prevention is the most effective method against acute viral hepatitis due to HAV and HEV through the maintaining of hygienic practices. All the nations should make efforts to increase the public awareness among citizens for the reduction of global morbidity, mortality, and economic burden.

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The Neurodevelopmental Architecture of ADHD: Executive Function, Emotional Dysregulation, and Circuit-Level Mechanisms

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Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) is a complex neurodevelopmental condition characterized by pervasive deficits in executive control, motivational regulation, and emotional stability. Contemporary neuroscience conceptualizes ADHD as a disorder of distributed neural systems rather than localized dysfunction. This paper examines the neurodevelopmental architecture of ADHD through the integration of cognitive, affective, and circuit-level perspectives. Longitudinal imaging studies demonstrate delayed cortical maturation and disrupted connectivity within prefrontal and parietal regions, contributing to deficits in working memory, inhibition, and sustained attention. Emotional dysregulation is traced to impaired prefrontal–limbic communication, particularly between the amygdala and ventromedial prefrontal cortex, resulting in heightened reactivity and poor affective control. At the systems level, functional network analyses reveal instability across frontostriatal, frontoparietal, default mode, limbic, and cerebellar circuits. These networks exhibit abnormal coupling, reduced segregation, and inconsistent transitions between internal and external attentional states. Genetic and neurochemical studies implicate dopaminergic and noradrenergic dysregulation as primary modulators of these circuit abnormalities. Translational evidence indicates that stimulant and non-stimulant pharmacotherapy partially normalize network activation, while behavioral, cognitive, and neuromodulatory interventions strengthen regulatory circuitry through neuroplastic adaptation. Collectively, these findings support a dynamic systems model in which ADHD emerges from disrupted developmental synchronization across executive and emotional networks. Understanding this architecture offers a foundation for precision interventions targeting the neural mechanisms underlying self-regulation across the lifespan.

Keywords: ADHD, executive function, emotional dysregulation, neurodevelopment, brain networks, frontostriatal circuit, default mode network, dopamine, prefrontal cortex, functional connectivity, neural maturation, cognitive control

1. Introduction

1.1 Conceptualizing ADHD as a Neurodevelopmental Disorder

Attention-Deficit/Hyperactivity Disorder (ADHD) is a prevalent neurodevelopmental condition characterized by persistent patterns of inattention, hyperactivity, and impulsivity that interfere with functioning across multiple contexts. The disorder emerges early in development, typically before adolescence, and affects approximately 5–7% of children worldwide. Symptoms frequently persist into adulthood, influencing occupational stability, interpersonal relationships, and emotional well-being. ADHD is not confined to a single behavioral or cognitive domain. It reflects a constellation of atypical developmental processes shaping the maturation of brain systems responsible for self-regulation, motivation, and executive control.

Historically, ADHD was framed as a disorder of attention or behavioral inhibition. Contemporary research in developmental neuroscience has shifted the perspective toward a multidimensional model encompassing cognitive, emotional, and motivational dysregulation. This shift recognizes that attention deficits are only one aspect of a broader neurobiological pattern involving alterations in cortical development and distributed neural network organization. The integration of cognitive neuroscience, genetics, and neuroimaging has established ADHD as a disorder of neural circuitry rather than a single-site brain dysfunction.

1.2 Global Impact and Lifespan Perspective

ADHD imposes substantial personal and societal costs. Across diverse cultural and socioeconomic settings, individuals with ADHD experience higher rates of academic underachievement, employment instability, and social exclusion. Longitudinal studies indicate that approximately two-thirds of children with ADHD continue to display significant symptoms into adulthood, suggesting that the disorder reflects a persistent deviation in neurodevelopmental trajectory rather than a transient childhood condition. Adult manifestations often include internal restlessness, disorganization, and difficulties managing affect, which collectively impair adaptive functioning. The chronic nature of ADHD underscores the need to understand not only symptom expression but also the underlying developmental mechanisms that sustain it over time.

At the population level, ADHD contributes to increased healthcare utilization and comorbidity with anxiety, mood, and substance use disorders. The overlap between cognitive and emotional regulation deficits suggests shared neural substrates that extend beyond the traditional diagnostic boundaries of ADHD. This complexity challenges categorical classification systems and highlights the importance of mechanistic approaches rooted in developmental neurobiology.

1.3 From Behavioral Phenotype to Neural Architecture

Advances in neuroimaging and computational modeling have transformed our understanding of ADHD from a behavioral syndrome to a disorder of brain network organization. Structural magnetic resonance imaging (MRI) studies reveal delayed cortical maturation, particularly within prefrontal and parietal regions responsible for top-down control. Functional MRI demonstrates altered activation and connectivity among the frontostriatal, frontoparietal, and default mode networks—circuits crucial for sustaining attention and regulating motivation. These patterns suggest that ADHD involves disrupted coordination among distributed neural systems rather than isolated regional deficits.

This network-based framework aligns with the concept of ADHD as a disorder of self-regulation, encompassing both executive function and emotional control. The same circuits that govern goal-directed behavior also modulate affective responses, implying that cognitive and emotional dysregulation share common neurobiological foundations. By examining ADHD through this lens, researchers can move toward a more integrated model that connects symptom expression to specific circuit-level mechanisms.

1.4 Aim and Scope of the Study

The purpose of this work is to examine the neurodevelopmental architecture of ADHD through three interrelated domains: executive function, emotional dysregulation, and circuit-level organization. Each domain contributes to the behavioral phenotype of ADHD and reflects underlying variations in brain development and connectivity. The discussion aims to synthesize empirical findings across developmental stages, highlight converging evidence from cognitive neuroscience and neuroimaging, and propose an integrative framework that bridges cognition and emotion within a unified neurobiological model.

This approach positions ADHD as a disorder of distributed neural systems shaped by developmental timing, genetic modulation, and experience-dependent plasticity. Understanding how these elements interact is essential for advancing diagnostic precision and for designing interventions that target the neural mechanisms underlying self-regulatory failure.

2. Neurodevelopmental Trajectories

2.1 Patterns of Cortical Maturation

ADHD is rooted in atypical brain maturation that begins early in childhood and persists throughout adolescence. Longitudinal neuroimaging studies reveal that children with ADHD display a delay in cortical thinning, particularly within the prefrontal cortex and parietal association areas. These regions are central to attention control, working memory, and planning. The delay does not imply neurodegeneration but rather a slower or desynchronized developmental trajectory, suggesting that the timing of neural maturation is a critical determinant of symptom persistence. Structural MRI studies have demonstrated that peak cortical thickness occurs several years later in children with ADHD compared to typically developing peers, especially in regions implicated in top-down regulation.

White matter integrity also shows developmental differences. Diffusion tensor imaging studies report reduced fractional anisotropy in frontostriatal and frontoparietal tracts, which reflects less efficient communication among brain regions responsible for executive function and inhibitory control. Such findings indicate that

ADHD involves not only regional gray matter differences but also impaired connectivity within large-scale systems that support goal-directed behavior.

2.2 Developmental Timing and Network Integration

Brain development follows a hierarchical pattern from subcortical to cortical regions. In ADHD, this sequence appears to be disrupted. Subcortical structures such as the striatum and amygdala may mature earlier or exhibit hyperreactivity relative to underdeveloped prefrontal regions. This imbalance may contribute to the characteristic impulsivity and emotional lability observed in affected individuals. During adolescence, when the prefrontal cortex typically assumes stronger regulatory control over limbic processes, individuals with ADHD often fail to achieve full synchronization between these systems.

Developmental neuroimaging has shown that the functional integration between the default mode network (DMN) and task-positive networks (such as the frontoparietal system) gradually improves with age in typical development. In ADHD, however, DMN activity remains intrusive during goal-directed tasks, resulting in mind-wandering and attentional lapses. This persistence of DMN activation is consistent with the hypothesis that ADHD involves a lag in network segregation, where brain systems responsible for internally focused thought fail to disengage when external attention is required.

2.3 Neurodevelopmental Models of ADHD

Multiple theoretical models have emerged to explain the developmental course of ADHD. The maturational delay model posits that ADHD reflects a general lag in cortical development, which may eventually normalize in some individuals, explaining symptom remission in late adolescence. The neural heterogeneity model, by contrast, suggests that distinct neurodevelopmental pathways lead to different ADHD subtypes, including those dominated by inattention, hyperactivity, or emotional dysregulation. A third framework, the developmental imbalance model, emphasizes the asynchronous maturation of prefrontal control systems and subcortical motivational circuits.

Evidence increasingly supports the imbalance model. Functional connectivity studies show that adolescents with ADHD exhibit overactivation of limbic and striatal regions in response to reward cues, paired with underactivation of the dorsolateral prefrontal cortex during tasks requiring inhibition. This dual pattern implies that emotional and motivational drives gain precedence over cognitive control processes, producing impulsive decisions and inconsistent task engagement.

2.4 Environmental Modulation and Plasticity

Although ADHD is highly heritable, environmental factors interact with genetic predispositions to shape neurodevelopmental outcomes. Prenatal exposure to nicotine, alcohol, and maternal stress has been associated with alterations in dopaminergic signaling and frontostriatal development. Early life stress may further affect amygdala reactivity and hypothalamic–pituitary–adrenal axis regulation, reinforcing emotional dysregulation. Socio-environmental enrichment, supportive parenting, and structured learning environments have been shown to enhance compensatory neural mechanisms, particularly in the prefrontal cortex.

Neuroplasticity plays a key role in modulating the severity and persistence of ADHD symptoms. Interventions such as cognitive training, aerobic exercise, and mindfulness have been found to strengthen prefrontal activation and functional connectivity with limbic structures. These findings indicate that ADHD is not a fixed structural anomaly but a dynamic developmental condition responsive to environmental and behavioral modulation.

Table 1.

Developmental Domain	**Typical Maturation Pattern**	**ADHD Trajectory**	**Functional Consequence**
Cortical thickness	Gradual thinning through adolescence	Delayed thinning, especially in PFC	Reduced executive control
White matter integrity	Progressive myelination	Lower frontostriatal connectivity	Inefficient information transfer
Network integration	Increased segregation of DMN and task networks	Persistent DMN interference	Mind-wandering, attentional lapses
Prefrontal–limbic balance	Gradual top-down regulation	Limbic dominance over PFC	Emotional reactivity, impulsivity
Neuroplastic response	Adaptive reorganization	Variable compensation	Individual differences in outcome

The convergence of structural, functional, and developmental findings suggests that ADHD reflects a pattern of delayed and desynchronized neural maturation. This framework provides the foundation for examining how specific domains of cognition and emotion emerge from these atypical developmental processes.

3. Executive Function and Cognitive Control

3.1 Defining Executive Function Within ADHD

Executive function refers to the set of higher-order cognitive processes that enable individuals to plan, sustain attention, inhibit responses, and adjust behavior in dynamic environments. These capacities rely primarily on prefrontal cortical systems and their communication with subcortical and parietal regions. In ADHD, impairments in executive function are consistently observed across lifespan and across cultural contexts, suggesting a core neurocognitive component rather than a secondary effect of motivation or environment.

Behaviorally, individuals with ADHD often show difficulty sustaining effort on tasks that require prolonged concentration or delayed gratification. They may initiate activities impulsively, fail to complete them, or shift goals prematurely. Neuropsychological testing highlights consistent deficits in response inhibition, working memory, and temporal processing—domains that collectively underlie self-regulatory control. These impairments form the basis of daily challenges in organization, time management, and persistence.

3.2 Neural Basis of Executive Dysfunction

Neuroimaging research links executive deficits in ADHD to structural and functional abnormalities in the prefrontal cortex and its connections with the basal ganglia and parietal cortex. The dorsolateral prefrontal cortex (DLPFC) is central to working memory and planning, while the anterior cingulate cortex (ACC) monitors performance and detects conflicts between goals and behavior. In ADHD, reduced activation in both DLPFC and ACC has been repeatedly demonstrated during inhibition and task-switching paradigms.

Functional connectivity analyses reveal weakened synchronization between the prefrontal cortex and striatal regions such as the caudate nucleus and putamen. This disruption leads to inefficient top-down control over motor and reward-driven behavior. The frontoparietal network, which coordinates attentional allocation and executive control, also shows reduced coherence. These findings indicate that executive dysfunction arises not from a single region's abnormality but from impaired coordination across distributed networks responsible for cognitive regulation.

3.3 Working Memory and Sustained Attention

Working memory supports the ability to maintain and manipulate information in the service of future goals. Individuals with ADHD often demonstrate limited working memory capacity and faster decay of stored information, particularly under high cognitive load. Functional MRI studies show that during working memory tasks, children and adults with ADHD exhibit hypoactivation in the DLPFC and posterior parietal cortex. The diminished activation correlates with slower reaction times and reduced accuracy.

Sustained attention deficits also represent a hallmark of ADHD. Electrophysiological studies demonstrate reduced amplitude of the P3 component, reflecting impaired attentional allocation. Resting-state imaging identifies instability in attention-related networks, where fluctuations in connectivity strength correspond to momentary lapses of focus. These results suggest that ADHD involves a fundamental difficulty in maintaining consistent neural engagement across time rather than a uniform inability to attend.

3.4 Inhibitory Control and Impulsivity

Response inhibition, the capacity to suppress prepotent actions, is among the most robustly impaired domains in ADHD. Tasks such as the stop-signal and go/no-go paradigms consistently show longer reaction times and higher error rates among individuals with ADHD. These behavioral findings align with hypoactivation of the right inferior frontal gyrus and pre-supplementary motor area—regions critical for implementing inhibitory control.

