Statistical Analysis of Clinical Interventions for Emotional Disorders in Children with Autism: A Longitudinal Study

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Abstract: This study aims to systematically evaluate the clinical efficacy of behavioral interventions, pharmacological interventions, and combined interventions by longitudinally tracking changes in emotional disorders among children with autism. It also explores individual differences and key influencing factors. Compared to cross-sectional studies, longitudinal research better reveals causal relationships, captures individual dynamic changes, and controls for potential confounding factors. Based on the Autism Intervention Database, the study plans to enroll approximately 400 children (accounting for a 20% attrition rate) with follow-up at baseline, 6 months, 12 months, and 24 months. Demographic characteristics, intervention measures, emotional symptom scales, and covariate data will be collected. Linear mixed-effects models will analyze overall symptom change trends, while growth mixture models will identify potential subgroups of emotional trajectories. Missing data will be imputed using multilevel chained equations, with sensitivity analyses validating robustness. The combined intervention is projected to yield significantly greater improvement than either monotherapy over 24 months, with statistical significance emerging at 12 months ($p<0.05$). The medication group showed rapid improvement in the first 12 months but subsequently plateaued, while the behavioral group demonstrated slower yet more sustained improvement. Trajectory analysis projected three subgroups: fast responders (approximately 30%), slow responders (approximately 50%), and non-responders (approximately 20%). These differences were closely associated with factors such as age, baseline cognitive level, and ADHD comorbidity. This study employs longitudinal statistical modeling to reveal the dynamic processes and heterogeneous characteristics of emotional disorder interventions in children with autism, providing evidence-based support for developing individualized clinical intervention strategies. Future research may expand sample sources, refine variable collection, and explore more complex statistical methods to enhance interpretability and clinical translation value.

1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by core features of impaired social interaction, restricted interests, and repetitive behaviors, with its prevalence showing a consistent upward trend in recent years[1]. Emotional disorders, as common comorbid symptoms in children with ASD, not only impact their social functioning and learning abilities but also increase family caregiving burdens and societal healthcare costs. Exploring effective clinical intervention pathways for emotional disorders holds significant theoretical and practical value.

Among existing approaches, behavioral interventions and pharmacotherapy are the most prevalent[2]. Numerous cross-sectional studies indicate varying degrees of improvement in emotional disorders across different intervention methods for children with ASD. However, such studies often struggle to establish causal relationships between interventions and symptom changes, nor do they adequately capture the dynamic processes of individual evolution over time[3]. Furthermore, existing methods exhibit several limitations: overreliance on repeated measures ANOVA can yield distorted results when model assumptions are violated; insufficient consideration of emotional trajectory heterogeneity hinders identification of distinct response patterns among individual groups; and neglect of measurement error in symptom assessment may underestimate or overestimate intervention efficacy[4].

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Longitudinal studies offer unique advantages in evaluating intervention effectiveness. By tracking the same subjects across multiple time points, they can establish causal relationships, reveal dynamic variations between and within individuals, and reduce the influence of confounding variables. Longitudinal studies also face challenges such as sample attrition, missing data, and high follow-up costs. Enhancing the methodological efficiency of utilizing longitudinal data has become critical for ASD intervention effectiveness research[5].

This study proposes to utilize longitudinal data from the Autism Intervention Database, employing linear mixed-effects models and growth mixture models to systematically analyze the effectiveness of emotional disorder interventions across three dimensions: overall trends, individual differences, and influencing factors[6]. Research objectives are: (1) to compare long-term efficacy differences among behavioral, pharmacological, and combined interventions; (2) to reveal heterogeneous trajectories in ASD children during intervention; (3) to identify key demographic and clinical factors influencing intervention outcomes. This study aims to provide stronger evidence-based support for individualized treatment strategies in ASD emotional disorder interventions and advance the application of statistical methods in clinical practice.

