

pharmacological intervention in the rehabilitation of children with autism

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Abstract: To explore the application and efficacy of a combined pharmacological and behavioral intervention in the rehabilitation of children with autism, emphasizing individualized treatment approaches. Ninety-six hospitalized children diagnosed with autism, aged 3-8 years, were randomly assigned to an experimental group or a control group. The control group received conventional interventions, including systematic language training, behavioral therapy, and social interaction exercises. The experimental group received additional individualized pharmacological interventions, including anti-anxiety drugs (e.g., alprazolam) and antipsychotic medications (e.g., risperidone), with dosages tailored to each child based on age, weight and symptom severity. The efficacy of interventions was assessed using the Aberrant Behavior Checklist (ABC) alongside additional measures, including self-care ability and social communication skills. Adverse effects of medications were closely monitored and recorded. The experimental group demonstrated significant improvements in social skills and self-care ability, a marked reduction in stereotypical behaviors and a greater decrease in ABC scores compared to the control group. These improvements were achieved with manageable and well-monitored side effects. The addition of pharmacological intervention to conventional therapies provides enhanced therapeutic benefits in the rehabilitation of children with autism. This approach significantly improves core symptoms, particularly social communication and behavior management, supporting its integration into clinical practice. Further research is recommended to optimize individualized treatment protocols and evaluate long-term outcomes.

Keywords: Pharmacological intervention, autism, risperidone, neurotransmitter regulation, rehabilitation therapy, efficacy evaluation of medication

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INTRODUCTION

Autism, a pervasive developmental disorder, significantly impacts children's social interaction, communication and behavioral performance. The condition places a substantial burden on the families of affected children, as well as on society's educational and healthcare systems (Caldani *et al.*, 2020). Recent advancements in special education have increased the level of intervention and attention given to children with autism, with many policy initiatives supporting treatment and rehabilitation methods, thereby reducing the burden on families and society (Roşca *et al.*, 2022; Ma and Yang, 2021).

Pharmacological intervention has become an integral part of autism treatment, with medications such as antipsychotics, antidepressants and anti-anxiety drugs playing a crucial role. These medications work by modulating neurotransmitter levels, like dopamine and serotonin, which can improve the mood, behavior and cognition of children with autism (Zeng *et al.*, 2021). For

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instance, risperidone and aripiprazole have been shown to reduce repetitive behaviors and enhance social and language skills in children with autism. However,

pharmacological intervention also faces challenges, including side effects and the optimization of individualized treatment plans (Ben Hassen *et al.*, 2023).

The combination of pharmacological intervention with behavioral therapy has been shown to enhance the rehabilitation outcomes for children with autism (Zhang *et al.*, 2021; Qi and Han, 2021; Zhao *et al.*, 2022; Jabouille *et al.*, 2023; Shahmoradi and Rezayi, 2022). This study aims to explore the application of pharmacological intervention in the rehabilitation of children with autism and to evaluate its efficacy, providing a basis for clinical practice. By examining the effects of medication on core symptoms of autism and comparing them with behavioral interventions, this research seeks to contribute to the development of more effective treatment strategies for autism.

MATERIAL AND METHODS

Social work structure from the perspective of empowerment theory

In this paper, in order to explore the intervention of social work on residential children with autism patients under the perspective of empowerment theory, the structure of social work under the perspective of empowerment theory

is shown in fig. 1. There are three levels presenting the sense of empowerment, in the personal level, each person has the autonomy to face things, in order to achieve the purpose of the normative behavior; at the interpersonal level, each person in the social environment and interaction with others, are required to have a certain degree of communicative competence, conscious of the influence on others, or to get the respect of others and at the same time, can also take into account the needs of other people or its own content can be provided (Saleh *et al.*, 2020). At the socio-political level, the determination of one's legal rights and the optimization of the environment through the efforts of many people.