The deficit in inhibitory control extends beyond motor behavior into cognition and emotion. Impulsive decision-making and rapid emotional reactions can be interpreted as failures of the same neural systems that govern response inhibition. This shared mechanism reinforces the view that cognitive and affective regulation in ADHD are interconnected through overlapping prefrontal circuits.

3.5 Temporal Processing and Reward Delay

Temporal processing refers to the ability to perceive, estimate, and respond to time intervals. Individuals with ADHD frequently underestimate time durations and struggle to delay gratification, favoring immediate rewards over larger delayed outcomes. Theoretical accounts such as the "delay aversion model" suggest that this temporal bias results from dysfunction within frontostriatal circuits that integrate timing with reward valuation.

Neurobiological evidence supports this view. Dopaminergic signaling in the striatum and prefrontal cortex underlies temporal prediction and motivation. In ADHD, reduced dopamine transporter regulation may impair the encoding of delay-related signals, leading to altered time perception and impulsive reward choices. These mechanisms connect executive dysfunction to motivational dysregulation, illustrating how cognitive control deficits translate into everyday behavioral impulsivity.

3.6 Integrative View of Executive Impairment

The executive deficits in ADHD represent a distributed network dysfunction encompassing both cognitive and motivational dimensions. Structural immaturity and functional disconnection within prefrontal circuits compromise the ability to sustain attention, manipulate information, and suppress inappropriate actions. The resulting behavioral pattern—variability in performance, impulsivity, and inconsistent goal pursuit—reflects the cascading effects of disrupted executive control on multiple levels of behavior.

This integrative understanding positions executive dysfunction as the cognitive foundation upon which emotional dysregulation and motivational abnormalities build. Subsequent sections address how these cognitive limitations intersect with affective systems to produce the full ADHD phenotype.

4. Emotional Dysregulation and Affective Circuits

4.1 Emotional Dysregulation as a Core Feature of ADHD

Emotional dysregulation, long considered a secondary symptom of ADHD, is now recognized as a central and defining component of the disorder. Individuals with ADHD experience rapid shifts in mood, heightened irritability, and difficulty recovering from negative affective states. These difficulties extend beyond normal variability in temperament and reflect structural and functional anomalies in brain systems that govern emotional reactivity and regulation. Clinical observations show that emotional instability often predicts functional impairment as strongly as inattention or hyperactivity. Children with ADHD who exhibit pronounced affective lability tend to experience higher rates of social rejection, academic failure, and comorbid mood disorders later in life.

4.2 Neurobiological Basis of Emotional Dysregulation

Neuroimaging studies reveal that emotional dysregulation in ADHD arises from disruptions in the interaction between the prefrontal cortex and subcortical limbic structures. The amygdala, a central node for emotion detection and salience processing, often shows hyperactivation in response to emotionally charged stimuli. The ventromedial prefrontal cortex (vmPFC) and orbitofrontal cortex (OFC), which normally exert top-down modulation of amygdala responses, display reduced activation and weaker functional connectivity in ADHD. This imbalance results in exaggerated emotional reactivity and diminished control over negative affect.

Structural imaging has demonstrated volumetric reductions in the amygdala and ventral striatum, as well as abnormal asymmetry in the OFC. Diffusion tensor imaging findings indicate reduced white matter integrity along prefrontal-limbic tracts, particularly in the uncinate fasciculus, a fiber bundle connecting the vmPFC with the amygdala. The functional implication of these abnormalities is a system that responds rapidly to emotional cues but lacks the regulatory precision needed to modulate those responses effectively.

4.3 Cognitive-Affective Interaction

Emotion and cognition are tightly integrated within shared neural systems. In ADHD, emotional dysregulation often exacerbates cognitive deficits by increasing distractibility and reducing working memory capacity under stress. Functional imaging studies using emotional Stroop or affective go/no-go tasks show that individuals with ADHD have difficulty suppressing attention to emotional stimuli, leading to greater interference and slower reaction times. The reduced engagement of prefrontal control regions during these tasks suggests that emotion-laden contexts amplify existing weaknesses in executive function.

This interaction also works in reverse. Impaired executive function limits the ability to employ cognitive reappraisal strategies, a key mechanism for downregulating emotional responses. The failure to engage cognitive control circuits during emotional arousal contributes to maladaptive coping strategies such as avoidance, impulsive reactions, or aggression. Thus, emotional dysregulation is both a consequence and a contributor to executive dysfunction, forming a reciprocal feedback loop that reinforces ADHD symptomatology.

4.4 Reward Sensitivity and Emotional Motivation

ADHD is characterized by altered reward processing, which intersects with emotional regulation. Individuals with ADHD often display increased sensitivity to immediate rewards and reduced sensitivity to delayed or abstract outcomes. Functional imaging implicates the ventral striatum and orbitofrontal cortex, where dopamine signaling plays a key modulatory role. Reduced activation in these regions during anticipation of delayed rewards corresponds with diminished motivation and poor delay tolerance.

This altered reward sensitivity contributes to emotional dysregulation by shaping the valence and intensity of affective responses. Frustration in the absence of immediate reinforcement triggers strong negative emotion and reactive behavior. The frontostriatal circuit's underactivation during delay tasks parallels hyperactivation of the amygdala and insula during frustration paradigms, indicating that motivational and emotional dysregulation share a common neurochemical substrate. These findings explain why emotional outbursts in ADHD often occur in contexts of delay, perceived unfairness, or unmet expectations.

4.5 Developmental Perspective on Emotional Control

Emotional regulation normally improves across childhood and adolescence as prefrontal systems mature and gain inhibitory control over subcortical responses. In ADHD, this developmental trajectory is altered. Longitudinal studies suggest that while some individuals show partial normalization of emotional control in adulthood, many continue to exhibit difficulties managing frustration and maintaining emotional balance. The persistence of these symptoms correlates with ongoing structural and functional deficits in prefrontal–limbic circuitry.

During adolescence, when social and emotional demands increase, the gap between typical and ADHD-related emotional control widens. This period coincides with a surge in limbic reactivity and ongoing prefrontal maturation, amplifying the imbalance between emotional drive and regulatory capacity. The result is a heightened risk for affective comorbidities such as depression and anxiety, particularly in individuals with prominent emotional instability.

4.6 Integrative Model of Emotional Dysregulation

Emotional dysregulation in ADHD reflects a failure of dynamic coordination between cognitive control networks and limbic systems. The prefrontal cortex, responsible for appraisal and inhibition, fails to exert sufficient modulation over limbic outputs, while the amygdala and ventral striatum exhibit heightened sensitivity to emotionally salient cues. This imbalance disrupts the equilibrium between approach and avoidance behavior, producing oscillations between impulsive emotional expression and withdrawal.

A conceptual model can be summarized as follows:

- **Limbic Overactivation:** Heightened amygdala and striatal reactivity to emotion and reward.
- **Prefrontal Hypoactivation:** Reduced regulatory control from vmPFC, OFC, and DLPFC.
- **Disrupted Connectivity:** Impaired communication via uncinate fasciculus and cingulum bundle.
- **Behavioral Outcome:** Rapid, poorly regulated emotional reactions and low frustration tolerance.

These neurobiological findings converge on a single principle: emotional and cognitive dysregulation in ADHD are not separate phenomena but interdependent manifestations of an underlying network imbalance. Understanding this interaction offers a framework for interventions that simultaneously target emotion and cognition through behavioral and neurobiological mechanisms.

5. Circuit-Level Mechanisms and Network Interactions

5.1 Distributed Network Dysregulation

ADHD involves widespread disruptions across neural circuits that integrate cognitive control, emotion regulation, and motivation. The disorder's neural architecture reflects not an isolated regional abnormality but a failure of large-scale systems to coordinate dynamically across time and context. Brain activity in ADHD is characterized by irregular synchronization among cortical and subcortical regions, producing inconsistent transitions between internally and externally directed states of attention. The interplay between multiple networks—the frontostriatal, frontoparietal, default mode, salience, limbic, and cerebellar systems—defines the condition's neurobiological profile.

Graph-theoretical analyses of functional connectivity provide quantitative evidence for this distributed dysregulation. Resting-state MRI data show decreased modularity and increased global efficiency, implying that the ADHD brain may be less segregated into distinct functional communities. This configuration reflects premature or inefficient integration across networks, where communication between unrelated systems becomes excessively coupled. The loss of functional segregation undermines the brain's ability to maintain specialized processing, resulting in cognitive variability and difficulty sustaining focus. Network hubs such as the anterior cingulate cortex (ACC) and precuneus exhibit altered centrality measures, suggesting that key relay nodes within the brain's communication hierarchy are either underactive or overconnected, contributing to instability in cognitive control.

5.2 Frontostriatal Circuit: Reward, Inhibition, and Volitional Control

The frontostriatal system serves as the neural backbone of goal-directed action and inhibitory regulation. In ADHD, reduced striatal volume and hypoactivation of the caudate nucleus disrupt feedback loops critical for suppressing impulsive responses and sustaining reward-driven motivation. Dopamine signaling within this circuit governs the evaluation of effort and reward, and its dysregulation produces inconsistent reinforcement learning. Neurophysiological recordings indicate delayed striatal response to reward prediction errors, which diminishes the motivational salience of delayed outcomes. The weakened prefrontal–striatal coupling therefore explains both the impulsive behavior and the preference for immediate gratification often observed in ADHD.

5.3 Frontoparietal Network: Cognitive Stability and Executive Coordination

The frontoparietal network functions as a domain-general control system that maintains task goals and reallocates attentional resources as environmental demands shift. Functional imaging consistently reveals hypoactivation in the dorsolateral prefrontal cortex (DLPFC) and inferior parietal lobule during working memory and set-shifting tasks. These areas exhibit weaker temporal coherence, indicating disrupted communication within the frontoparietal loop. Reduced network stability correlates with greater behavioral variability, suggesting that ADHD involves a breakdown in the brain's capacity to sustain continuous cognitive engagement.

Dynamic functional connectivity (dFC) studies have deepened this understanding by analyzing temporal fluctuations in network coupling rather than static averages. Individuals with ADHD exhibit higher variability in frontoparietal connectivity across time, reflecting unstable transitions between engagement and disengagement states. This temporal instability mirrors behavioral inconsistency, where performance quality oscillates within short intervals. The phenomenon supports a model of ADHD as a disorder of network temporal regulation rather than purely of activation strength.

5.4 Default Mode Network: Task Disengagement and Mind-Wandering

The default mode network (DMN) is typically active during rest and internally directed cognition and deactivates during externally oriented tasks. In ADHD, this system shows persistent activation during task engagement, leading to interference with attention and goal maintenance. The medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC), key hubs of the DMN, fail to suppress their activity when cognitive control networks are engaged. This overlap results in competing demands between introspective and task-relevant processing, producing mind-wandering and attentional lapses.

Resting-state connectivity data indicate that DMN hyperconnectivity correlates with symptom severity, particularly in inattention and distractibility. The interaction between the DMN and task-positive networks, such as the frontoparietal and dorsal attention systems, appears unbalanced. The inefficiency of network switching mechanisms may arise from dysfunction within the salience network, which normally acts as a switch between internal and external modes of processing.

5.5 Salience Network: The Neural Switch Between Internal and External Attention

The salience network (SN), centered on the anterior insula and dorsal anterior cingulate cortex (dACC), detects behaviorally relevant stimuli and coordinates transitions between the DMN and task-positive systems. In ADHD, functional connectivity within the SN is reduced, and its regulatory influence on other networks is weakened. fMRI studies have demonstrated that the anterior insula exhibits delayed or inconsistent responses to salient events, impairing the system's ability to reorient attention from internal thoughts to external tasks.

This network plays a key role in maintaining mental readiness and balancing emotional and cognitive priorities. Its dysfunction explains why individuals with ADHD may fluctuate between hyperfocus and distractibility, reflecting inconsistent triggering of attentional engagement. The SN also integrates interoceptive and affective signals, linking emotional regulation to cognitive control. Thus, its dysregulation contributes to both attentional instability and emotional impulsivity.

5.6 Cerebellar–Prefrontal Pathways

The cerebellum, traditionally associated with motor coordination, has emerged as a significant contributor to cognitive and emotional regulation. Structural and functional abnormalities in cerebellar lobules VI and VII, which connect with the prefrontal cortex via the dentate nucleus and thalamus, have been repeatedly documented in ADHD. These regions support temporal prediction, sequencing, and performance monitoring—functions essential for executive control. Cerebellar hypoactivation leads to impaired estimation of time intervals and deficits in the synchronization of cognitive operations.

Neurodevelopmentally, the cerebellum matures earlier than the prefrontal cortex and may scaffold early regulatory skills. Atypical cerebellar development could thus disrupt the calibration of prefrontal circuits, resulting in persistent timing and coordination difficulties. This account aligns with evidence that cerebellar–prefrontal connectivity predicts variability in response inhibition and temporal foresight in ADHD populations.

5.7 Graph Theory Metrics and Network Topology

Recent advances in network neuroscience enable quantitative characterization of ADHD-related connectivity changes using graph theory. Metrics such as **modularity**, **clustering coefficient**, and **path length** reveal the degree of integration and segregation across brain networks. ADHD brains tend to exhibit reduced modularity, indicating weaker specialization among functional subsystems, and shortened characteristic path length, reflecting over-integration. The presence of this “noisy connectivity” pattern supports the view that excessive cross-talk among networks disrupts efficient information processing.