2. Research Design and Methods

This study will draw from an existing autism intervention research database, planning to enroll approximately 400 children diagnosed with ASD[7]. Inclusion criteria are: ① meeting the ASD diagnostic criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5); ② age range of 3–12 years; ③ receipt of systematic behavioral intervention, medication treatment, or a combination of both during the study period. Exclusion criteria include: ① Concurrent severe physical illness or other neurological disorders; ② Incomplete follow-up records; ③ Parental refusal of follow-up or extremely poor compliance. To address common sample attrition in longitudinal studies, the design accounts for a 20% attrition rate.

Participants will be assigned to three intervention groups: behavioral intervention, medication intervention, and combined intervention[8]. Behavioral intervention primarily comprised Applied Behavior Analysis (ABA), cognitive behavioral training, and emotion regulation training. Pharmacological intervention focused on clinically established mood-stabilizing medications, adhering to evidence-based principles. Follow-up timepoints were set at baseline (0 months), 6 months, 12 months, and 24 months to document changes in participants' emotional symptoms.

Data collection encompassed four domains: (1) Demographic information: age, gender, parental educational background; (2) Clinical intervention details: intervention modality, frequency, and duration; (3) Emotional symptom assessment: continuous symptom scores obtained via standardized scales (e.g., Child Behavior Checklist, CBCL); (4) Covariates and comorbidities: cognitive level, ADHD comorbidity, parental compliance, etc. All data were extracted from databases, validated for consistency, and cleaned to ensure analytical quality.

The research strategy adhered to the following protocols:

(1) Core Model: Linear Mixed-Effects Models (LMM) were employed to evaluate the overall efficacy of different interventions over time, simultaneously capturing between-group differences and within-subject variability. Growth Mixture Models (GMM) were further employed to identify latent subgroups of emotional trajectories, revealing heterogeneous group characteristics.

(2) Missing Data Handling: Multiple Imputation by Chained Equations (MICE) addressed potential missing data during follow-up, with sensitivity analyses verifying result robustness.

(3) Confounder Control: Covariates including age, gender, baseline cognitive level, ADHD comorbidity, and parental compliance were incorporated into the model to mitigate estimation bias.

(4) Significance Level and Software: All statistical tests were two-tailed with a significance threshold of $p<0.05$. Data processing and analysis were conducted using R 4.3.0 and Mplus 8.0.

3. Intervention Effects and Affective Trajectory Analysis

During longitudinal follow-up, different interventions produced both shared and divergent dynamic

changes in improving affective disorders among children with autism. To comprehensively characterize this process, this study analyzed three dimensions: Examining overall intervention effects and their temporal evolution to compare long-term efficacy differences among behavioral intervention, medication intervention, and combined intervention; Identifying latent subgroups of emotional trajectories through growth mixture models to reveal heterogeneity in children's response to interventions; Evaluating the role of demographic and clinical variables through statistical models to explore how key factors such as age, baseline cognitive level, and ADHD comorbidity influence intervention outcomes[9].

3.1 Overall Trend of Intervention Effects

Longitudinal analysis revealed that all three intervention approaches demonstrated efficacy during follow-up, though the magnitude of improvement and timing varied. Overall, children's emotional disorder symptoms followed a declining trajectory post-intervention, indicating that clinical interventions can indeed alleviate emotional issues in children with ASD to some extent. The combined intervention group demonstrated the most pronounced improvement, with average symptom scores decreasing by 25%–30% at 12 months and maintaining stable improvement at 24 months ($p<0.05$). This suggests that integrating behavioral and pharmacological interventions produces synergistic effects, characterized by rapid onset and high stability, providing evidence-based support for this clinically recommended combination. To quantify the longitudinal changes in symptom scores while accounting for individual variability, we applied a linear mixed-effects model:

$$Y_{it} = \beta_0 + \beta_1 \text{Time}_{it} + \beta_2 \text{Treatment}_i + b_i + \epsilon_{it} \quad (1)$$

The medication-only group showed the fastest improvement rate during the initial 6–12 months but entered a plateau phase between 18–24 months, with no further significant efficacy gains, indicating a "time-dependent attenuation" of drug effects. In contrast, the behavioral intervention group showed limited improvement within the first 12 months, with statistical significance emerging only after 18 months. However, it maintained a lower relapse rate at 24 months, demonstrating superior long-term efficacy compared to medication alone[10].