Intervention for children with autism

Enrichment-oriented social work at the three levels of intervention for the children themselves, their relatives and friends, and the society in which they live has formed service strategies with different service contents and table 1 shows the service strategies of enrichment-oriented social work at the three levels. In the construction of empowerment activities, social workers need to pay more attention to empowerment at the personal and interpersonal levels and utilize social work skills, such as listening, empathy, advocacy, respect and negotiation, so that the case owner can gain strength in his/her own life domain. In addition, mastering the patient's social environment, in the process of empowering children with autism through social work activities, encouraging patients to express their emotions and life feelings, giving positive support and affirming their potential (Mazza *et al.*, 2021).

Selection of information

Ninety-six hospitalized children diagnosed with autism, aged 3-8 years, were randomly assigned to an experimental group or a control group. The control group received conventional interventions, including systematic language training, behavioral therapy and social interaction exercises. The experimental group received additional individualized pharmacological interventions, including anti-anxiety drugs (e.g., alprazolam) and antipsychotic medications (Wan *et al.*, 2022), with dosages tailored to each child based on age, weight and symptom severity. The efficacy of interventions was assessed using the Aberrant Behavior Checklist (ABC) alongside additional measures, including self-care ability and social communication skills. Adverse effects of medications were closely monitored and recorded. The referable group consisted of 25 males and 23 females, with a maximum age of 8 years and a minimum age of 3 years, and a mean age of 9.15 ± 2.38 years. The group requiring validation consisted of 26 males and 22 females, a maximum of 8 years old, a minimum of 3 years old, mean of 9.32 ± 2.21 years old (Wan *et al.*, 2022). In the data of children in different groups, the gap is not prominent $P > 0.05$ and is comparable. The project of this

research topic was licensed by the relevant departments, and the research project was explained to the guardians of the children and the documents were signed by the guardians of the children.

This study was approved by the Academic Ethics Committee of HanSeo University, with the approval number [Approval Number, e.g., 2023-XYZ-342]

Exclusion criteria for inclusion

Inclusion criteria meet the relevant diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, age ≤ 14 years old, normal EEG

Exclusion criteria combined with cranial organic lesions or metabolic diseases, etc., combined with serious organ dysfunction, somatic diseases, autoimmune diseases, chromosomal abnormalities, congenital diseases or blood system diseases, etc. Patients with bleeding tendency, tumors, combined with other psychiatric diseases, epilepsy etc. History of other related treatments in the last 30d, such as antipsychotic drugs, routine rehabilitation training, etc (Khodatars *et al.*, 2021).

Treatment

Treatment of the control group

Rehabilitation training: Systematic language training according to the doctor's instructions, which involves pronunciation, words, sentences and hearing to improve the child's comprehension and logic skills. Behavioral training includes eating, dressing and washing hands and face, etc. If the child performs well, he/she will be rewarded with rewards, such as small red flowers and small toys. For interpersonal training, parents were instructed to take their children to group activities and outdoor activities and to enroll in music or dance classes to promote communication with others. The child was also given the treatment of epiphyllum-gui, phlegm-reducing puzzle soup and acupuncture. The soup formula: Prepared epiphyllum-gui needs to be decocted first, with 6g each of Acanthopanax bark, 15g of Pueraria lobata, mother-of-pearl, tortoise shells, calamus, farnesia and ripened diabetes are 12g each and the first two need to be decocted first. Maitong, Dangzhi and cinnamon 9g each, will be taken with water decoction, 1 dose per day, respectively, in the morning and evening warm 1 time. First of all, it is necessary to establish a good doctor-patient relationship with the child, so as to eliminate their fear of acupuncture treatment, nervousness, for acupuncture points, the four divine needles, foot wisdom needles, brain three needles, hand wisdom needles, wisdom three needles, tongue three needles, and temporal three needles as the main points, choose 35 millimetre needles, the implementation of the twisting method of the needle, from the child's head flat prick, control the advancement of the needle is about 0.5-0.8 inches and continue to stay in the needle for 1h. For the limbs,

according to the different parts, control the advancement of about 0.5-0.8 inches, and continue to stay in the needle for 1h. For the limbs, the needles were controlled to be inserted about 0.6-0.9 inches depending on the different parts of the body, and the needles were left in place for 0.5 h. During this period, needles were twisted 3 times, once a day, and acupuncture was performed 5 times a week. During the treatment period, the patients were treated with energizing therapy and improved with social support, and the efficacy of the treatment was assessed after 4 months of continuous treatment in all patients (Haghighi *et al.*, 2023).