Altered hub organization further differentiates ADHD from typical development. Central hubs within the prefrontal cortex, anterior cingulate, and precuneus often show reduced betweenness centrality, signifying weakened influence over network communication. In contrast, compensatory hyperconnectivity in sensory and motor regions may reflect attempts to stabilize network performance through alternative pathways. These findings reinforce the concept of ADHD as a disorder of network topology, where imbalance between segregation and integration compromises flexibility and control.

Table 2.

Circuit/System	Primary Function	Alteration in ADHD	Key Regions
Frontostriatal	Reward processing, inhibition	Hypoactivation, reduced dopamine signaling	Prefrontal cortex, striatum
Frontoparietal	Executive control, attention	Weakened connectivity, instability	DLPFC, inferior parietal cortex
Default Mode Network	Internal mentation	Incomplete task-related suppression	mPFC, PCC
Limbic Network	Emotion regulation	Hyperreactivity, weak top-down control	Amygdala, vmPFC, insula
Cerebellar Circuit	Temporal coordination	Structural reduction, hypoactivation	Lobules VI–VII, dentate nucleus

5.8 Integrative Model: Dynamic Instability and Network Competition

The convergence of findings across static and dynamic network analyses suggests that ADHD involves a fundamental instability in neural coordination. Instead of consistent transitions between attention, control, and rest states, the ADHD brain exhibits erratic oscillations among networks. Excessive DMN persistence, weakened salience detection, and inconsistent frontoparietal activation form a triad of dysfunction that underlies attentional variability. The cerebellum and striatum, by contributing timing and reward signals, modulate these transitions but fail to maintain synchronization when connectivity is unstable.

This model integrates molecular, structural, and functional levels: dopaminergic and noradrenergic dysregulation impair the precision of network signaling, which in turn disrupts circuit timing and inter-network switching. Behavioral outcomes—impulsivity, distractibility, and emotional lability—emerge as expressions of this unstable neural architecture. Future interventions aimed at restoring network stability, whether through pharmacology, neurostimulation, or behavioral retraining, may thus correct the disorder at its systems level rather than its surface symptoms.

6. Genetic and Neurochemical Underpinnings

6.1 Molecular Foundations of ADHD

ADHD arises from a complex interaction of genetic variation and neurochemical imbalance that shapes brain development and circuit function. Twin and family studies estimate its heritability at approximately 70–80%, marking it as one of the most genetically influenced psychiatric conditions. Genetic factors primarily affect the dopamine and norepinephrine systems, which are central to attention, reward processing, and executive control. These neurotransmitter systems modulate the efficiency of communication between cortical and subcortical regions, especially within the frontostriatal and frontoparietal circuits. Dysregulation at this molecular level leads to the functional and behavioral phenotypes that define ADHD.

Genome-wide association studies (GWAS) have identified multiple loci associated with ADHD risk, though each exerts a small individual effect. The cumulative influence of these polymorphisms contributes to altered neurotransmission and synaptic signaling. Many of the implicated genes are involved in dopamine synthesis, transport, and receptor regulation, supporting the centrality of dopaminergic mechanisms.

6.2 Dopaminergic System: Reward, Motivation, and Timing

Dopamine plays a crucial role in reward prediction, reinforcement learning, and temporal processing—all functions disrupted in ADHD. The mesocorticolimbic dopamine pathway, extending from the ventral tegmental area to the nucleus accumbens and prefrontal cortex, is particularly implicated. Reduced dopamine transporter availability and altered receptor binding have been demonstrated through positron emission tomography (PET) and single-photon emission computed tomography (SPECT) imaging.

One of the most studied genetic variants in ADHD is the dopamine transporter gene (DAT1 or SLC6A3). The 10-repeat allele of a variable number tandem repeat (VNTR) polymorphism in the DAT1 gene is associated with hyperactivity and altered response to stimulant medication. Similarly, the dopamine receptor D4 gene (DRD4) features a 7-repeat allele that has been linked to novelty seeking, impulsivity, and reduced receptor efficiency. These polymorphisms collectively contribute to weaker dopaminergic tone in the prefrontal cortex, impairing the maintenance of task-related motivation and temporal precision.

Functional consequences of dopaminergic dysregulation are evident in neuroimaging studies. Individuals with ADHD display blunted ventral striatal responses during reward anticipation, reflecting an impaired encoding of incentive salience. This deficit disrupts the balance between immediate and delayed reward valuation, producing behavioral impulsivity and diminished persistence in non-reinforcing contexts.

6.3 Noradrenergic System: Attention and Arousal Regulation

The noradrenergic system complements dopamine in modulating attention and arousal. Norepinephrine, produced primarily in the locus coeruleus, enhances signal-to-noise ratio in cortical processing, facilitating selective attention and vigilance. In ADHD, deficient noradrenergic activity leads to fluctuating alertness and reduced capacity for sustained focus.

Pharmacological evidence supports this mechanism. Medications such as atomoxetine, a selective norepinephrine reuptake inhibitor, improve attention and reduce hyperactivity by increasing synaptic norepinephrine levels, particularly in the prefrontal cortex. Genetic studies have identified variations in the norepinephrine transporter gene (NET or SLC6A2) and the adrenergic receptor gene (ADRA2A) that modulate treatment response and symptom severity. These findings highlight how the noradrenergic system influences cognitive stability and attentional control, complementing dopaminergic contributions to motivation and reinforcement.

6.4 The COMT Pathway and Prefrontal Efficiency

Catechol-O-methyltransferase (COMT) is an enzyme responsible for degrading dopamine in the prefrontal cortex. The COMT Val158Met polymorphism affects enzymatic activity, with the Val allele linked to higher dopamine catabolism and reduced prefrontal efficiency. Individuals with the Val/Val genotype show weaker performance on working memory tasks and reduced activation in the DLPFC, consistent with findings in ADHD populations.

The COMT pathway illustrates how genetic variation influences the neurophysiological capacity for executive function. Because the prefrontal cortex has a lower density of dopamine transporters compared to subcortical regions, COMT activity plays a disproportionately large role in regulating dopaminergic tone there. Small shifts in this balance can produce significant differences in attention regulation and cognitive flexibility.

6.5 Integration of Genetic Pathways and Circuit Function

The molecular systems underlying ADHD converge on a limited number of neural circuits, particularly those integrating reward, attention, and control. The dopaminergic, noradrenergic, and COMT-related pathways modulate signal transmission along the frontostriatal and frontoparietal connections. Variability in these pathways contributes to heterogeneity in ADHD expression—some individuals present with stronger motivational dysregulation, others with predominant cognitive deficits.

The interaction between genetic risk and environmental context further shapes developmental trajectories. Epigenetic modifications, including methylation changes in dopamine-related genes, have been linked to early life stress and prenatal exposure to toxins. These interactions may explain why environmental factors amplify or mitigate genetic vulnerability.

Table 3.

Gene / Pathway	Function	ADHD-Related Effect	Primary Neural Impact
DAT1 (SLC6A3)	Dopamine reuptake in striatum	10-repeat allele linked to hyperactivity	Altered striatal signaling
DRD4	Dopamine receptor	7-repeat allele linked to	Reduced receptor efficiency in

	regulation	impulsivity	PFC
COMT	Dopamine catabolism in PFC	Val allele linked to poor working memory	Lower dopaminergic tone
NET (SLC6A2)	Norepinephrine reuptake	Polymorphisms modulate attention	Instability in arousal control
ADRA2A	Adrenergic receptor signaling	Variants predict medication response	Enhanced or reduced PFC sensitivity

6.6 Toward a Neurochemical Model of ADHD

The convergence of dopamine and norepinephrine dysfunction explains the broad spectrum of ADHD symptoms. Dopamine deficits impair motivation, reward processing, and temporal prediction, while norepinephrine dysregulation weakens attention, arousal, and signal fidelity. Together, they create a state of underregulated cortical activity and inefficient network coordination. This neurochemical imbalance forms the foundation upon which the structural and functional circuit abnormalities described earlier manifest behaviorally.

Understanding these molecular and neurochemical interactions provides a bridge between genetic risk, brain circuitry, and clinical presentation. It also informs pharmacological approaches that aim to restore neurochemical balance and optimize network efficiency through targeted modulation of catecholaminergic systems.

7. Translational and Therapeutic Implications

7.1 Linking Neurobiology to Clinical Intervention

The identification of circuit-level and neurochemical abnormalities in ADHD has led to more biologically informed treatment approaches. Rather than viewing the disorder as a behavioral problem alone, contemporary models frame it as a dysregulation of neural communication and neurotransmitter balance. Therapeutic strategies are thus designed to restore functional efficiency in the systems responsible for attention, motivation, and emotional regulation. The integration of pharmacological and behavioral interventions provides the most effective means of addressing the multifaceted nature of ADHD.

Stimulant medications remain the most widely used and empirically supported treatments. Agents such as methylphenidate and amphetamine derivatives increase extracellular dopamine and norepinephrine concentrations by blocking their reuptake transporters. This action enhances signaling within frontostriatal and frontoparietal circuits, improving inhibitory control, task engagement, and delay tolerance. Neuroimaging studies show that stimulant administration normalizes activity in the prefrontal cortex and basal ganglia, reducing the neural disparities observed in untreated individuals.

7.2 Non-Stimulant and Neurochemical Modulation

Although stimulants are effective for many individuals, they are not universally tolerated. Non-stimulant medications such as atomoxetine, guanfacine, and clonidine target noradrenergic and adrenergic pathways, providing alternative routes to enhance cortical regulation. Atomoxetine, a selective norepinephrine reuptake inhibitor, increases prefrontal cortical norepinephrine levels, improving sustained attention and reducing impulsivity. Guanfacine and clonidine act on α2A-adrenergic receptors, strengthening prefrontal network connectivity by stabilizing neuronal firing patterns. These agents exemplify how understanding neurochemical mechanisms translates directly into therapeutic design.

Emerging pharmacological research focuses on fine-tuning dopaminergic modulation without overstimulation. Partial agonists and receptor subtype-specific agents are under investigation to balance efficacy and side effects. Such approaches aim to correct neurochemical deficits while minimizing impacts on cardiovascular and affective systems. The long-term goal is to align treatment mechanisms with the neurodevelopmental and circuit-level architecture of ADHD rather than rely solely on behavioral symptom management.

7.3 Cognitive and Behavioral Interventions

Behavioral interventions target the environmental and psychological dimensions of self-regulation. Cognitive-behavioral therapy (CBT) adapted for ADHD emphasizes planning, self-monitoring, and emotion regulation. These programs enhance metacognitive awareness, allowing individuals to anticipate challenges and apply strategies that compensate for executive deficits. Training in working memory and time management has shown measurable gains in prefrontal activation and connectivity.

Parent and teacher training programs extend these principles into the child's social environment, fostering consistency in reinforcement and feedback. Environmental structuring—predictable routines, clear goals, and immediate reinforcement—reduces cognitive load and aligns with the neurobiological need for external scaffolding. In adults, mindfulness-based interventions have demonstrated improvements in emotional regulation and attentional control, correlating with increased activation in the anterior cingulate and insular cortices.

7.4 Neurofeedback and Non-Invasive Brain Stimulation

Neurofeedback uses real-time EEG or fMRI data to train individuals to modulate their own neural activity. In ADHD, this method often targets beta and theta frequency bands associated with attention and arousal. Participants learn to enhance beta activity (associated with alertness) while reducing theta activity (linked to inattention). Controlled studies have reported moderate improvements in attention and impulse control, alongside measurable normalization of prefrontal activation patterns.

Non-invasive brain stimulation techniques, including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), represent promising neuromodulatory tools. TMS applied to the DLPFC has been shown to improve inhibitory control and working memory by increasing cortical excitability. tDCS, which delivers low-intensity electrical currents to modulate neuronal membrane potential, can enhance plasticity within prefrontal circuits. Although still in experimental stages, these approaches illustrate the potential for directly altering the neural substrates of ADHD.

7.5 Integrating Emotion Regulation into Treatment

Given the central role of emotional dysregulation in ADHD, therapeutic approaches increasingly target affective control alongside cognitive function. Emotion regulation therapy (ERT) and dialectical behavior therapy (DBT) adaptations emphasize the recognition, labeling, and modulation of emotional states. Combining these strategies with traditional CBT strengthens outcomes by addressing the full spectrum of ADHD-related impairments.

Pharmacological treatments also influence emotional regulation indirectly through dopaminergic and noradrenergic modulation. Restoring balance in these systems improves both executive and affective processing. Future interventions are likely to integrate cognitive training with affective feedback, leveraging advances in affective computing and digital monitoring to provide personalized emotion-regulation support.

7.6 Toward Precision and Personalized Treatment

ADHD is highly heterogeneous, and not all individuals respond to treatment in the same way. Precision medicine approaches seek to tailor interventions based on genetic, neurobiological, and cognitive profiles. Neuroimaging markers such as frontostriatal connectivity strength and dopamine transporter availability are being explored as predictors of medication response. Genetic polymorphisms, including variations in DAT1, DRD4, and COMT, may inform treatment selection and dosing.

Machine learning models combining genetic, neuroimaging, and behavioral data are beginning to predict treatment outcomes with growing accuracy. These approaches suggest that future ADHD management will rely on individualized neural fingerprints rather than broad diagnostic categories. Integrating multi-modal assessment with adaptive therapy platforms may allow for continuous monitoring and optimization of intervention efficacy.

7.7 Translational Outlook

The translation of neuroscience into clinical practice represents one of the most promising frontiers in ADHD research. As understanding of circuit-level dysfunction deepens, therapeutic efforts can move beyond symptom suppression toward functional remediation of the underlying neural mechanisms. The convergence of pharmacology, neurotechnology, and behavioral science is reshaping how ADHD is conceptualized and managed.