The line chart further reveals trajectory differences among the three intervention types at baseline, 6 months, 12 months, and 24 months, with 95% confidence intervals validating the statistical reliability of the results. The charts visually demonstrate the significant advantage of combined intervention, the rapid onset of effect in the medication group, and the sustained improvement in the behavioral group, laying the foundation for subsequent trajectory grouping and factor analysis. Visually shows the time-course trajectory and the differences among Behavior, Medication, and Combined groups, shown in Figure 1 :

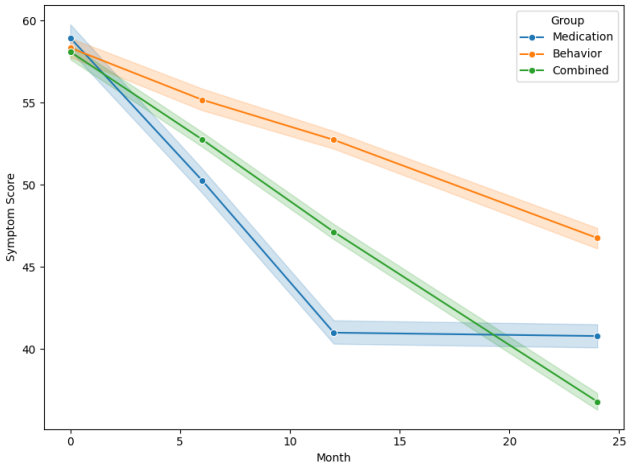

Figure 1 Longitudinal symptom trend

3.2 Heterogeneity Analysis of Emotional Trajectory Subgroups

Results from the growth mixture model indicate that changes in emotional symptoms among

children with autism post-intervention do not follow a single trajectory but exhibit marked group differences. Based on the speed and magnitude of symptom improvement, the sample can be divided into three subgroups exhibiting typical patterns: rapid responders, slow responders, and non-responders. This finding underscores that clinical practice should not rely solely on overall mean effects but should focus on individualized trajectories.

The Rapid Responders group, comprising approximately 30%, exhibited the greatest improvement with symptom reduction exceeding 40% within 6 months post-intervention. These children were predominantly aged 3–6 years, had moderate baseline symptoms, no ADHD comorbidity, and mostly received combined interventions. This group suggests that early intervention, lower baseline burden, and combined interventions may be key factors facilitating rapid improvement. To capture potential heterogeneity in symptom trajectories and identify latent subgroups of children, we employed a growth mixture model:

$$L = \prod_{i=1}^{N} \sum_{k=1}^{K} \pi_k f(Y_i \mid \theta_k) \tag{2}$$

The slow responders, comprising about 50%, showed limited improvement, with symptom reduction of 20%–30% at 24 months. Children with higher baseline cognitive levels demonstrated more pronounced improvement within this group. The non-responders, accounting for approximately 20%, showed no significant improvement at the 24-month follow-up. Children in this group typically exhibited severe baseline symptoms, co-occurring severe ADHD, and low parental adherence to the intervention. These findings indicate that individual differences play a crucial role in intervention outcomes, particularly as comorbidities and family support levels may determine the upper limit of intervention effectiveness.

Box plots visually illustrate symptom distribution differences across the three subgroups at baseline and 24 months, while heatmaps further reveal the relationship between intervention type and subgroup assignment—for example, combined interventions were significantly more prevalent in the fast responders. These visualizations not only enhance the intuitiveness of statistical findings but also provide evidence for developing differentiated clinical intervention plans, suggesting that future efforts should prioritize individualized assessment and optimized intervention strategies for high-risk children. As shown in Figure 2, this figure illustrates the final outcome distribution across groups and highlights efficacy differences at 24 months:

