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The effectiveness of personalized medication based on drug-related genes, for schizophrenia patients with resistance to traditional drugs.

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Keywords: inflammatory cytokines; neurotrophic factors; PANSS; BPRS; social skills; ADL; CYP2D6.

Abstract. We aimed to study the impact of personalized medication based on drug-related genes for schizophrenia patients with resistance to traditional drugs. One hundred and ten schizophrenia patients who sought treatment at our medical facility between June 2021 and February 2023 were chosen and divided at random into two groups: one group (n=55) received conventional medication, while the other group (n=55) received personalized medication based on their genetic profile. The study compared the levels of inflammatory cytokines and neurotrophic factors, as well as the scores on the Positive and Negative Symptoms Scale (PANSS), Brief Psychiatry Rating Scale (BPRS), Social Skills Psychometric Instruments (SSPI), and Ability of Daily Living Scale (ADL) between the two groups. Following the treatment, both groups exhibited reduced levels of TNF-α and IL-1β compared to pre-treatment levels, with the gene-guided group showing even lower levels ($p<0.05$). Conversely, the levels of NGF and BDNF increased in both groups post-treatment, with the gene-guided group demonstrating even higher levels ($p<0.05$). Additionally, the PANSS and BPRS scores decreased in both groups after treatment, with the gene-guided group showing even lower scores ($p<0.05$). On the other hand, both groups'

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SSPI and ADL scores increased post-treatment, with the gene-guided group exhibiting higher scores ($p<0.05$). The overall efficacy of the treatment in the gene-guided group was superior to that in the conventionally treated group ($p<0.05$). Personalized medication guided by pharmacogenetics has the potential to enhance cognitive function, facilitate neurological recovery, improve social functioning, and enhance the daily living skills of individuals with schizophrenia, thereby facilitating their successful reintegration into society.

La eficacia de la medicación personalizada basada en genes relacionados con fármacos, para pacientes con esquizofrenia resistente a los fármacos tradicionales.

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Palabras clave: citoquinas inflamatorias; factores neurotróficos; PANSS; BPRS; habilidades sociales; ADL; CYP2D6.

Resumen. Nuestro objetivo fue estudiar el impacto de la medicación personalizada basada en genes relacionados con medicamentos para pacientes con esquizofrenia resistentes a los medicamentos tradicionales. Se seleccionaron 110 pacientes con esquizofrenia que buscaron tratamiento en nuestra instalación médica entre junio de 2021 y febrero de 2023, y se dividieron al azar en dos grupos: un grupo (n=55) recibió medicación convencional, mientras que el otro grupo (n=55) recibió medicación personalizada basada en su perfil genético. El estudio comparó los niveles de citocinas inflamatorias y factores neurotróficos, así como las puntuaciones en la Escala de Síntomas Positivos y Negativos (PANSS), la Escala Breve de Evaluación Psiquiátrica (BPRS), los Instrumentos Psicométricos de Habilidades Sociales (SSPI) y la Escala de Habilidades de Vida Diaria (ADL) entre los dos grupos. Después del tratamiento, ambos grupos mostraron niveles reducidos de TNF-α y IL-1β en comparación con los niveles previos al tratamiento, con el grupo guiado por genes mostrando aún niveles más bajos ($p<0,05$). Por el contrario, los niveles de NGF y BDNF aumentaron en ambos grupos después del tratamiento, con el grupo guiado por genes demostrando incluso niveles más altos ($p<0,05$). Además, las puntuaciones de PANSS y BPRS disminuyeron en ambos grupos después del tratamiento, con el grupo guiado por genes mostrando incluso puntuaciones más bajas ($p<0,05$). Mientras que las puntuaciones de SSPI y ADL aumentaron en ambos grupos después del tratamiento, con el grupo guiado por genes mostrando puntuaciones más altas ($p<0,05$). La eficacia general del tratamiento en el grupo guiado por genes fue superior a la del grupo tratado convencionalmente ($p<0,05$). La medicación personalizada guiada por farmacogenética tiene el potencial de mejorar la función cognitiva, facilitar la recuperación neurológica, mejorar el funcionamiento social y mejorar las habilidades de vida diaria de las personas con esquizofrenia, facilitando así su reintegración exitosa en la sociedad.