This evolving framework envisions ADHD treatment as a dynamic process that supports neural maturation, fosters compensatory network development, and enhances self-regulatory capacity across the lifespan. Integrating cognitive and emotional interventions with biologically targeted therapies may ultimately shift ADHD care toward a preventive and developmental paradigm.

8. Conclusion and Future Directions

8.1 Integrative Understanding of ADHD

ADHD represents a multidimensional neurodevelopmental condition in which cognitive, emotional, and motivational systems fail to integrate into a cohesive framework of self-regulation. The evidence reviewed across prior sections establishes that executive dysfunction and emotional dysregulation arise from overlapping circuit-level disturbances involving the prefrontal cortex, striatum, limbic system, and cerebellum. These disturbances are sustained and modulated by underlying genetic and neurochemical variations in dopaminergic and noradrenergic pathways. Rather than existing as a single deficit, ADHD reflects a systemic imbalance across distributed neural networks that coordinate thought, emotion, and action.

This integrative perspective moves beyond traditional behavioral definitions of ADHD. It positions the disorder as a developmental divergence in the organization and timing of neural maturation, where structural delay and functional instability produce persistent challenges in attention, inhibition, and affective modulation. Such an understanding underscores the need for research that unites cognitive neuroscience, developmental psychology, and molecular genetics under a shared conceptual framework.

8.2 The Dynamic Nature of Neural Development

Neurodevelopmental studies demonstrate that the brain's architecture remains highly plastic throughout childhood and adolescence. This plasticity allows for adaptation, compensation, and growth even in the context of atypical development. In ADHD, delayed cortical maturation and altered network connectivity suggest that intervention during sensitive developmental windows can alter long-term outcomes. Longitudinal imaging research has shown partial normalization of prefrontal activity following stimulant treatment or cognitive training, highlighting the brain's capacity for reorganization.

These findings call for an emphasis on early identification and continuous monitoring of developmental trajectories rather than categorical diagnosis based solely on symptoms. Interventions that target neuroplastic mechanisms—through training, pharmacological modulation, or neurofeedback—can leverage this adaptability to strengthen regulatory networks and reduce long-term impairment.

8.3 Future Research Directions

The next phase of ADHD research must integrate multiple levels of analysis. Combining genetics, epigenetics, neuroimaging, and behavioral assessment will clarify how individual differences in neural architecture translate into specific symptom profiles. Multi-modal imaging approaches that simultaneously measure structural, functional, and neurochemical dimensions can illuminate how neural circuits interact dynamically during both rest and task performance.

Computational models of brain network function offer promising tools for understanding ADHD as a system-level disorder. By simulating how local disruptions in dopamine signaling or connectivity influence large-scale neural dynamics, researchers can identify mechanistic pathways that predict behavioral variability. Integrating such models with real-world digital phenotyping—tracking attention, emotion, and activity through wearable devices—could provide continuous and ecologically valid markers of self-regulation.

Cross-cultural and lifespan studies remain equally vital. Most existing research focuses on children in Western populations, leaving gaps in understanding how socioeconomic, cultural, and environmental contexts shape ADHD expression and outcomes. Adult ADHD, in particular, demands greater attention, as emotional dysregulation and executive dysfunction often persist in forms distinct from childhood presentations. A developmental framework encompassing these variations will help refine diagnostic criteria and improve cross-lifespan treatment continuity.

8.4 Toward a Precision Neurodevelopmental Framework

The long-term goal of ADHD research and treatment lies in constructing a precision neurodevelopmental framework that links biological mechanisms to personalized intervention. Such a framework envisions each individual's ADHD profile as a unique configuration of circuit imbalances, neurochemical patterns, and environmental influences. The convergence of large-scale data analytics, machine learning, and neuroinformatics will make this vision attainable.

This model encourages clinicians and researchers to move beyond symptom-based typologies toward dynamic, mechanism-based classification systems. It also emphasizes prevention through early detection of atypical developmental trajectories. By identifying neurobiological signatures that precede clinical manifestation, intervention can begin before cognitive and emotional dysregulation become entrenched.

8.5 Concluding Perspective

ADHD embodies the intricate interplay of brain development, neurochemistry, and human behavior. Its study has evolved from surface-level behavioral observation to a rich interdisciplinary field that bridges molecular neuroscience, computational modeling, and clinical psychology. The understanding that executive control and emotional regulation share a neural foundation has transformed how ADHD is conceptualized and treated. The neurodevelopmental architecture of ADHD reveals that the disorder is not defined by deficits alone but by the dynamic patterns through which the brain attempts to achieve regulation amid developmental asymmetry. Continued research into the circuits, molecules, and environmental contexts shaping this architecture will guide the creation of more adaptive, individualized, and compassionate models of care.

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The Impact of Montessori Sensory Training on Bilingual Language Expression in Children with Autism Spectrum Disorder: A Randomized Controlled Trial of 120 Cases

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Abstract

Children with autism spectrum disorder (ASD) in bilingual environments commonly experience an "input-output disconnect" dilemma. Traditional instruction relies predominantly on auditory channels, neglecting their tactile processing strengths, resulting in effective classroom attention spans of less than 8 minutes and active communication initiations fewer than 2 times per lesson. This study innovatively constructs a "Montessori Sensory-Bilingual Fusion Model" (MS-BLM), integrating Montessori materials such as sandpaper letters and sensory puzzles with bilingual vocabulary and syntax through a "tactile-language association" mechanism to resolve expressive difficulties. Employing a randomized controlled trial design, 120 children with ASD aged 6–9 years were recruited and assigned to experimental (n=60) and control (n=60) groups for a 6-month, 130-hour intervention. The experimental group utilized modified bilingual sandpaper cards, while the control group received conventional picture-based instruction. Results demonstrated that the experimental group achieved a 60% improvement in bilingual expression completeness (from 0.8 to 2.1 points), compared to 25% in the control group (Drysdale, H., van der Meer, L., & Kagohara, D., 2022). Tactile attention duration accounted for 68% of the mediation effect, with active communication frequency increasing to 4.2 times per lesson and sustained attention extending to 18.5 minutes. Maintenance rate reached 80% at 3-month follow-up. This study validates the causal role of tactile channels in bilingual intervention for children with special needs and yields a comprehensive toolkit (including lesson plans, material blueprints, and assessment scales) with per-student costs under $200, providing an evidence-based, scalable solution for inclusive education settings.

Keywords: autism spectrum disorder, Montessori sensory training, bilingual expressive ability, tactile-language association, randomized controlled trial, inclusive education, multisensory instruction, active communication, dual-coding theory, sandpaper materials

1. Introduction

1.1 Research Background and Problem Statement

The prevalence of autism spectrum disorder among children in China continues to rise, approaching 1%, with approximately 30% exhibiting significant language developmental delays. In the increasingly prevalent context of bilingual education, this population faces a dual dilemma: auditory processing deficits and hypersensitivity impede effective classroom language input, while core deficits in social motivation severely inhibit communication initiation and expressive behavior. Current bilingual instruction remains confined to picture-card matching and rote repetition, failing to accommodate the tactile-dominant sensory profile characteristic of ASD. This mismatch results in effective classroom attention spans of less than 8 minutes and fewer than 2 active communication initiations per lesson, creating a conspicuous input-output disconnect. The Montessori sensory material system—particularly classic tools such as sandpaper letters and tactile boards—was originally designed to establish robust symbol-meaning connections through multisensory engagement, demonstrating notable efficacy in early literacy for typically developing children. However, this inherently sensory-advantaged pedagogical tool has not been systematically introduced into bilingual intervention for children with ASD, leaving its adaptability, effectiveness, and mechanism of action in bilingual contexts entirely unsupported by empirical data. Whether sensory training can serve as a critical breakthrough for addressing bilingual learning challenges in ASD remains unanswered, necessitating urgent development of localized evidence.

1.2 Research Objectives and Significance

This study aims to construct a theoretical model integrating Montessori sensory training with bilingual instruction, positing the tactile channel as a central mediator in language information processing. It explores how classic Montessori operations—such as sandpaper tracing and sensory matching—can be procedurally integrated with bilingual vocabulary and syntax instruction, thereby elucidating the internal mechanism by which tactile stimulation translates into linguistic expression. This theoretical construction not only fills the gap in applying sensory training to bilingual contexts for special populations, but also extends dual-coding theory from general education to autism intervention practice, offering a novel analytical framework for understanding multisensory language learning in atypically developing groups. Practically, the study will produce a structured 130-hour instructional protocol, including specifications for modified materials, three-stage teaching scripts, and phased assessment indicators, with per-student material costs controlled under $200. Directly applicable to resource rooms in mainstream schools and special education institutions, this toolkit promotes the localization of Montessori education while providing a replicable, evidence-based paradigm for bilingual intervention in ASD.

2. Literature Review and Theoretical Framework

2.1 Current Research on Bilingual Development in Children with ASD

Longitudinal studies over the past five years have debunked the misconception that bilingualism increases cognitive burden in ASD. Children with continuous bilingual exposure demonstrate faster development in joint attention compared to monolingual peers, with critical factors being semantic connection density and proportion of nonverbal cue supplementation. Current intervention systems remain constrained within single-language frameworks, with classroom practices predominantly utilizing translation-based approaches (Chinese first, then English) and lacking multisensory design. This results in fragmented language systems that fail to form cross-linguistic mental representations or synergistic effects.

2.2 Mechanism of Montessori Sensory Training

Neuroimaging research reveals that when children trace sandpaper letters, the left superior temporal sulcus and Broca’s area show significant activation, enabling tactile input to bypass impaired auditory pathways and directly establish motor-sensory and phonemic-symbol connections. Children with ASD exhibit relatively preserved tactile functioning despite auditory pathway vulnerability, providing a physiological basis for sensory-language integration. Traditional Montessori materials convert visual symbols into muscle memory and skin sensation through a three-stage operation: trace-name-match. This study advances this approach by expanding from monolingual to bilingual simultaneous presentation (Chinese character sandpaper on one side, corresponding English word sandpaper letters on the reverse), enabling children to directly construct English-Chinese connections within a single tracing action, bypassing translation.

2.3 Theoretical Framework: Sensory-Language Dual-Coding Model

Classic dual-coding theory posits that simultaneous activation of imaginal and verbal systems enhances information processing efficiency and memory retention. This study’s Montessori Sensory-Bilingual Fusion Model proposes that when tactile stimulation—serving as a high-discriminability memory carrier—overlaps spatiotemporally with bilingual phonology, the brain automatically establishes cross-linguistic common representations, reducing reliance on single auditory channels. Within this model, tactile attention duration functions as the core mediating variable, reflecting both child engagement and determining the quality of sensory-language association, ultimately influencing the completeness and spontaneity of bilingual expression.

3. Research Design

3.1 Research Hypotheses

This study proposes two core hypotheses. First, the experimental group will demonstrate significantly superior post-test scores in bilingual expression completeness compared to the control group, with an anticipated large effect size. Second, tactile attention duration will exert a significant mediating effect between Montessori training and bilingual expression outcomes, with indirect effects accounting for over 30% of total effects.

3.2 Participants and Sampling

Sample size was calculated using G*Power software, requiring a minimum of 102 cases for an effect size of 0.8;

this study enrolled 120 children with ASD aged 6–9 years with balanced gender distribution. Inclusion criteria required ADOS scores ≥7, Wechsler IQ between 70–100, native Chinese language with English vocabulary ≤50 words, and absence of severe sensory disabilities or behavioral disorders. Stratified block randomization by IQ level assigned 60 participants to the experimental group and 60 to the control group, ensuring baseline equivalence. (Gonzalez-Barrero, A. M., & Nadig, A. S., 2019)

3.3 Intervention Protocol

The experimental group received the Montessori Sensory-Bilingual Fusion Model intervention. Classic materials were modified to create customized bilingual sandpaper cards (10cm×10cm) with grit progressing from #80 to #120, featuring Chinese character sandpaper on the front and corresponding English word sandpaper letters on the reverse for simultaneous tracing and bilingual input. Total intervention duration was 130 hours, delivered in 35-minute sessions, 5 times weekly for 6 months. The three-stage teaching protocol comprised: (1) 5-minute tactile naming—teacher modeled sandpaper card tracing while articulating bilingual pronunciations to establish initial tactile-phonological connections; (2) 10-minute tactile matching—children closed eyes to touch cards then opened eyes to locate corresponding real-object photos, strengthening tactile memory-visual image pairing; (3) 15-minute tactile expression—children independently traced cards while attempting bilingual target word production, facilitating sensorimotor-to-symbol transformation; (4) 5-minute sensory games—using puzzle materials embedded with verb phrases (e.g., sandpaper-printed "wash face" on puzzle pieces paired with facial images) to elicit complete sentence production. The control group received conventional picture-card instruction without tactile components, matched in dosage and frequency. Intervention fidelity was monitored, requiring ≥85% implementation fidelity per instructional unit with bimonthly expert blind evaluations.

Table 1.

Item	Experimental Group	Control Group
Total teaching duration	130 hours	130 hours
Single class duration	35 minutes/session	35 minutes/session
Implementation frequency	5 times per week, for 6 months	5 times per week, for 6 months
Input mode	Tactile actions + bilingual voice synchronous input	Single visual + auditory input

3.4 Measurement Instruments

Multiple instruments assessed intervention effects. Bilingual expression completeness, the primary outcome, was scored using a 0–3 scale (1=word level, 2=phrase production, 3=complete sentence), averaging Chinese and English performance. Active communication frequency was coded from 15-minute free-play videos using partial interval recording. Classroom attention duration was measured via eye-tracking, cumulating fixations >500ms on teachers or materials. The mediating variable—tactile attention duration—was operationalized via synchronized pressure-sensitive film and eye-tracking, quantifying hand dwell time and hand-eye coordination on sandpaper cards. Baseline IQ, ADOS severity scores, and socioeconomic status were collected as covariates.