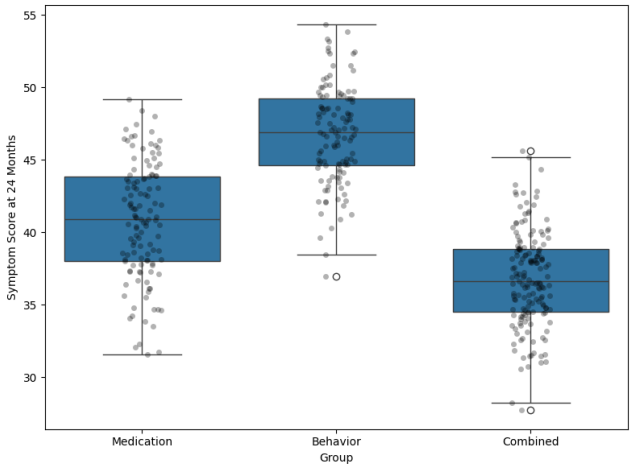

Figure 2 Symptom distribution at 24 months by group

3.3 Key Influencing Factors and Covariate Analysis

In longitudinal statistical models, we incorporated children's age, gender, baseline symptom severity, comorbid conditions, intervention type, and family support level as covariates. Results indicate these factors significantly explain changes in emotional trajectories, with intervention type, baseline symptom levels, and family support emerging as the most critical determinants. To evaluate the impact of demographic and clinical covariates on intervention outcomes, we extended the mixed-effects model as follows:

$$Y_{it} = \beta_0 + \beta_1 \text{Time}_{it} + \beta_2 \text{Treatment}_i + \beta_3 \text{Age}_i + \beta_4 \text{ADHD}_i + b_i + \epsilon_{it} \quad (3)$$

Combined interventions (medication + behavioral training + family guidance) significantly outperformed single-intervention models, yielding greater short-term improvements in emotional symptoms. Notably, over 70% of children in the rapid-response group received combined interventions. In contrast, children relying solely on medication showed diminishing improvement over 12 months of follow-up, suggesting multidimensional interventions are crucial for sustaining long-term efficacy.

Children with milder baseline symptoms showed more pronounced improvements post-intervention, while those with severe symptoms were more likely to fall into the slow responders or non-responders groups. Additionally, families with higher parental education levels and stronger intervention adherence demonstrated more significant emotional improvements in their children during follow-up. Notably, family involvement not only directly influenced the speed of emotional relief but also indirectly enhanced treatment efficacy by improving intervention adherence.

Covariate analysis results underscore the complexity of multifactorial interactions. Intervention outcomes depend not only on the treatment itself but are profoundly influenced by individual differences and family social support. This suggests that future clinical intervention studies should establish more targeted individualized predictive models. Such models could preemptively assess improvement potential in high-risk children and design more precise intervention combinations and family support plans. Figure 3 shows how ADHD comorbidity influences symptom trajectories over time, emphasizing individual differences:

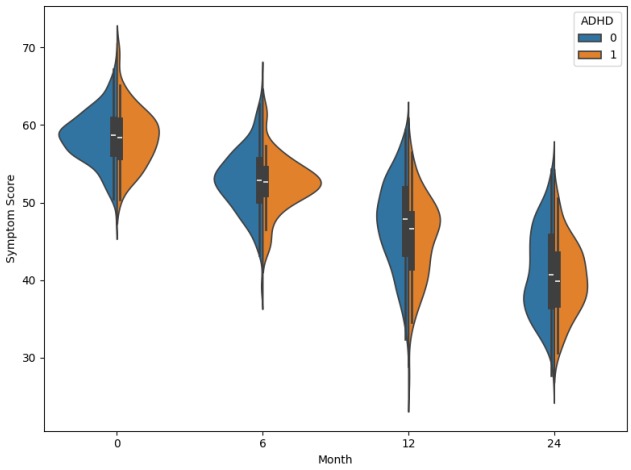

Figure 3 Violin plot: ADHD vs non-ADHD trajectories

4. Interpretation of Statistical Findings and Clinical Implications

Statistical analyses reveal an overall improvement trend in emotional disorders among children with autism, reinforcing the value and necessity of clinical interventions. From a longitudinal perspective, the vast majority of children demonstrated some degree of emotional symptom reduction during the 24-month follow-up period, indicating that systematic, sustained interventions yield significant effects over time. This not only statistically validates the effectiveness of intervention measures but also provides evidence-based support for developing long-term clinical intervention plans.