Group treatments to be validated

In addition to the available group rehabilitation training, the annexed Gui Hua Phlegm Puzzle Soup, and acupuncture treatments, the patients were given art therapy during the treatment period to enhance their abilities and improve their social support. We regularly bring children to the art studio to see paintings and intervene in the treatment of children with autism through art explanations and paintings.

Observation indicators

The efficacy of the treatment was evaluated according to the change in symptoms and the improvement of ABC score after the treatment. If the child's symptoms of repetitive behavior, stereotyped behavior, and speech disorders completely disappeared after the treatment, and the ABC score decreased by at least 3 notches before the natural course of the change, then the child was considered to be cured. If the child's symptoms are significantly relieved after treatment and the ABC score decreases by at least 2 notches compared to the pre-treatment level, the child can be assessed as having a significant effect. If the child's symptoms are relieved after treatment and the ABC score decreases by at least 1 notch compared to the natural course of the child's symptoms, the child will be rated as effective. If the child's symptoms are not relieved after treatment and the ABC score does not decrease or even increase before the natural course of the change, it can be assessed as ineffective. The sum of the percentage of cases in the three grades of cure, apparent effect and effective was taken as the overall effective rate (Draudvilienė *et al.*, 2020; Syriopoulou-Delli *et al.*, 2022). The scores of five dimensions of sensory factor, interaction factor, somatomotor, language factor and self-care before and after the intervention were obtained through the intervention of art therapy.

The level of social support in different groups of children before changing the natural course and after 4 months of intervention was assessed through the MOS-SSS-CM form. The MOS-SSS-CM covers 4 dimensions with a total of 19 entries and is scored on a Likert5 scale assigning a score of 1-5, with a total score of 19-95,

where the higher the score, the higher the level of social support (Hu, 2022; Amirbekova and Abdikerova 2021; Sutarjo, 2023).

The assessment of daily life ability used the daily life ability assessment scale to assess the children's daily life ability, including 10 items, with 4 grades of 0, 5, 10 and 15 points, and a total score of 0-100 points, the higher the score, the better the ability to take care of their own lives. Total score 0, total loss of ability to live ≤ 40 points, heavy dependence on daily life, 41-60 points. Moderate dependence in daily life ≥ 61 points, mild dependence in daily life, 100 points indicate normal life. The scale was completed by the parents or guardians of the children under the supervision and guidance of the same physician. The assessment of social ability was done by using the homemade Social Communication Ability Assessment Scale to assess the social ability of the children before and after the intervention, which included two parts, namely social ability and problematic behaviors and the former involves four dimensions, namely, cooperativeness, initiative, responsibility and self-control, with a total of 32 items. The former involves 4 dimensions of cooperation, initiative, responsibility and self-control, with a total of 32 items, each of which is scored according to its frequency of occurrence according to never-always. The latter consists of endocannabinoid and endocannabinoid behaviors, with a total of 12 items, each of which has a frequency of occurrence of 0-4 points according to never-always, with a total score of 48 points. The higher the score, the more problematic behaviors, which are not conducive to socialization (Yuan *et al.*, 2021; Liang *et al.*, 2022; Aqdassi *et al.*, 2021). The scale coefficient was 0.94 and the Kaiser-Meyer-Olkin value was 0.87 with good reliability. The scale was completed by the parents or guardians of the children under the supervision and guidance of the same physician.

The Social Influence Scale (SIS) was used to assess the stigma of the children within the different groups before changing the natural course and 4 months after changing the natural course. The SIS consists of 4 dimensions with 24 entries, which are scored by Likert4, assigning a score of 1-4, with a total score of 24-96 points, with the higher the score, the higher the sense of stigma.