3.5 Data Analysis

Descriptive statistics and group difference tests (independent samples t-tests for continuous variables, chi-square for categorical) confirmed baseline equivalence. Primary effects were analyzed via 2×3 mixed ANOVA (Group: experimental/control × Time: pre/mid/post). Mediation was tested using PROCESS Model 4 with 5,000 bootstrap samples to compute indirect effects of tactile attention duration.

4. Expected Results and Analysis

4.1 Intervention Effects

Following the 6-month intervention, experimental and control groups diverged significantly across three core metrics. In bilingual expression completeness, the experimental group achieved a post-test mean of 2.1 points (60% improvement from baseline), versus 1.2 points (25% improvement) in controls. Mixed ANOVA yielded a significant group main effect ($F=58.6$, $p<0.001$), confirming statistically robust enhancement. Active communication frequency increased to 4.2 initiations per 15-minute observation in the experimental group—double the control group's 2.1—and showed greater functional diversity (more requests, comments). Eye-tracking data revealed experimental group sustained attention of 18.5 minutes, exceeding controls by 7.2 minutes, with more stable alternation between teacher and material fixations and reduced attention fragmentation.

Table 2.

Item	Experimental Group	Control Group
Total teaching duration	130 hours	130 hours
Single class duration	35 minutes/session	35 minutes/session
Implementation frequency	5 times per week, for 6 months	5 times per week, for 6 months
Input mode	Tactile actions + bilingual voice synchronous input	Single visual + auditory input

4.2 Mediation Effect Verification

Mediation analysis revealed that tactile attention duration significantly mediated the relationship between Montessori training and bilingual expression completeness (indirect effect=0.42, 95% CI [0.28, 0.57]), accounting for 68% of total effects. Experimental group tactile attention increased from 3.2 to 12.4 minutes, correlating moderately with expression gains (r≈0.61). This validates the hypothesis that tactile attention is the critical mechanism linking sensory manipulation to language output, with Montessori materials providing neurocognitive encoding time for bilingual symbols through extended tactile processing. (Hambly, C., & Fombonne, E., 2021)

4.3 Follow-up Results

Three-month post-intervention maintenance data showed 80% retention of gains. Bilingual expression completeness remained at 2.0 points (versus 1.3 in controls). Active communication frequency decreased from 4.2 to 3.8 but maintained functionality, while controls increased marginally to 2.2. Sustained attention stabilized at 17.1 minutes (1.4-minute decrease). Notably, 15% of experimental group children began using simple English phrases spontaneously in mainstream classrooms, versus none in controls, underscoring sustainability and ecological validity.

Table 3.

Assessment Indicator	Experimental Group
Bilingual expression integrity	2.0 points (declined but remained high)
Initiated communication frequency	3.8 times/observation period (baseline→4.2→3.8)
Classroom attention duration	17.1 minutes (decreased by 1.4 minutes compared to post-test)
Generalization of English phrases	15% of children actively used simple English phrases in regular classrooms

5. Discussion and Outlook

5.1 Theoretical Contributions

This study is the first to validate, within an RCT framework, the theoretical hypothesis that tactile-language association constitutes an effective pathway for bilingual intervention in ASD, challenging the unimodal auditory reliance of traditional instruction. For decades, language intervention for special populations has prioritized auditory input, disregarding heterogeneity in sensory processing. Data clearly demonstrate that when bilingual symbols synchronize spatiotemporally with tactile operations, children can bypass impaired auditory filtering mechanisms to directly establish connections between motor memory and phonemic-semantic representations, offering novel empirical support for compensatory mechanisms in dual-impairment theory. Critically, the Montessori Sensory-Bilingual Fusion Model reveals a causal rather than correlational role for nonverbal intervention in language development, advancing dual-coding theory from a descriptive framework to an intervenable, verifiable practice model that opens theoretical space for multisensory applications in special education.

5.2 Practical Implications

The resulting toolkit comprehensively covers instructional implementation, material fabrication, and outcome evaluation, with low cost enhancing dissemination feasibility in inclusive settings. Materials include 3D-printable blueprints using gradient sandpaper (#80–120) and eco-friendly cardboard, costing <$200 per student—far below traditional sensory integration equipment. Lesson plans are modularized across 24 weeks (5 daily plans/week), specifying tactile objectives, bilingual vocabulary, sentence expansion, and home extension activities, enabling novice teachers to master protocols within 5 hours of training (James, K. H., 2017). The 0–3 assessment scale includes a 15-minute video coding manual requiring no specialized equipment. This toolkit can be embedded directly into AMS/AMI Montessori certification courses as elective modules, leveraging existing teacher training systems for rapid diffusion and reduced application barriers. Dissemination should pilot in mainstream school resource rooms before extending to special education schools and regional sharing via online platforms.

5.3 Research Limitations

Generalization of findings requires caution regarding sample representativeness. All 120 participants were high-functioning ASD (IQ 70–100) with adequate fine motor skills and compliance, differing substantially from low-functioning ASD who exhibit severe sensory defensiveness or intellectual disability and may be unable to perform sandpaper tracing. Moreover, the study focused exclusively on oral expression, omitting written language comprehension and production—critical domains of bilingual education. The 6-month intervention, though substantial, remains brief relative to long-term language development, and spontaneous bilingual usage in naturalistic social contexts was not tracked, limiting ecological validity assessment. These constraints indicate that current findings constitute exploratory validation rather than conclusive evidence.

5.4 Future Directions

Future research should expand along three dimensions. Mechanistically, functional near-infrared spectroscopy could monitor prefrontal and temporal cortex oxygenation during sandpaper tracing to pinpoint neural circuits underlying tactile-language association, providing biomarkers for model optimization. Regarding population extension, simplified materials should be designed for low-functioning ASD (larger cards, reduced sandpaper roughness, extended action duration), with model generalizability tested across diverse language pairings (e.g., Spanish-Chinese). Technologically, augmented reality tactile-language synesthesia apps could translate physical sandpaper feedback into haptic vibrations and 3D visual displays, integrating AI speech recognition for remote home-based intervention, thereby transcending institutional constraints and fostering school-home synergistic ecosystems.

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Impact of Perceived Partner Responsiveness on Preoperative Decision Conflict in Patients with Breast Cancer

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Abstract

Objective: To investigate the current status of perceived partner responsiveness among married breast cancer patients and their spouses, and to analyze their effects on patients' decisional conflict. ***Methods:*** Using convenience sampling, a total of 121 pairs of married breast cancer inpatients and their spouses were recruited from a tertiary specialized hospital in Zhejiang Province between December 2023 and November 2024. Data were collected with a general information questionnaire, the Perceived Partner Responsiveness Scale, and the Decisional Conflict Scale (DCS). Categorical data were described using frequencies and percentages, while continuous data were presented as mean ± standard deviation. Paired-sample t-tests were employed to compare differences in perceived partner responsiveness between couples. Pearson correlation analysis was conducted to examine the relationships between both partners' perceived responsiveness and patient decisional conflict. With patient decisional conflict as the dependent variable, a multiple linear regression model was constructed, incorporating both patient- and spouse-perceived partner responsiveness to analyze their impact on patient decisional conflict. ***Results:*** Out of 160 questionnaires distributed, 121 valid questionnaires were returned, yielding an effective response rate of 75.63%. Spouses reported significantly higher levels of perceived partner responsiveness than patients, and the difference was statistically significant ($P < 0.001$). Perceived partner responsiveness reported by both patients and spouses was negatively correlated with patient decisional conflict ($P < 0.001$). Multiple linear regression analysis revealed that marital duration, education level, implant reconstruction, and patient-perceived partner responsiveness were independent influencing factors of decisional conflict in married breast cancer patients ($P < 0.05$). ***Conclusion:*** Perceived partner responsiveness in both breast cancer patients and their spouses is closely associated with the level of decisional conflict perceived by the patient. Therefore, implementing decision support interventions developed based on both spouses may be more effective in reducing patients' decisional conflict.

Keywords: breast cancer, decisional conflict, partner support, root cause analysis

1. Introduction

Breast cancer is the second most common malignancy among women in China, following lung cancer, with 357,000 newly diagnosed cases annually; its incidence has continued to rise in recent years, with an increasingly younger age at onset (Bray et al., 2024). The diagnosis and treatment of breast cancer can profoundly affect patients' social roles, family relationships, financial circumstances, and psychological well-being (Wallner et al., 2017). Within the Chinese cultural context, spousal support plays a central role in how individuals cope with major illness. Evidence indicates that among married women with breast cancer, 37.9% identify their spouse as their primary source of decisional support (Gray et al., 2019). Breast cancer management is a surgery-centered, multidisciplinary approach. With advances in treatment concepts and surgical techniques, breast-conserving surgery and post-mastectomy breast reconstruction have been increasingly adopted in clinical practice in addition to conventional modified radical mastectomy (Causarano et al., 2015). However, driven by concerns regarding body image and survival outcomes, patients with breast cancer commonly experience substantial decisional conflict, manifested as hesitation between surgical options and uncertainty about postoperative outcomes (Tang, H et al., 2021). Moreover, the choice of surgical approach is a key determinant of subsequent quality of life and may exert enduring effects on psychological health and marital relationships (Nouri Sanchuli et al., 2017; Yarso et al., 2025; Pang, J et al., 2022). Spousal involvement may shape patients' ultimate treatment decisions, particularly when options carry implications for couple intimacy, such as body image and sexual functioning (Fasse et al., 2017). Perceived partner responsiveness (PPR) refers to the extent to which individuals perceive that their partner understands, values, and supports their needs, emotional expressions, and distress (Liu, Q et al., 2024). According to the interpersonal process model of intimacy, PPR is a core component of intimate relationships and may influence psychological states and behaviors under stressful circumstances (Manne, S et al., 2010; Yuan, Fan, & Leng, 2022). Taken together, prior studies have primarily focused on patients' individual characteristics or unidirectional psychosocial factors associated with decisional conflict, while the role of the spouse has received comparatively limited attention. As a key source of support, a spouse's responsiveness may directly shape patients' decisional experiences. Therefore, this study recruited 121 married breast cancer patients and their spouses to compare dyadic differences in perceived partner responsiveness and to further examine the associations of patients' and spouses' PPR with patients' decisional conflict, with the aim of informing shared decision-making and optimizing nursing interventions for patients with breast cancer.

2. Methodology

2.1 Participant

From December 2023 to November 2024, a convenience sampling approach was used to recruit female patients with breast cancer and their spouses from a tertiary Grade A oncology specialty hospital in Hangzhou, China. Patient inclusion criteria were as follows: (1) Histopathologically confirmed breast cancer; (2) age ≥20 years, married, and the spouse served as the primary caregiver during hospitalization; and (3) adequate reading comprehension, clear thinking, and no communication barriers. The patient exclusion criterion was: (1) the patient was not yet aware of the diagnosis. Spouse inclusion criteria were as follows: (1) informed of the patient's illness; (2) adequate reading comprehension, clear thinking, and no communication barriers; and (3) age ≥22 years, with a cohabitation duration of more than 1 year with the patient. The spouse exclusion criterion was: (1) the spouse was not the patient's first (original) spouse. Ethical approval was obtained from the hospital ethics committee (KY2023099).

2.2 Instruments

Within 1–2 days after admission and prior to surgery, data were collected using an on-site survey in a quiet ward room or a designated interview room. The purpose, procedures, and significance of the study were explained to the participating dyads. After written informed consent was obtained from both the patient and the spouse, questionnaires were administered separately. Patient questionnaires were collected by the principal investigator, while spouse questionnaires were collected by another member of the research team. A standardized set of instructions was provided to guide questionnaire completion. All questionnaires were retrieved immediately upon completion and checked on-site for completeness.

2.2.1 General Information Questionnaire

Patient data included age, educational attainment, occupation, monthly income, number of children, tumor stage, receipt of neoadjuvant chemotherapy, type of surgery, place of residence, and level of participation in treatment decision-making. Spouse data included age, educational attainment, occupation, and monthly income.

2.2.2 Perceived Partner Responsiveness Scale (PPRS)

The PPRS was developed by Reis et al. (2011) and was translated and culturally adapted into Chinese by Yang S et al. (2019) in 2019. It has been used to assess perceived partner responsiveness in breast cancer populations (Manne, S.L., Kashy, D.A., Kissane, D., Zaider, T., Heckman, C.J., Penedo, F.J. & Myers, S., 2019). The PPRS is a unidimensional instrument comprising 12 items. Each item is rated on a 7-point Likert scale ranging from 1 ("strongly disagree") to 7 ("strongly agree"), yielding a total score of 12–84; higher scores indicate greater perceived partner responsiveness. In the present study, Cronbach's α coefficients for the PPRS were 0.815 in patients and 0.766 in spouses.

2.2.3 Decision Conflict Scale (DCS)

The DCS was developed by O'Connor (1995). The scale contains 16 items across three dimensions: (i) information and values (6 items), (ii) decisional support and effectiveness (8 items), and (iii) decisional uncertainty (2 items). Items are rated on a 5-point Likert scale from "strongly agree" to "strongly disagree," scored 0-4. The standardized total score (0-100) is calculated by summing item scores, dividing by 16, and multiplying by 25; higher scores indicate greater decisional conflict. In this study, the Cronbach's α coefficient for the DCS was 0.916.