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INTRODUCTION

Schizophrenia stands as one of the most prevalent mental disorders globally, often afflicting young adults and characterized by prolonged duration, frequent relapses, and abrupt onset [1]. Individuals with schizophrenia typically exhibit disturbances in thought, consciousness, behavior, and emotion, along with inappropriate psychological and physical activities. Concurrently, they experience negative emotions encompassing fear, anger, and depression. In severe cases, some patients may even demonstrate self-destructive tendencies or resort to suicide [2]. Integration into society proves challenging for schizophrenia patients due to their limited sense of affiliation and prominent negative emotional states. These significantly hamper their subjective well-being and self-esteem [3,4]. While antipsychotic medications can effectively manage the condition for the majority of schizophrenia patients, approximately 30% exhibit poor or partial responses to these treatments, categorizing them as drug-resistant individuals [5]. Thus, improving the efficacy of antipsychotics on mental diseases has become an attractive issue in the psychiatry department. At the same time, individualized medication can be made based on genetic evidence derived from the analysis of drug-related genes and gene polymorphisms to select the drugs and doses more precisely [6]. Gene detection has been widely applied to develop antipsychotic drugs, but fewer studies report the efficacy of drugs on drug-resistant patients with schizophrenia. Consequently, we carried out this study to investigate the efficacy of drug-related-gene-guided individualized medication on drug-resistant patients with schizophrenia and its effect on patients.

PATIENTS AND METHODS

Subjects

One hundred and ten individuals diagnosed with schizophrenia admitted to the Department of Psychosomatic Medicine at The First People's Hospital of Chenzhou, Luojiajing, Chenzhou, Hunan, People's Republic of China, during the period spanning June 2021 to February 2023, were enrolled in this study. They were subsequently categorized into the regular medication group (Group A) and the gene-guided medication group (Group B), each comprising 55 patients.

Comprehensive information about the study was provided to all patients and their families, and written informed consent was obtained. The Ethical Committee of the Hospital approved the study.

Criteria for inclusión: 1. Patients with manifestations conforming to the diagnostic criteria of schizophrenia of *The Diagnostic and Statistical Manual of Mental Disorders (4th edition). 2.* Patients aged between 18 and 60 years, with no response to the high-dose treatment of three kinds of antipsychotics. 3. Patients with a disease course not shorter than five years.

Criteria for exclusion: 1. Patients with other diseases. 2. Patients who had received appropriate treatment prior to this study. 3. Patients with communication difficulties. 4. Patients who were uncooperative with the staff. 5. Patients with severe adverse responses to the drugs used in this study. 6. Patients with a history of drug use that might affect the result of this study.

Methods

In the current study, two distinct approaches to medication were compared: Group A received antipsychotics selected by physicians based on their expertise, whereas Group B received personalized medication determined through drug-related gene tests and the evaluation of physicians and clinical pharmacists.

Group A

The specific antipsychotic medications used in Group A included Haloperidol at doses of 2-10 mg per day, chosen for pa-

tients with positive symptoms like hallucinations and delusions based on its efficacy for these symptoms; Risperidone at 2-6 mg per day, selected for patients with both positive and negative symptoms given its broader efficacy profile; Olanzapine at 5-20 mg per day, used for patients with predominant negative symptoms like social withdrawal due to its efficacy for these symptoms; Quetiapine at 150-750 mg per day, chosen for patients with mood or sleep issues given its sedating and mood-stabilizing effects; and Aripiprazole at 10-30 mg per day, used for patients susceptible to side effects like tardive dyskinesia due to its lower risk of these effects.

Group B

In the Group B, medication was personalized based on drug-related gene tests and the collaborative analysis of physicians and clinical pharmacists. The gene tests identified genetic variations that could influence an individual's response to specific antipsychotic medications. For example, the CYP2D6 gene was of particular interest, as it encodes an enzyme responsible for the metabolism of many antipsychotic drugs. Variations in this gene can lead to differences in how quickly medications are metabolized, potentially affecting their efficacy and side-effect profiles [7,8].