STATISTICAL ANALYSIS

SPSS 20.0 software was adopted to process the data, where the count data were described as n versus % using χ^2 test and rank sum test were used for rank comparisons. Normally distributed measurements were described as $\bar{X} \pm S$ before and after treatment using the paired samples t test. Different groups were tested using the independent samples t test and $P < 0.05$ was considered statistically significant.

RESULTS

Comparison of ABC scores and efficacy grades between the two groups

In order to verify the effect of the groups that can be referenced in this paper and the groups that need to be verified after 4 months of treatment, the ABC scores and efficacy ratings before and after the intervention are shown in table 2. In the pre-intervention ABC scores, there were 32 child patients with severe autism and 16 child patients with moderate autism in the study group. While in the control group, there were 21 cases of child patients with severe autism and 27 cases of child patients with moderate autism. The ABC scores of both the groups before and after the treatment change of natural course were lower than their respective scores before the change of natural course, the post-intervention score of the group needing validation was 37.31, whereas the ABC score of the control group after the change of natural course was 41.71, thus it can be seen that the ABC scores of the group needing validation were significantly less than the group available for reference, $p < 0.05$. Comparison of efficacy levels showed that different groups The difference in overall efficacy comparison was statistically significant $P < 0.05$, the total effective rate of treatment in the group that needs to be verified was 100%, while the total effective rate of treatment in the group that can be referenced was 91.7%, so the total effective rate of the study group was significantly higher than that of the group that can be referenced $P < 0.05$.

Comparison of evaluation scale factors before and after intervention between groups

The effective rate of different groups before and after changing the natural process was obtained from the ABC scale evaluation scores, here in order to conduct a detailed validation analysis of the ABC scale evaluation content under art therapy. Sensory factor, interaction factor, somatomotor, language factor to life self-care as five evaluation indexes to evaluate the effectiveness of the treatment of children with autism before and after changing the natural process between the groups, table 3 shows the evaluation of the treatment of patients before and after the intervention. The patients in the referable group had a pre-intervention sensory factor index score of 7.5, interaction factor index score of 8.55, somatomotor index score of 6.45, language factor index score of 11.05, and self-care of life index score of 8.85, whereas there was a small change in all the indexes in the control group after the intervention, with a sensory factor index score of 9.25, interaction factor index score of 10.9, somatomotor Indicator score 8.05, language factor indicator score 14.15, and self-care indicator score 9.6, so the indicators of the referable group after changing the natural course were higher than the indicator scores before changing the natural course. The patients in the study group had pre-intervention sensory factor indicator scores of 6.15, interaction factor indicator scores of 7.95, somato-motor indicator scores of 6.45, language factor indicator scores

of 10.35, and self-care of life indicator scores of 6.2, whereas the indicators in the group that needed to be verified after changing the natural course showed stronger changes, with sensory factor indicator scores of 12.95, interaction factor indicator scores of 15.25, somato-motor indicator score 15.25, language factor indicator score 19.55, and self-care indicator score 13.25, which shows that there is no statistical significance in the different groups of factor indicator scores before changing the natural process. However, after changing the natural process in the group that obviously needs to be verified, there is no statistical significance between groups for each factor indicator score, and the five factor indicator scores have improved substantially compared to the pre-intervention period, whereas the indicator scores of the control group after the intervention, although improved compared to the pre-intervention period, the improvement is not obvious, and the effect is not significant.

Comparison of social support between groups

To evaluate the level of social support among groups from the perspective of social support theory, the Medical Outcomes Study Social Support Survey - Chinese Version for Medical Patients (MOS-SSS-CM) was employed. This tool was used to assess the level of social support in different groups of patients both before the intervention and after a four-month intervention period. The results, as depicted in table 4, reveal significant improvements in the study group's social support scores post-intervention. Specifically, the practical support score increased from 10.22 to 17.14, marking a 67.71% rise. The message and emotional support score saw a 55.68% increase, climbing from 21.32 to 33.19. The social interactive cooperation score improved by 45.76%, from 11.18 to 17.20. Affective support showed the most substantial growth, with a 75.98% increase from 7.12 to 12.53, and the overall score jumped by 58.72%, from 50.44 to 80.06.