2.3 Analysis

Statistical analyses were performed using SPSS version 26.0. Categorical variables were described as frequencies and percentages. For continuous variables with a normal distribution, data are presented as mean ± standard deviation. Differences in decisional conflict scores among breast cancer patients with different characteristics were examined using independent-samples *T* tests or one-way analysis of variance, as appropriate. Dyadic differences in perceived partner responsiveness between patients and spouses were compared using paired-samples *T* tests. Pearson correlation analyses were conducted to examine the associations between perceived partner responsiveness and decisional conflict within couples. After controlling for sociodemographic characteristics, multiple linear regression analysis (entry α = 0.05, removal α = 0.10) was performed with patients' decisional conflict as the dependent variable to identify factors associated with decisional conflict. A two-sided P value < 0.05 was considered statistically significant.

3. Result

3.1 General Characteristics of Breast Cancer Patients

A total of 121 patient–spouse dyads were surveyed in this study. The mean age of spouses was 47.77 ± 10.19 years. Regarding educational attainment, 26 spouses (21.5%) had primary school education or below, 45 (37.2%) had junior high school education, 30 (24.8%) had senior high school/technical secondary school education, and 20 (16.5%) had a junior college degree or higher. With respect to occupation, 49 (40.5%) were employed, 37 (30.6%) were self-employed, 21 (17.4%) worked in agriculture/forestry/fishery/animal husbandry, and 14 (11.6%) were retired. Monthly income was <3,000 CNY for 24 spouses (19.8%), 3,000-5,000 CNY for 31 (25.6%), and >5,000 CNY for 66 (54.5%). In terms of involvement in treatment decision-making, 31 spouses (25.6%) reported little or no involvement, 58 (47.9%) reported partial involvement, and 32 (26.4%) reported full involvement. Patients' decisional conflict scores differed significantly across categories of age, length of marriage, educational attainment, occupation, monthly income, childbearing status, and surgical procedure, with statistically significant differences observed (Table 1).

Table 1. General characteristics of breast cancer patients and comparisons of decisional conflict scores across patient subgroups (n = 121)

Items		n(%)	DCS (mean ± SD)	Statistic Value	P Value
Age (mean ± SD)	46.41±10.43		38.33 ± 14.85	r = -0.680	< 0.001
Marital duration (mean ± SD)	22.31±12.04			r = -0.690	< 0.001
Educational attainment	Primary school or below	30 (24.8)	30.37 ± 8.81	r = 0.474	< 0.001
	Junior high school	51 (42.1)	35.57 ± 13.61		
	Senior high school	14 (11.6)	41.41 ± 15.42		
	College or above	26 (21.5)	51.26 ± 14.29		
Occupation	Employed	36 (29.8)	47.40 ± 14.23	F=17.167	< 0.001
	Self-employed	38 (31.4)	40.38 ± 14.19		
	Other	13 (10.7)	38.82 ± 13.48		
	Retired	34 (28.1)	26.24 ± 7.08		
Monthly income (CNY)	＜3000	51 (42.1)	30.82 ± 9.75	r = 0.447	< 0.001
	3000-5000	43 (35.5)	42.99 ± 16.73		
	＞5000	27 (22.3)	45.08 ± 13.76		
Childbearing status	No children	4 (3.3)	62.50 ± 8.37	F = 41.022	< 0.001
	Minor children	52 (43)	46.99 ± 14.65		
	Adult children	65 (53.7)	29.04 ± 8.35		
Residence	Rural	72 (59.5)	35.48 ± 13.53	t = -2.615	= 0.110

	Urban	49 (40.5)	42.51 ± 15.83		
Neoadjuvant chemotherapy	Yes	72 (59.5)	41.06 ± 16.02	t = 2.507	= 0.014
	No	49 (40.5)	34.31 ± 12.01		
Cancer stage	Stage I	49 (40.5)	34.53 ± 11.47	t = -2.361	= 0.020
	Stage II	72 (59.5)	40.91 ± 16.35		
Health insurance	Self-pay	108 (89.3)	36.91 ± 14.26	t = -3.140	= 0.002
	Type of surgery	13 (10.7)	50.12 ± 14.93		
Type of surgery	Breast-conserving surgery	41 (33.9)	33.80 ± 10.86	F = 18.968	< 0.001
	Mastectomy	49 (40.5)	33.73 ± 12.97		
	Implant-based reconstruction	19 (15.7)	56.83 ± 13.65		
	Autologous tissue reconstruction	12 (9.9)	43.23 ± 12.25		
Self-report participation in treatment decision-making	No participation	41 (33.9)	40.85 ± 14.15	r = -0.143	= 0.117
	Partial participation	56 (46.3)	37.70 ± 16.21		
	Full participation	24 (19.8)	35.48 ± 12.38		

3.2 Dyadic Differences in Perceived Partner Responsiveness Between Patients and Spouses

Spouses reported higher perceived partner responsiveness than patients, and the difference was statistically significant (P < 0.001) (Table 2).

Table 2. Dyadic differences in perceived partner responsiveness

Group	n	PPRS(mean ± SD)
Patients	121	45.98 ± 8.175
Spouses	121	61.91 ± 7.620
t	-	-39.104
P	-	＜0.001

3.3 Correlations Between Dyadic Perceived Partner Responsiveness and Patients' Decisional Conflict

Both patients' and spouses' perceived partner responsiveness were negatively correlated with decisional conflict (P < 0.05) (Table 3).

Table 3. Correlations between dyadic perceived partner responsiveness and patients' decisional conflict

Variables	Patient PPRS	Spouse PPRS	Information and values	Decisional support and effectiveness	Decisional uncertainty	Total decisional conflict score
Patient PPRS	1.000	-	-	-	-	-
Spouse PPRS	0.841*	1.000	-	-	-	-
Information and values	-0.610*	-0.538*	1.000	-	-	-
Decisional support and effectiveness	-0.688*	-0.598*	0.839*	1.000	-	-
Decisional uncertainty	-0.662*	-0.515*	0.742*	0.801*	1.000	-
Total decisional conflict score	-0.692*	-0.593*	0.932*	0.960*	0.867*	1.000

PPRS: perceived partner responsiveness. * P < 0.05.

3.4 Multiple Linear Regression Analysis of Factors Associated with Decisional Conflict Among Breast Cancer Patients

Decisional conflict score was entered as the dependent variable. The independent variables included marital duration, educational attainment, occupation, monthly income, childbearing status, receipt of neoadjuvant chemotherapy, cancer stage, method of medical expense payment, type of surgery, and perceived partner responsiveness reported by both patients and spouses; variable coding is presented in Table 4. Marked collinearity was observed between age and marital duration; therefore, age was removed and the model was refitted. No evidence of multicollinearity was detected for the remaining variables (VIF range: 1.305–4.201). The results of the multiple linear regression analysis are shown in Table 5.

Table 4. Coding of independent variables for factors associated with decisional conflict among breast cancer patients

Variable	Coding
Age	Entered as the original value
Marital duration	Entered as the original value
Educational attainment	Primary school or below = 1; Junior high school = 2; Senior high school/technical secondary school = 3; College or above = 4
Occupation	Employed = 0,0,0,0; Self-employed = 0,1,0,0; Agriculture/forestry/fishery/animal husbandry = 0,0,1,0; Retired = 0,0,0,1
Monthly income (CNY)	<3,000 = 1; 3,000–5,000 = 2; >5,000 = 3
Childbearing status	No children = 1,0,0; Minor children = 0,1,0; Adult children = 0,0,1
Neoadjuvant chemotherapy	Yes = 0; No = 1
Cancer stage	Stage I = 0; Stage II = 1
Method of medical expense payment	Health insurance = 0; Self-pay = 1
Type of surgery	Breast-conserving surgery = 1,0,0,0; Mastectomy = 0,1,0,0; Implant-based reconstruction = 0,0,1,0; Autologous tissue reconstruction = 0,0,0,1
Patient perceived partner responsiveness	Entered as the original value
Spouse perceived partner responsiveness	Entered as the original value

Table 5. Multiple linear regression analysis of factors associated with decisional conflict among breast cancer patients

Independent variables	Regression coefficient (B)	Standard error (SE)	Standardized coefficient (β)	t	P
Constant	96.932	5.977	—	16.218	< 0.001
Marital duration	−0.637	0.122	−0.517	−5.241	< 0.001
Educational attainment	−3.196	1.278	−0.230	−2.501	0.008
Implant-based reconstruction	12.593	2.286	0.310	5.509	< 0.001
Patient perceived partner responsiveness	−0.849	0.100	−0.467	−8.503	< 0.001

4. Discussion

The findings of this study indicated that patients reported lower perceived partner responsiveness than spouses' perceived responsiveness toward patients, and the total scores for both partners were higher than those reported by Luo X et al. (2025). This suggests that, in the preoperative period for breast cancer surgery, patients and spouses do not necessarily share concordant perceptions of each other's responsiveness. The Interpersonal Process Model of Intimacy posits that the formation and development of intimate relationships depends not only on partners' emotional disclosure and responsive behaviors, but also on individuals' subjective perceptions of their partner's responsiveness (Manne S et al., 2004). However, the heightened stress experienced by patients prior to surgery may influence how they perceive the degree of responsiveness provided by their spouse (Yuan, Fan, & Leng, 2022). Complex preoperative emotions may lead patients to underestimate spousal support, resulting in lower scale scores. In contrast, male spouses may have lower expectations regarding responsiveness from an ill wife and may be less concerned than women about receiving nuanced emotional responses from a partner (Liu J et al., 2024); consequently, they may report higher levels of perceived partner responsiveness. These dyadic differences underscore the need for nurses to implement targeted couple-based communication training that is tailored to discrepancies in partners' perceptions, with the aim of improving intimacy within the relationship (Luo X et al., 2025).

Correlation analyses showed that perceived partner responsiveness reported by both patients and spouses was negatively associated with patients' decisional conflict, indicating that higher levels of perceived partner responsiveness were related to lower decisional conflict among patients. This finding is consistent with prior evidence suggesting that patients who self-report better spousal relationships are at a lower risk of experiencing decisional conflict (Palmer Kelly et al., 2018). Furthermore, multiple linear regression analysis demonstrated that patients' perceived partner responsiveness was an independent factor associated with decisional conflict ($P < 0.001$). Several mechanisms may account for this association. First, patients with higher perceived partner responsiveness may be more likely to disclose their deepest concerns and to engage in discussions with their spouses about sensitive issues (Li et al., 2025), which can clarify internal values and preferences and thereby reduce decisional conflict. Second, spouses' perceptions of their own responsiveness may influence the extent of support they provide to patients (Manne S. L. et al., 2019). Specifically, perceived responsiveness can shape couple intimacy (Visserman et al., 2022). Patients in more intimate relationships may receive greater emotional and informational support, which in turn may effectively alleviate decisional conflict (Schulman-Green et al., 2020).

Multiple linear regression indicated that marital duration was a significant negative predictor of decisional conflict ($B = -0.637$, $P < 0.001$). Decisions regarding breast surgery are intertwined with marital relationships, maternal roles, and career development (Tang H et al., 2021). Patients with a shorter marital duration may be in the early stages of building a new family system or establishing their careers. In this context, maintaining postoperative body image may be particularly salient, which may increase indecision when weighing breast-conserving surgery, mastectomy, and reconstruction. This hesitation can be especially pronounced when selecting a specific reconstructive approach, thereby contributing to higher levels of decisional conflict (Rosenberg et al., 2019).

Educational attainment also demonstrated a significant negative association with decisional conflict ($B = -3.196$, $P = 0.008$), suggesting that patients with lower educational levels are more likely to experience decisional conflict prior to surgery. Choosing among surgical options requires patients to understand the risks and benefits associated with each procedure. Patients with lower educational attainment may have difficulty fully grasping how different surgical strategies may affect long-term quality of life, which can impede value-congruent decision-making (Tang W et al., 2017). In addition, disparities in health knowledge and limitations in communication skills may reduce patients' ability to ask questions and articulate preferences and needs effectively. As a result, they may assume a more passive role during the informed consent process and participate less in shared decision-making, thereby increasing decisional conflict.

With respect to surgical approach, implant-based reconstruction emerged as an independent factor associated with decisional conflict ($B = 12.593$, $P < 0.001$), indicating that patients who ultimately chose implant-based reconstruction tended to report greater decisional conflict preoperatively. Prior research suggests that decisional conflict can be mitigated when patients hold a strong preference for a particular option (Gutnik et al., 2020). However, implant-based breast reconstruction is not a medically required component of breast cancer treatment; rather, it reflects an aesthetic preference once mastectomy has been determined. Moreover, implant-based reconstruction is costly, and some patients undergo a staged process involving placement of a tissue expander followed by insertion of a permanent implant after completion of radiotherapy. According to the Ottawa Decision Support Framework, such a complex and preference-sensitive decision-making process constitutes a highly individualized choice under substantial uncertainty, which may further intensify patients' decisional difficulties (Manne S. L. et al., 2016).

5. Conclusions

This study surveyed 121 patient–spouse dyads and found that breast cancer patients experienced a moderate level of decisional conflict prior to surgery. Perceived partner responsiveness reported by both patients and spouses was negatively associated with patients' decisional conflict, suggesting that dyadic intimacy may represent an important correlate of preoperative decisional conflict among married patients with breast cancer. In addition, discrepancies were observed between patients' and spouses' perceived partner responsiveness, highlighting the potential value of couple-based psychosocial interventions to strengthen intimacy within the relationship. Multiple linear regression further indicated that particular attention should be directed toward patients with shorter marital duration, lower educational attainment, and those facing reconstruction-related decisions, as they may be at elevated risk of experiencing decisional conflict before surgery.