Patients with the 'poor metabolizer' phenotype, characterized by certain SNP combinations, were prescribed lower doses or given antipsychotics not primarily metabolized by the CYP2D6 enzyme to avoid drug accumulation and subsequent side effects. In contrast, 'rapid metabolizers' may have required higher doses or more potent medications to achieve therapeutic drug levels.

The treatment protocol was adjusted within two weeks after the gene test, including maintaining, increasing, or reducing the initial drug dose or its combination with other antipsychotics or switching to other antipsychotics. The specific medications and doses used were determined based on a comprehensive analysis of the recommended drugs by the DSM4, the patient's gene test results, and the individual's symptomatology and treatment history.

The distribution of crucial CYP2D6 genotypes in Group B were as follows:

- Poor metabolizers: 7 patients (12.7%).
- Intermediate metabolizers: 18 patients (32.7%).
- Normal metabolizers: 25 patients (45.5%).
- Ultra-rapid metabolizers: 5 patients (9.1%).

Medications were adjusted based on this genotype data. For example, poor metabolizers were prescribed lower doses of risperidone, switched from Haloperidol to Quetiapine, or changed from Olanzapine to Aripiprazole. Ultra-rapid metabolizers were given higher doses of Haloperidol or switched from Quetiapine to Olanzapine. Table 1 shows examples of specific medication changes made.

Gene test

A customized tube obtained from Shanghai Conlight Medical Laboratory Co., Ltd was utilized to gather detached cells from the oral epithelium. This was achieved by gently swabbing the buccal region of the mouth with a cotton swab. The collected cells were then securely sealed within the tube, ensuring no contact with external materials. Two sets of samples were procured from both the left and right sides of the mouth for subsequent DNA extraction. These samples were subsequently stored at room temperature.

The genotypes and allele frequencies of three single nucleotide polymorphisms (SNPs) within the CYP2D6 gene (rs16947, rs1065852, and rs5030865) were examined. The analysis used the general sequencing kit (NovaSeq 6000 Reagent Kits) and the fluorescence in situ hybridization (FISH Tag™ DNA Multicolor Kit by Invitrogen).

Table 1
Medication adjustments based on CYP2D6 genotypes in Group B.

Genotype	Patients n (%)	Initial Medication and Dose	Adjusted Medication and Dose	Rationale for Adjustment
Poor metabolizer	7 (12.7%)	Haloperidol 5mg daily	Quetiapine 100mg twice daily	Haloperidol is primarily metabolized by CYP2D6 [31]. Due to poor metabolism, it was switched to quetiapine, which has alternate metabolic pathways to avoid drug accumulation.
		Risperidone 3mg daily	Risperidone 1mg daily	Risperidone dosage was reduced by 50% to avoid side effects due to poor CYP2D6 metabolism [32].
Intermediate metabolizer	18 (32.7%)	Olanzapine 10mg daily	Olanzapine 5mg daily	The dose was reduced as metabolism was expected to be slower in intermediate metabolizers.
		Risperidone 4mg daily	Risperidone 2mg daily	
Normal metabolizer	25 (45.5%)	Haloperidol 5mg twice daily	No change	Normal metabolizer phenotype indicates haloperidol metabolism is expected to be typical. No dose adjustment was needed.
		Quetiapine 400mg daily	Quetiapine 400mg twice daily	As a normal metabolizer, can tolerate higher doses of quetiapine. The dose was increased for improved efficacy.
Ultra rapid metabolizer	5 (9.1%)	Risperidone 4mg daily	Risperidone 6mg daily	More rapid CYP2D6 metabolism is expected in ultra-rapid metabolizers. The risperidone dose was increased by 50% to ensure therapeutic levels were achieved.
		Quetiapine 400mg daily	Olanzapine 20mg daily	Switched from quetiapine to olanzapine due to concerns that quetiapine might be metabolized too rapidly in ultra-rapid metabolizers, affecting its effectiveness.