In contrast, the control group exhibited more modest improvements. Their practical support score rose by 22.34%, from 10.70 to 13.09. The message and emotional support score increased by 22.83%, from 21.55 to 26.47. The social interactive cooperation score improved by 23.14%, from 11.32 to 13.94. The affective support score increased by 28.71%, from 7.07 to 9.10, and the overall score improved by 23.62%, from 50.64 to 62.60.

A comparative analysis of the pre-intervention scores using the MOS-SSS-CM indicated no significant differences between the study and control groups. However, post-intervention, the study group demonstrated significantly higher scores across all dimensions and overall social support when compared to the control group, suggesting the efficacy of the intervention in enhancing perceived social support among patients.

Table 1: Three Levels of Enrichment Oriented Social Work Service Strategies

Interventional level	Services	Service Strategy	Service Focus
Patient level	Simulation of Social Life	Class open management	Personal Ability Enhancement
Patient's family and friends level	Volunteer Team for Retirees	Volunteer teams organize their own activities	Interpersonal Relationship Growth
Social level	Social Integration	Out-of-hospital Resource Experience	Respect for Needs

Table 2: ABC scores and efficacy grades before and after intervention ($\bar{x} \pm s$)

Sports event ABC($\bar{x} \pm s$)	Study group (n=48)	Control group (n=48)	t/Z/x ²	P-value
Pre-intervention	71.15±5.94	70.88±3.45	0.228	0.785
Post-intervention	37.31±9.65*	41.71±9.63*	2.234	0.028
Efficacy rating [n (%)]			2.543	0.011
Show an effect	27(56.3)	16(33.3)	/	/
Effective	21(43.7)	28(58.4)	/	/
Ineffective	0(0)	4(8.3)	/	/
Total Effective	48(100)	44(91.7)	4.174	0.041

Table 3: Evaluation of patient treatment before and after intervention ($\bar{x} \pm s$)

Score Factor	Control group (n=48)		Study group (n=48)	
	Pre	Post	Pre	Post
Feeling Factor	7.5000±7.7968	9.2500±7.8262	6.1500±6.8154	12.9500±8.4135
Interaction Factor	8.5500±7.4514	10.9000±8.8252	7.9500±7.4231	15.2500±8.9199
Somatic Movement	6.4500±7.8995	8.0500±9.1334	6.4500±6.9998	15.2500±8.9199
Language Factor	11.0500±6.3285	14.1500±8.4372	10.3500±7.4641	19.5500±7.6809
Self-Care	8.8500±5.9052	9.6000±5.7711	6.2000±4.7749	13.2500±5.4856

Table 4: MOS-SSS-CM scores of patients in group before and after intervention ($\bar{x} \pm s$)

Enterprise	Practical support	Messages and emotional support	Social interactive cooperation	Emotional support	Emotional support
Pre-intervention					
Study group n=48	10.22±1.41	21.32±3.28	11.18±1.64	7.12±0.66	50.44±6.75
Control group n=48	10.70±1.19	21.55±3.84	11.32±1.48	7.07±0.81	50.64±6.87
t-value	1.517	0.384	0.369	0.279	0.121
P-value	0.134	0.702	0.713	0.781	0.904
Post-intervention					
Study group n=48	17.14±2.39	33.19±5.36	17.20±2.57	12.53±1.57	80.06±9.62
Control group n=48	13.09±1.68	26.47±4.02	13.94±2.20	9.10±1.04	62.60±7.94
t-value	8.202	5.934	5.701	10.775	8.281
P-value	<0.001	<0.001	<0.001	<0.001	<0.001

Table 5: Intergroup daily living and social interaction skills ($\bar{x} \pm s$)