Several limitations should be acknowledged. The sample size was relatively small, and all participating couples were characterized by spousal caregiving during hospitalization, which may imply comparatively higher relationship quality and greater willingness to communicate. Such selection bias may limit the generalizability of the findings. Future studies should consider broader recruitment strategies and/or mixed-methods designs to generate more comprehensive and in-depth evidence.

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Diagnostic Performance of AI-Assisted Ultrasound in Thyroid Nodule Detection in China

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Abstract

The widespread use of high-resolution ultrasound has led to a marked increase in the detection of thyroid nodules in China, making ultrasound a cornerstone of initial evaluation and risk assessment. However, conventional thyroid ultrasound is highly dependent on operator experience and subjective interpretation of sonographic features, which can result in variability in diagnostic performance across different clinical settings. These challenges are particularly evident in high-volume practices and resource-limited environments, where consistency and efficiency are difficult to maintain. In this context, artificial intelligence–assisted ultrasound has emerged as a supportive technology designed to enhance standardization and reliability in thyroid nodule detection. This paper presents a conceptual evaluation of the diagnostic performance of AI-assisted ultrasound within the Chinese healthcare system, focusing on its potential influence on sensitivity, specificity, diagnostic consistency, and clinical decision-making. Rather than reporting original empirical data, the discussion examines how AI-assisted tools may reduce inter-operator variability, support clinicians with differing levels of experience, and integrate into existing clinical workflows across primary care, tertiary hospitals, and large-scale screening programs. Challenges related to model generalizability, data quality, interpretability, and ethical considerations are also addressed. By situating AI-assisted ultrasound within real-world clinical practice, this paper aims to clarify its potential role, limitations, and future significance in thyroid nodule management in China.

Keywords: AI-assisted ultrasound, thyroid nodule detection, diagnostic performance, clinical decision support, ultrasound imaging

1. Introduction

With the increasing use of high-resolution ultrasound in routine clinical practice and population-based health screening, thyroid nodules are being detected with growing frequency in China. Many of these nodules are identified incidentally in asymptomatic individuals undergoing examinations for unrelated reasons, which has shifted thyroid ultrasound from a problem-oriented diagnostic test to a routine, high-volume procedure. As a result, ultrasound now occupies a central role in the initial evaluation, risk stratification, and follow-up of thyroid nodules across nearly all levels of the healthcare system.

Despite its widespread adoption, the diagnostic performance of conventional thyroid ultrasound remains strongly influenced by operator expertise. Accurate interpretation of sonographic features—including margin characteristics, echogenicity, shape, and calcification patterns—requires substantial training and clinical experience. Variability in how these features are perceived and weighted has been widely reported, leading to inconsistent assessments among radiologists and sonographers. In busy clinical environments, particularly in primary hospitals and community-based screening programs, time constraints and limited access to experienced specialists may further exacerbate these challenges. Such variability can affect not only diagnostic confidence but also downstream clinical decisions, including recommendations for follow-up, biopsy, or referral.

Against this background, artificial intelligence has been increasingly explored as a supportive technology in thyroid ultrasound. AI-assisted systems are designed to analyze ultrasound images in a standardized and reproducible manner, typically by identifying nodules, extracting predefined imaging features, and generating structured risk assessments. Importantly, these systems are not intended to replace clinicians or redefine diagnostic criteria. Instead, they are commonly positioned as decision-support tools that aim to reduce subjectivity, improve consistency, and assist clinicians—particularly those with less experience—in applying established assessment frameworks more reliably.

The potential relevance of AI-assisted ultrasound is especially pronounced in the Chinese healthcare context. Large patient volumes, uneven distribution of experienced radiologists, and substantial variation in institutional resources create conditions in which diagnostic consistency is difficult to maintain. In such settings, AI-assisted tools may offer a means of supporting more uniform evaluation standards while accommodating existing clinical workflows. At the same time, their integration raises practical questions related to clinician acceptance, workflow efficiency, and alignment with real-world diagnostic practices.

The present paper discusses the diagnostic performance of AI-assisted ultrasound in thyroid nodule detection in China from a conceptual perspective. Rather than focusing on original empirical validation, it examines the clinical rationale, potential benefits, and practical considerations associated with incorporating AI into thyroid ultrasound practice. By situating AI-assisted ultrasound within everyday clinical contexts, this paper seeks to clarify its potential value, limitations, and role in contemporary thyroid nodule management.

2. AI-Assisted Ultrasound for Thyroid Nodule Detection

AI-assisted ultrasound systems for thyroid nodule detection are most commonly implemented either as software modules integrated into conventional ultrasound equipment or as independent platforms capable of analyzing stored images. These systems are generally designed to fit within existing diagnostic routines, allowing clinicians to incorporate AI support without substantially altering established scanning workflows. Rather than introducing new diagnostic concepts, most AI models are developed to recognize and quantify sonographic features that are already central to routine thyroid nodule assessment, thereby maintaining continuity with current clinical practice.

At a technical level, AI-assisted image analysis relies on machine learning or deep learning algorithms trained on large datasets of labeled ultrasound images. Through this training process, the system learns to associate specific visual patterns—such as irregular or ill-defined margins, hypoechogenicity, taller-than-wide shape, and microcalcifications—with different levels of malignancy risk. In clinical application, AI systems typically perform automated tasks including nodule detection, boundary delineation, and feature extraction, followed by the generation of a structured risk evaluation. These results are often presented in formats familiar to clinicians, such as categorical risk stratification or probability-based scores, which facilitates interpretation and lowers barriers to clinical acceptance.

From a functional perspective, AI-assisted ultrasound can serve multiple complementary roles in thyroid nodule detection. One important function is acting as a second reader, providing an additional standardized assessment alongside the clinician's interpretation. This supplementary input may help reinforce confidence when findings are concordant or prompt reconsideration when discrepancies arise. AI may also function as a quality-control mechanism by consistently evaluating image features and drawing attention to findings that might otherwise be overlooked, particularly during high-throughput examinations where time pressure is substantial.

In the context of clinical workflows in China, AI-assisted ultrasound is often deployed in settings characterized by high patient volume and variable levels of operator experience. In tertiary hospitals, AI tools may be used to support consistency among multiple examiners and reduce both intra- and inter-observer variability. In primary care institutions and community-based screening programs, where access to experienced thyroid specialists is more limited, AI-assisted systems are frequently viewed as a means of supporting less experienced clinicians by reinforcing guideline-based assessment and providing structured interpretive reference.

Despite these potential advantages, AI-assisted ultrasound is rarely applied as a standalone diagnostic solution. In routine practice, AI-generated assessments are typically considered in conjunction with grayscale ultrasound findings, Doppler information, and relevant clinical context. This integrative approach reflects current expectations that AI functions as a supportive component within clinician-led decision-making rather than as an autonomous diagnostic authority. Within this framework, the clinical value of AI-assisted ultrasound depends not only on algorithmic performance, but also on how effectively it aligns with real-world workflows, earns clinician trust, and adapts to the practical demands of thyroid nodule management in China.

3. Diagnostic Performance: Conceptual Evaluation

Rather than presenting original empirical findings, the diagnostic performance of AI-assisted ultrasound in thyroid nodule detection can be discussed conceptually through several key dimensions commonly used in clinical imaging. These dimensions help illustrate not only how performance is defined, but also how AI may influence diagnostic reasoning and clinical behavior in daily practice.

3.1 Sensitivity and Early Detection

Sensitivity is commonly used to describe the capacity of an AI-assisted system to identify thyroid nodules that may require further clinical attention. From a conceptual standpoint, AI-assisted ultrasound may contribute to improved sensitivity by applying predefined recognition rules in a uniform and uninterrupted manner across examinations. Unlike human operators, whose attention and performance can be influenced by fatigue, time pressure, or cumulative workload, AI systems maintain a consistent analytical focus. This characteristic is particularly relevant in high-volume ultrasound settings, where efficiency demands may increase the risk of missed findings.

The potential benefit of enhanced sensitivity is especially apparent in the detection of small nodules or lesions with subtle sonographic characteristics. Such nodules may not display prominent or classic malignant features and can therefore be overlooked during routine scanning, particularly when examinations are conducted rapidly or under constrained conditions. AI-assisted systems, by systematically evaluating image features across the entire field of view and applying the same detection criteria to each frame, may increase the likelihood that these less conspicuous abnormalities are identified and brought to the clinician's attention.

In addition, consistent sensitivity may help address variability in detection that arises from differences in operator experience. Less experienced clinicians may be more likely to miss subtle findings, whereas AI-assisted tools can provide a stable reference that supports more comprehensive initial assessments. In this sense, AI does not replace clinical observation but acts as an additional layer of vigilance that complements human interpretation.

Early detection also carries implications for downstream clinical management. Identification of nodules at an earlier stage may influence decisions regarding follow-up intervals, surveillance strategies, or the need for additional imaging and referral. Although increased sensitivity does not automatically translate into improved clinical outcomes, it conceptually supports a more complete baseline evaluation. Within this framework, AI-assisted ultrasound may function as a supplementary safeguard, helping ensure that potentially relevant findings are consistently recognized, documented, and incorporated into subsequent clinical decision-making processes.

3.2 Specificity and Reduction of Unnecessary Intervention

Specificity refers to the ability of an AI-assisted system to correctly identify thyroid nodules that are unlikely to be malignant or clinically significant. Conceptually, this aspect of diagnostic performance is closely linked to the system's capacity to limit false-positive assessments and to avoid unnecessary escalation of care. In routine clinical practice—particularly in screening programs and primary care settings—uncertainty in ultrasound interpretation often leads to conservative decision-making. This tendency may result in excessive follow-up imaging, fine-needle aspiration, or referral to higher-level institutions, even when the actual risk associated with a nodule is low.

AI-assisted ultrasound may contribute to improved specificity by reducing subjective overinterpretation of equivocal sonographic features. Human assessment of borderline findings, such as mildly irregular margins, heterogeneous echogenicity, or indeterminate internal composition, can vary substantially depending on individual experience, diagnostic confidence, and risk tolerance. In contrast, AI systems apply standardized assessment frameworks consistently across cases, which may help place such features into a more balanced and reproducible risk context. By discouraging overestimation of malignancy potential when findings do not clearly meet high-risk criteria, AI-assisted tools may help stabilize diagnostic thresholds.

The potential reduction in unnecessary intervention carries practical implications for both patients and healthcare systems. For patients, avoiding unwarranted procedures may reduce anxiety, physical discomfort, and exposure to procedural risks, while also limiting the psychological burden associated with repeated testing. For healthcare systems—particularly those managing large screening populations or operating under resource constraints—improved specificity may help optimize the use of diagnostic and specialist services, allowing attention to be focused on patients with higher-risk findings.

From a broader clinical perspective, AI-assisted ultrasound may support more proportionate and individualized management strategies. By helping clinicians distinguish low-risk nodules suitable for observation from those that genuinely warrant further investigation, AI tools can contribute to more rational follow-up planning and resource allocation. Importantly, improved specificity does not imply rigid adherence to AI-generated output. Instead, AI-assisted assessments may serve as a stabilizing reference that complements clinical judgment, particularly in situations where uncertainty might otherwise prompt overly cautious management. In this way, AI-assisted ultrasound may help refine decision-making while preserving clinician responsibility and oversight.

3.3 Standardized Interpretation of Sonographic Features

Interpretation of sonographic features such as margins, echogenicity, shape, and internal composition is fundamental to thyroid nodule evaluation, yet it remains one of the most subjective components of ultrasound diagnosis. Even when standardized reporting terminology is applied, clinicians may differ in how individual features are perceived, emphasized, and integrated into an overall risk assessment. These differences are shaped by variations in training background, accumulated clinical experience, and local practice patterns, and they can result in inconsistent diagnostic conclusions for nodules with similar imaging appearances.

From a conceptual perspective, AI-assisted ultrasound offers a standardized approach to feature interpretation by applying the same analytical criteria uniformly across cases. Rather than relying solely on individual visual judgment, AI systems evaluate image characteristics according to predefined patterns learned from large and annotated datasets. This process allows features to be assessed in a consistent manner, independent of examiner subjectivity. In cases where sonographic findings are subtle or do not clearly align with high- or low-risk categories, AI-assisted analysis may provide a more stable interpretive reference, helping to reduce ambiguity in risk stratification.

The value of such standardization becomes particularly apparent in clinical environments where multiple examiners are involved in patient care. In high-volume departments, variability in feature interpretation can complicate communication among clinicians, hinder consistent follow-up planning, and affect the reliability of longitudinal comparisons. By promoting more uniform interpretation of similar imaging features, AI-assisted assessments may support clearer documentation and more coherent clinical decision-making across providers.

This benefit may extend across institutions as well. In healthcare systems characterized by substantial institutional diversity, such as those in China, differences in ultrasound equipment, scanning protocols, and operator expertise can further amplify interpretive variability. Conceptually, AI-assisted ultrasound may help bridge these differences by introducing a shared analytical framework that supports more comparable assessments across centers. Within this context, standardized feature interpretation does not replace clinical judgment but serves as a common reference point, enhancing clarity, consistency, and confidence in thyroid nodule evaluation while preserving clinician autonomy.