Genomic analysis and protocol adjustment

Genomic analysis was conducted on patients belonging to Group B, encompassing the identification of metabolic, responsive, and toxic gene phenotypes, along with their distribution frequencies. Within two weeks after the gene testing, the treatment regimen was modified based on a comprehensive analysis that considered the recommendations provided by the DSM4 and the outcomes of the gene tests.

These adjustments entailed the maintenance, augmentation, or reduction of the initial drug dosage, either in isolation or in combination with other antipsychotic medications. In some cases, a transition to alternative antipsychotic drugs was also considered. The recommended medications were categorized into primary, secondary, and tertiary options. Furthermore, medications were selected sequentially, following the gene test outcomes, and were tagged as suitable for direct use, utilization with caution, or utilization with caution accompanied by frequent monitoring.

Observation of indicators

Before and after treatment, a fasting 6 mL elbow venous blood sample was collected from each patient and subsequently centri-

fuged at 3000 rpm to facilitate the separation of the supernatant. This supernatant was then carefully preserved at a temperature of -70°C.

The quantification of TNF-α, IL-1β, NGF, BDNF, PI3K, and mTOR levels was done utilizing a double sandwich enzyme-linked immunosorbent assay (ELISA). The procedure encompassed the following steps: an ELISA plate was appropriately labeled at room temperature, and a standard curve was meticulously prepared using the appropriate standard reagents. The patient samples and the standard reagents were appropriately diluted and introduced into individual wells (100 μL per well). Subsequently, incubation was carried out at 37°C within a humid environment.

Following the incubation period, the plate underwent repeated rinsing steps, after which an antibody-working solution was meticulously added to each well at a dilution of 1:100 (100 μL per well). This was followed by an additional incubation at 37°C for 45 minutes. The plate was then rinsed again, and solutions of TNF-α, IL-1β, NGF, BDNF, PI3K, and mTOR were introduced to the respective wells (100 μL per well), followed by another incubation under humid conditions for 45 minutes.

The enzymatic reaction was eventually halted by introducing a termination solution (100 μL per well). Subsequently, a microplate reader obtained an optical density reading at a wavelength of 450 nm. This reading was then utilized to calculate the alterations in the concentrations of the factors mentioned above.

The assessment of clinical responses in patients involved the utilization of the Positive and Negative Syndrome Scale (PANSS) and the Brief Psychiatric Rating Scale (BPRS) [9,10]. The PANSS comprises 30 items, each scored on a scale of 1 to 7. Similarly, the BPRS encompasses five items, specifically targeting anxiety, depression, thought disturbance, and excitability, with a pivotal score of 35 points. It should be noted that both PANSS and BPRS scores exhibit a negative correlation with the observed clinical response. In other words, as the scores on these scales increase, the corresponding clinical response tends to decrease, indicating a greater severity of symptoms.

Social skills psychometric instruments (SSPI) and activities of daily living (ADL) scale were used to evaluate patients' social and living abilities [11,12]. The SSPI scale includes ten dimensions, such as familial activity, social activity, responsibility, and planning, and scores according to the following criteria: 1 point for no anomaly or only slight functional defect; 2 points for a definite functional defect; 3 points for severe functional defect. Patients who scored not fewer than 2 points should be considered as having social dysfunction. The ADL scale includes 14 items, such as diet, medication, and housekeeping, and patients are scored as per the following criteria: 1. Patients can take care of themselves independently; 2. Patients have difficulties in taking care of themselves independently; 3. Patients need help in taking care of themselves; 4. Patients fail to take care of themselves independently.

Evaluation of clinical response

Clinical responses were classified into three grades: remarkable response, response, and failure. Remarkable response: no psychotic symptoms, with a decrease in PANSS scores between 50% and 74%. Response: no significant psychotic symptoms, with a decrease in PANSS score between 25% and 49%. Failure: no significant improvement in psychotic symptoms, with a decrease in PANSS score lower than 25%. Total effectiveness rate = Rate of remarkable response + rate of response.