Meters	Study group (n=48)	Control group (n=48)	t	P
ADL				
Pre-intervention	40.31±5.28	40.21±6.35	0.087	0.931
Post-intervention	81.33±15.25*	75.15±13.83*	2.083	0.040
Social accomplishment				
Pre-intervention	49.63±6.06	48.56±6.35	0.839	0.404
Post-intervention	93.85±14.07*	86.52±11.21*	2.825	0.006
Problematic behavior				
Pre-intervention	36.58±2.34	36.65±2.36	0.13	0.897
Post-intervention	19.21±4.38*	22.23±4.07*	5.153	0.001

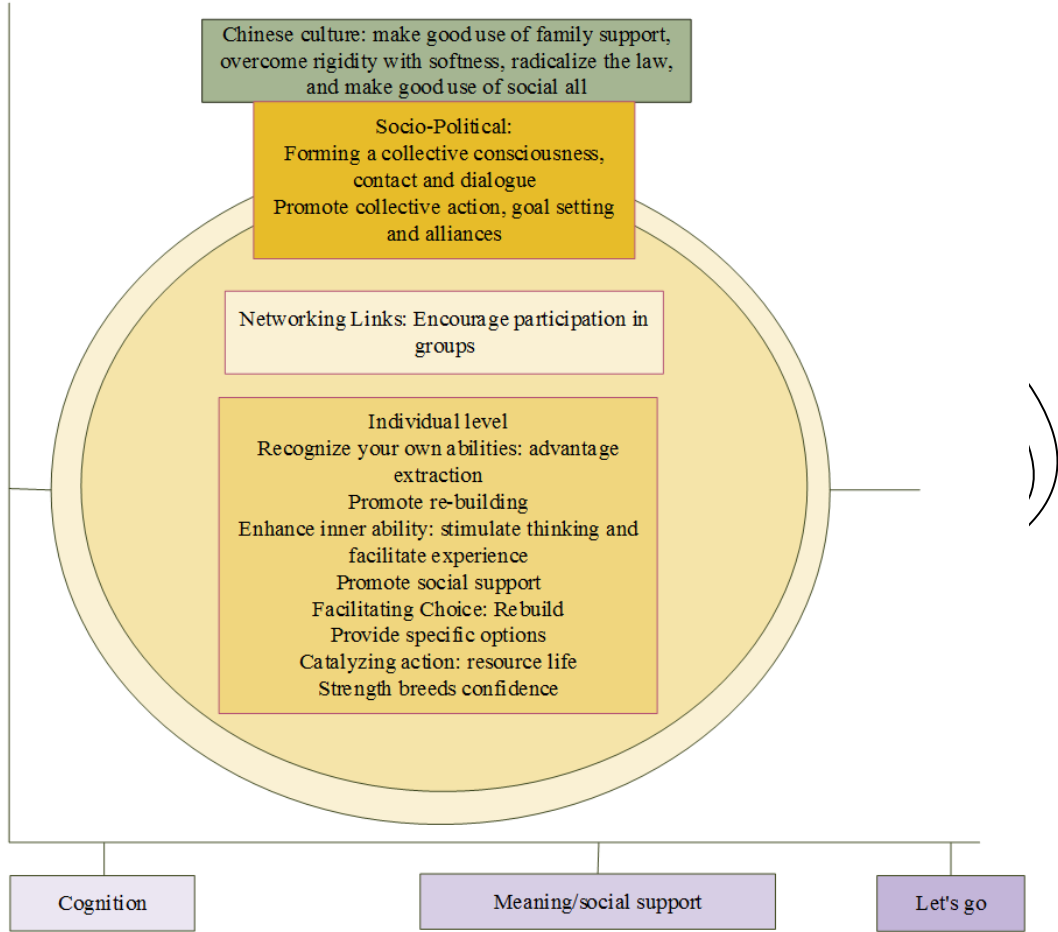


Fig. 1: Social work architecture from the perspective of empowerment theory

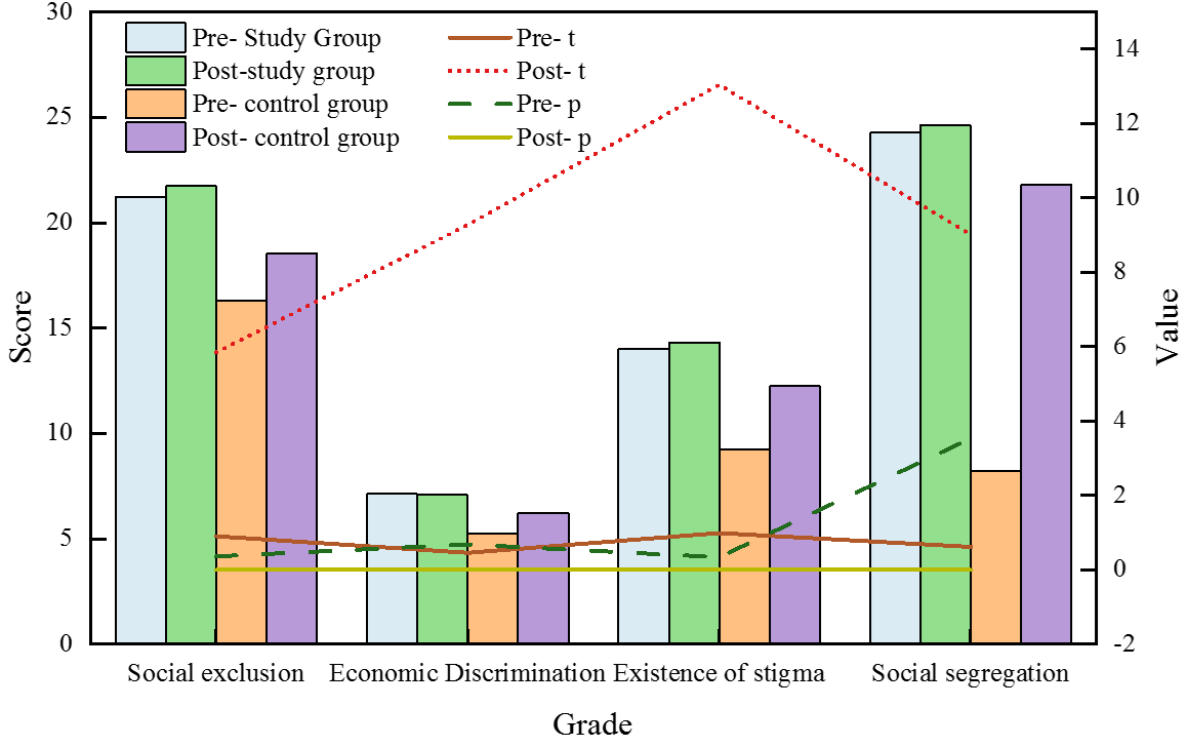


Fig. 2: SIS scores before and after intervention for patients between groups

Comparison of daily living skills and social interaction skills between groups under enrichment activities

The self-assessment scale and The Social Interaction Skills Assessment Scale were used to assess the children's self-assessment before and after the intervention as well as their social skills, and the daily living and social interaction skills between the groups are shown in table 5. In the assessment of daily living skills, the pre-intervention score of the group requiring validation was 40.31 and the post-intervention score was 81.33, which was 101.76% better than the pre-intervention score before changing the natural course. While the control group had a pre-intervention score of 40.21 and a post-intervention score of 75.15, which was an improvement of 86.89% compared to the pre-intervention score, it is clear that the post-intervention score of daily living ability of the research group improved more than that of the control group; in the area of socialization ability, the pre-intervention score of the research group was 49.63 and the post-intervention score of the research group was 93.85, which was an improvement of 89.10% compared to the pre-intervention score. In the control group, the pre-intervention score was 48.56 and the post-intervention score was 86.52, which was 78.17% higher than the pre-intervention score, obviously the post-intervention social competence score of the study group improved more than that of the control group; in the area of problematic behaviors, the pre-intervention problematic behaviors score of the study group was 36.58, and the score after changing the natural process dropped to 19.21, which was a decrease of 47.48%. The problem behavior score of the referable group was 36.65 before the intervention and dropped to 22.23 after the intervention, a decrease of 39.35%, so the effect of the group that needed to be verified after changing the natural process in terms of problem behavior was more pronounced than the control group.