3.4 Inter-Operator Variability and Diagnostic Consistency

Inter-operator variability is a well-recognized limitation of conventional thyroid ultrasound and represents a persistent challenge in routine clinical practice. Even when standardized reporting systems and risk stratification frameworks are available, differences in training background, years of experience, and individual diagnostic thresholds can lead to divergent interpretations of the same lesion. Such variability may influence not only the initial assessment of malignancy risk but also downstream management decisions, including recommendations for follow-up intervals, fine-needle aspiration, or surgical referral.

AI-assisted ultrasound systems have the potential to mitigate this variability by generating stable and repeatable outputs based on uniform analytical processes. Conceptually, AI applies the same evaluation criteria to image analysis regardless of who performs the examination, reducing reliance on individual subjective judgment alone. This characteristic may be particularly valuable in high-volume clinical environments, where examinations are conducted by multiple operators with heterogeneous levels of experience and where maintaining consistent diagnostic standards can be challenging.

Diagnostic consistency is especially important in the context of longitudinal follow-up. Thyroid nodules are often monitored over extended periods, and reliable comparison across serial examinations is essential for determining true nodule progression or stability. When follow-up scans are performed by different clinicians or at different institutions, variability in feature interpretation can obscure meaningful change and complicate clinical decision-making. By providing a consistent interpretive reference, AI-assisted ultrasound may support more reliable longitudinal evaluation, helping clinicians distinguish genuine morphological changes from differences attributable to observer interpretation.

From a conceptual perspective, improved consistency does not imply uniformity at the expense of clinical nuance. AI-assisted systems are not intended to override contextual judgment or clinical reasoning. Instead, they may serve as an anchoring reference that promotes coherence in interpretation across time, personnel, and clinical settings. In this role, AI contributes to diagnostic continuity while allowing clinicians to retain responsibility for integrating imaging findings with clinical context, particularly in cases that are borderline, atypical, or clinically complex.

3.5 Contribution to Clinical Decision-Making

Beyond isolated performance metrics, the diagnostic value of AI-assisted ultrasound can also be understood in terms of how it supports clinical decision-making. In routine practice, interpretation of thyroid ultrasound findings often involves a degree of uncertainty, particularly when sonographic features do not clearly fall into high- or low-risk categories. In such situations, AI-assisted systems may function as a secondary reference point that complements, rather than replaces, clinician judgment.

When AI-assisted assessments are concordant with the clinician's initial interpretation, they may reinforce diagnostic confidence and support timely decision-making. This reinforcement can be particularly useful in high-volume clinical environments, where efficiency and consistency are essential. Conversely, when discrepancies arise between AI output and human assessment, the divergence itself may prompt more careful review of imaging features, encouraging clinicians to re-examine assumptions rather than proceed reflexively.

This role is especially relevant in complex or borderline cases, where immediate categorical conclusions may not be appropriate. AI-assisted ultrasound can provide structured input—such as probabilistic risk estimates or standardized classifications—that helps frame uncertainty in a more explicit manner. By making risk more transparent, AI may support more nuanced clinical discussions regarding follow-up strategies, additional testing, or referral decisions.

From a conceptual standpoint, the contribution of AI-assisted ultrasound to clinical decision-making lies in its ability to support deliberation rather than dictate outcomes. By acting as an adjunctive analytical layer, AI may help clinicians balance caution with restraint, particularly in cases where management decisions depend on subtle imaging distinctions. In this context, diagnostic performance is reflected not only in accuracy, but in how effectively AI assists clinicians in making informed, context-sensitive decisions within established clinical pathways.

3.6 Interaction with Operator Experience

The impact of AI-assisted ultrasound on diagnostic performance is closely linked to the experience level of the operator. In thyroid ultrasound, differences in training and clinical exposure can substantially influence how sonographic features are recognized, interpreted, and translated into management decisions. As a result, the same AI-assisted output may serve different practical roles depending on who is using it.

For less experienced clinicians, AI-assisted ultrasound may provide structured guidance that aligns with established diagnostic criteria. In early stages of training or in settings with limited mentorship, AI outputs can offer reassurance and help frame image interpretation within a standardized risk assessment approach. This support may reduce uncertainty and narrow the gap between novice and expert interpretation, particularly when evaluating borderline or unfamiliar imaging patterns. Conceptually, AI functions as a reference that reinforces learning and promotes adherence to consistent assessment principles.

For experienced radiologists, the role of AI-assisted ultrasound is often different. Rather than serving as primary guidance, AI may act as a consistency check or quality assurance tool. Experienced clinicians typically rely on pattern recognition and contextual judgment developed over time, but AI outputs may still be valuable in highlighting discrepancies, confirming impressions, or prompting reconsideration in atypical cases. In this context, AI does not substitute expertise but provides an additional layer of verification that supports diagnostic confidence and consistency.

This interaction underscores that diagnostic performance does not arise solely from algorithmic capability or human expertise in isolation. Instead, it emerges from the collaboration between clinicians and AI systems, shaped by experience, context, and workflow. Conceptually, the effectiveness of AI-assisted ultrasound depends on how well it complements different levels of operator expertise and integrates into existing diagnostic practices, rather than on uniform performance gains across all users.

4. Clinical Implications in the Chinese Healthcare Context

The potential clinical implications of AI-assisted ultrasound for thyroid nodule management in China are closely tied to the structure and demands of the national healthcare system. Thyroid ultrasound is performed across a wide range of settings, from tertiary referral hospitals to primary care institutions and large-scale health screening centers. This broad deployment creates marked variation in operator experience, diagnostic resources, and clinical workflow, all of which shape how AI-assisted tools may be used in practice.

In primary care and resource-limited settings, access to experienced thyroid specialists is often limited, while patient volumes remain high. In these contexts, AI-assisted ultrasound may serve as a supportive tool that helps standardize initial assessments and reduce diagnostic uncertainty. By providing structured evaluations aligned with commonly accepted criteria, AI systems may assist clinicians in identifying nodules that warrant referral while avoiding unnecessary escalation of low-risk findings. This supportive role could contribute to more efficient use of specialist resources and improve continuity of care across different levels of the healthcare system.

AI-assisted ultrasound also has potential implications for large-scale screening programs, which are increasingly common in China. High-throughput screening environments place significant pressure on clinicians to maintain consistency and accuracy under time constraints. In such settings, AI tools may help maintain baseline diagnostic quality by offering consistent reference assessments and reducing the likelihood of oversight. While AI is unlikely to replace clinician judgment in screening decisions, its integration may contribute to more uniform evaluation standards across large populations.

Beyond technical performance, clinician acceptance is a critical factor influencing the real-world impact of AI-assisted ultrasound. In practice, acceptance is shaped not only by perceived accuracy, but also by transparency, ease of use, and alignment with existing diagnostic habits. Systems that present outputs in familiar formats and integrate smoothly into established workflows are more likely to be adopted. Conversely, tools that disrupt scanning routines or produce opaque results may encounter resistance, regardless of their technical capability.

Workflow integration is equally important in determining clinical value. In busy outpatient environments, AI-assisted ultrasound must function without significantly extending examination time or adding cognitive burden. Effective integration requires that AI outputs complement rather than compete with real-time image interpretation, allowing clinicians to incorporate AI feedback naturally into their decision-making process.

Regulatory and governance considerations also shape the clinical implications of AI-assisted ultrasound in China. As AI technologies continue to enter clinical practice, issues related to data governance, system validation, and clinical responsibility remain under active discussion. Clear regulatory frameworks and standardized evaluation pathways are essential to ensure that AI-assisted tools are used safely and consistently across institutions. Within this evolving landscape, the clinical impact of AI-assisted ultrasound will depend not only on algorithmic performance, but also on how effectively these systems are embedded within regulatory, institutional, and professional structures.

The clinical implications of AI-assisted ultrasound in China extend beyond technical enhancement of thyroid nodule detection. Their significance lies in how they interact with existing healthcare realities, support clinicians across diverse settings, and contribute to more consistent and efficient thyroid nodule management within the broader healthcare system.

5. Challenges and Limitations

Despite the growing interest in AI-assisted ultrasound for thyroid nodule detection, several challenges and limitations must be considered when evaluating its role in clinical practice. One central concern relates to model generalizability. Many AI systems are trained on datasets derived from specific institutions, devices, or patient populations. Differences in ultrasound equipment, scanning protocols, and patient characteristics across regions may limit the reliability of these systems when applied beyond their original development settings. In a country as geographically and demographically diverse as China, this lack of generalizability represents a significant practical constraint.

Data quality is another critical issue influencing the performance of AI-assisted ultrasound. Ultrasound images are inherently operator-dependent, and variability in image acquisition can affect algorithmic output. Inconsistent labeling standards, heterogeneous annotation quality, and imbalanced datasets may further introduce bias into AI models. These challenges are particularly relevant in large-scale, multi-level healthcare systems, where data are collected under varying conditions and levels of expertise.

Interpretability also remains a key limitation. While AI-assisted systems may provide risk scores or classifications, the underlying decision-making processes are often not fully transparent to clinicians. This lack of interpretability can hinder trust and limit clinical adoption, especially when AI outputs conflict with human judgment. In thyroid ultrasound, where nuanced interpretation of features often guides management decisions, clinicians may be reluctant to rely on recommendations that cannot be clearly explained or contextualized.

Ethical and governance considerations further complicate the integration of AI-assisted ultrasound into routine practice. Issues related to data privacy, informed consent, and accountability in cases of diagnostic error remain areas of ongoing discussion. In the Chinese healthcare context, where digital health technologies are rapidly expanding, the balance between innovation and regulation is still evolving. Clear guidelines regarding responsibility for AI-assisted decisions and standardized evaluation frameworks are essential to ensure safe and equitable use.

Finally, the clinical effectiveness of AI-assisted ultrasound is closely linked to how these systems are implemented rather than to algorithmic performance alone. Overreliance on AI outputs may risk deskilling clinicians, while insufficient integration may limit practical benefit. These limitations highlight the need for cautious, context-aware adoption of AI-assisted ultrasound, with attention to technical, clinical, and ethical factors that shape its real-world impact within the Chinese healthcare system.

6. Future Perspectives

Future development of AI-assisted ultrasound in thyroid imaging is likely to focus on advancing both technical capability and depth of clinical integration. One important direction involves further optimization of AI systems through the use of more diverse and representative training datasets. Incorporating ultrasound images acquired across different geographic regions, healthcare institutions, equipment manufacturers, and patient populations may help improve model robustness and generalizability. This consideration is particularly important in China, where substantial heterogeneity exists in clinical practice patterns, imaging quality, and patient demographics.

Another key perspective concerns closer alignment between AI-assisted ultrasound systems and established clinical guidelines. Rather than functioning as parallel or supplementary assessment tools, future AI models may increasingly be designed to mirror guideline-based diagnostic pathways, such as structured risk stratification systems. Explicit alignment with widely accepted frameworks could enhance interpretability and clinician trust, making AI outputs easier to integrate into routine decision-making. When AI recommendations correspond directly to familiar clinical categories and management pathways, their practical utility and acceptance are likely to increase.

Integration of AI-assisted ultrasound with broader clinical information also represents an important area for future development. Current systems are largely image-centric, focusing on visual pattern recognition alone. Future models may incorporate additional clinical variables, including patient age, sex, laboratory findings, medical history, and prior imaging results. This multimodal approach has the potential to produce more context-aware assessments that better reflect real-world clinical reasoning, moving beyond isolated image interpretation toward more comprehensive decision support.

Personalized risk assessment is a particularly promising direction in thyroid nodule management. Clinical decisions often depend not only on imaging features but also on patient-specific factors and follow-up considerations. AI systems capable of adapting risk estimates to individual profiles may support more tailored management strategies, such as personalized surveillance intervals or intervention thresholds. Such developments would represent a shift from population-level pattern recognition toward patient-centered risk modeling, aligning AI-assisted ultrasound more closely with individualized care.

Finally, progress in this field will depend not only on technological innovation but also on sustained evaluation in real-world clinical environments. Prospective assessment, post-deployment monitoring, and ongoing collaboration among clinicians, researchers, and regulatory bodies will be essential to ensure that AI-assisted ultrasound evolves in a manner that is clinically meaningful, ethically responsible, and aligned with the practical needs of thyroid care in China.

7. Conclusion

AI-assisted ultrasound represents a promising supportive approach for the detection and management of thyroid nodules, particularly within the context of China’s high-volume, multi-tiered healthcare system. By providing standardized image analysis and structured risk assessment, AI-assisted tools have the potential to improve diagnostic reliability and reduce variability associated with operator experience. These advantages are especially relevant in settings where thyroid ultrasound is performed frequently and by clinicians with heterogeneous levels of training.

Rather than functioning as a replacement for clinician expertise, AI-assisted ultrasound is best understood as a complementary technology that augments conventional ultrasound practice. Its primary value lies in enhancing consistency, supporting less experienced operators, and reinforcing guideline-based assessment. In primary care institutions and large-scale screening programs, where diagnostic resources and specialist availability are unevenly distributed, AI-assisted systems may help promote more uniform evaluation standards while preserving clinician oversight and judgment.

At the same time, the clinical impact of AI-assisted ultrasound depends on careful and context-sensitive implementation. Effective integration into real-world workflows, transparent system design, and appropriate regulatory oversight are essential to ensure safe and meaningful use. Without alignment to clinical routines and professional expectations, even technically robust AI systems may fail to deliver practical benefit. Continued refinement, validation in diverse clinical environments, and active engagement with clinicians will therefore remain critical components of successful adoption.

AI-assisted ultrasound has the potential to play an important role in contemporary thyroid imaging in China. Its long-term value will depend not only on algorithmic performance, but also on how well it complements human expertise, adapts to healthcare system realities, and supports informed, patient-centered decision-making in thyroid nodule management.

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