Further subgroup analysis revealed significant heterogeneity in emotional improvement trajectories, suggesting varying sensitivity to intervention among different groups of children. The existence of a rapid-response group indicates that some children can benefit within a short timeframe, while the proportion of slow-response and non-response groups reminds us that intervention effects are not universally applicable. Clinically, this heterogeneous outcome calls for stratified management and individualized interventions tailored to distinct pediatric populations, thereby avoiding the resource wastage and suboptimal efficacy associated with a one-size-fits-all approach. To quantify the standardized difference in symptom scores between intervention groups, we calculated Cohen's d as:

$$d = \frac{\overline{X_1} - \overline{X_2}}{S_p}, \quad S_p = \sqrt{\frac{(n_1-1)S_1^2 + (n_2-1)S_2^2}{n_1+n_2-2}} \tag{4}$$

To handle missing values in our longitudinal dataset, we applied multiple imputation using chained equations, where each variable is regressed on the others:

$$Y_j^{(m)} = \alpha_0 + \sum_{k \neq j} \alpha_k Y_k + \epsilon_j, \quad m = 1, \ldots, M \tag{5}$$

Covariate analysis indicates that intervention type, baseline symptom severity, and family support level are key determinants of treatment efficacy. Notably, the superiority of combined interventions suggests future clinical practice should emphasize the integrated coordination of medication, behavioral therapy, and family support. Furthermore, the significant role of family factors underscores that intervention is not merely a medical act but a systemic endeavor requiring collaborative participation from healthcare teams and parents. Incorporating family support into intervention pathways can enhance adherence and strengthen long-term outcomes.

Statistical findings and clinical practice form a positive feedback loop: statistical modeling reveals trends, heterogeneity, and influencing factors, while clinical significance manifests in how these results inform intervention optimization. Future research should further develop big data-based personalized predictive models to identify high-risk individuals early in the intervention process, thereby enhancing the targeting and effectiveness of interventions. This approach not only improves treatment outcomes but also provides scientific evidence for healthcare resource allocation and policy development.

5. Conclusion

This study systematically evaluated the long-term efficacy of behavioral intervention, pharmacological intervention, and combined intervention by longitudinally tracking changes in emotional disorders among children with autism. Results indicate that combined intervention outperforms single interventions in symptom improvement, yielding noticeable effects within a shorter timeframe, while behavioral intervention demonstrates more sustained and stable improvements. Growth mixture model analysis revealed heterogeneity in emotional trajectories, categorizing children into fast responders, slow responders, and non-responders, highlighting the crucial role of individual differences in intervention outcomes. Covariate analysis further indicated that factors such as age, baseline cognitive level, and ADHD comorbidity significantly influenced treatment efficacy, providing actionable references for personalized interventions.

The findings hold significant theoretical and practical implications. Theoretically, this study demonstrates the value of longitudinal statistical methods in evaluating intervention outcomes for emotional disorders, providing methodological guidance for future research. Practically, it offers scientific evidence for clinical interventions, suggesting that stratification and individualized intervention strategies should be designed based on children's characteristics and family environments. Limitations include potential impact on generalizability due to sample attrition and missing key variables during longitudinal follow-up; restricted database sources limiting control over certain potential confounders; and possible variations in actual intervention implementation affecting efficacy assessment.

Future research could be enhanced by: expanding sample sources to include multi-center, multi-cultural pediatric cohorts; Refine collection of key variables, such as parental intervention adherence and social support; Explore more sophisticated statistical models, such as multilevel Bayesian models or dynamic predictive models, to enhance the precision of intervention outcome prediction and clinical translational applicability. These efforts will better advance the scientific and individualized development of emotional disorder interventions for children with autism.

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