SIS scores of patients before and after intervention between groups

The Social Influence Scale SIS was used to assess the stigma of the disease in different groups of patients before changing the natural course and after 4 months of intervention. fig. 2 shows the SIS scores of the patients before and after the intervention between the groups, the social exclusion score of the study group was 21.22 before the intervention and became 16.29 after the intervention, which is a decrease of 23.23%. The economic discrimination score in the pre-intervention was 7.14 and post-intervention was 5.27, a decrease of 26.19%. The internal shame score in the pre-intervention was 14.04 and post-intervention was 9.25, a decrease of 34.12%. The social isolation score was 24.27 before the natural course of change and 18.24 after the natural course of change, a decrease of 24.85%. The overall score of the study group was 66.67 before the change in natural course and 49.05 after the change in natural course, a decrease of 26.43%. The social exclusion score for the

referable group was 21.74 before the natural course of change and became 18.54 after the natural course of change, a decrease of 14.72%. The economic discrimination score was 7.08 before the intervention and 6.24 after the intervention, a decrease of 11.86%. The pre-intervention intrinsic shame score was 14.33 and post-intervention it was 12.24, a decrease of 14.58%. The social isolation score was 24.63 pre-intervention and 21.81 post-intervention, a decrease of 11.45%. The overall score of the control group was 68.18 pre-intervention and 58.83 post-intervention, a decrease of 13.71%. After the intervention it was found that the treatment effect of the study group was significantly better than that of the control group $P < 0.05$, so the treatment method in this paper has important clinical significance for the rehabilitation of the children.

DISCUSSION

Our study's findings underscore the pivotal role of pharmacological intervention in the comprehensive treatment plan for children with autism. The modulation of neurotransmitters such as dopamine and serotonin through medication has been instrumental in attenuating the core symptoms of autism, including reducing anxiety and repetitive behaviors and enhancing social interaction abilities (Syriopoulou-Delli and Gkiolnta E, 2022). This neurochemical approach complements behavioral interventions, providing a stable emotional baseline that facilitates the child's engagement in therapeutic activities and bolsters the enduring impact of such interventions (Hu, 2022).

The synergistic effect of medication and behavioral therapy is particularly noteworthy. By managing the underlying neurochemical imbalances, pharmacological treatment prepares the groundwork for behavioral therapy to be more effective (Amirbekova and Abdikerova, 2021). This is evident in our study, where the experimental group, which received both medication and behavioral therapy, showed superior outcomes compared to the control group which received only behavioral therapy.

However, the variability in treatment response among individuals with autism suggests that a one-size-fits-all approach is not suitable. The challenge lies in the complexity of autism, where genetic, environmental, and neurobiological factors contribute to the heterogeneity of the condition (Sutarjo, 2023). Therefore, the development of personalized treatment plans that consider an individual's unique profile is crucial. This includes the careful selection of medication, dosage adjustments, and regular monitoring of treatment response and side effects (Yuan et al., 2021).

The implications of our findings advocate for a more nuanced understanding of autism treatment, where pharmacological intervention is not viewed in isolation

but as part of an integrated care model. This model should also incorporate family support, educational strategies, and community-based programs to address the multidimensional needs of children with autism and their families (Liang *et al.*, 2022; Aqdassi *et al.*, 2021).

CONCLUSION

The addition of pharmacological intervention to conventional therapies provides enhanced therapeutic benefits in the rehabilitation of children with autism. This approach significantly improves core symptoms, particularly social communication and behavior management, supporting its integration into clinical practice. Further research is recommended to optimize individualized treatment protocols and evaluate long-term outcomes.

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