Statistical methods

The SPSS 20.0 software was applied for data analysis. Measurement data were described as means ± standard deviations ($\bar{X}\pm SD$), and the difference between the two groups was validated by an independent sample *t*-test. Enumeration data were expressed

as ratios, and the chi-square test validated the difference. $P<0.05$ indicated that the difference had statistical significance.

RESULTS

Demographic characteristics

In Group A, there were 32 males and 23 females, aged 25 to 67 years (mean ± SD: 44.5±20.1 years). Education varied: 21 had diplomas below high school, 18 had high school diplomas, and 16 had diplomas beyond high school. Illness duration ranged from 2 to 24 years (mean ± SD: 13±9 years), with onset age from 18 to 37 years (mean ± SD: 24±9 years); three patients reported familial cases. In Group B, 30 males and 25 females were aged 26 to 67 years (mean ± SD: 45.5±20.1 years). Education-wise, 25 had diplomas below high school, 16 had high school diplomas, and 14 had diplomas beyond high school. Illness duration ranged from 2 to 25 years (mean ± SD: 12±9 years), with onset age from 18 to 35 years (mean ± SD: 25±9 years); four patients reported familial cases (Table 2).

Comparison of the inflammatory cytokines

As depicted in Fig. 1, a comparison of TNF-α and IL-1β levels between the two groups before treatment revealed no statistically significant differences ($p>0.05$). However, substantial reductions were observed following treatment in both TNF-α and IL-1β levels. Notably, the declines in Group B were more pronounced than Group A's ($p<0.05$).

Comparison of nerve growth factors between the two groups

Before treatment, we found no significant differences in the levels of NGF and BDNF between the two groups ($p>0.05$); after treatment, significant increases were found in the levels of NGF and BDNF of the two groups, while the increases in Group B were more evident ($p<0.05$), (Fig. 2).

Comparison of the PANSS and BPRS scores between two groups

As shown in Fig. 3, comparing the scores of PANSS and BPRS between the two groups before treatment showed no significant differences ($p>0.05$). However, after treatment, significant decreases were noted in scores of PANSS and BPRS, and decreases in Group B were more pronounced than those in Group A ($p<0.05$).

Social function and daily living activities

Before treatment, we found no significant differences when comparing the scores

Table 2
Demographic characteristics.

		Group A	Group B
Participants		55	55
Sex	Male	32	30
	Female	23	25
Age (Mean ± SD)		44.5 ± 20.1	45.5 ± 20.1
Education Level	Lower Secondary	21	25
	Diploma	18	16
	Post-High School	16	14
Disease Duration (Mean ± SD)		13 ± 9	12 ± 9
Age of Onset (Mean ± SD)		24 ± 9	25 ± 9
Familial Positivity		3	4

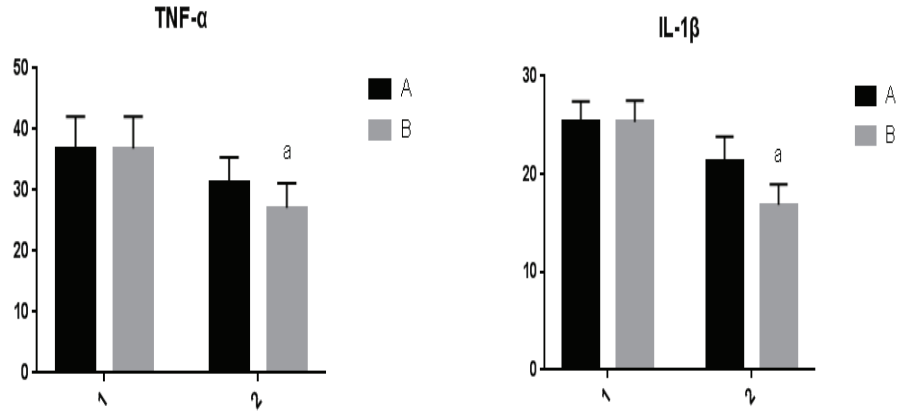

Fig. 1. Comparison of the levels of TNF-α and IL-1β between two groups (ng/mL).
Note: Group A for the regular medication group, Group B for the gene-guided medication group, 1 for before treatment, 2 for after treatment; a for $p<0.05$.

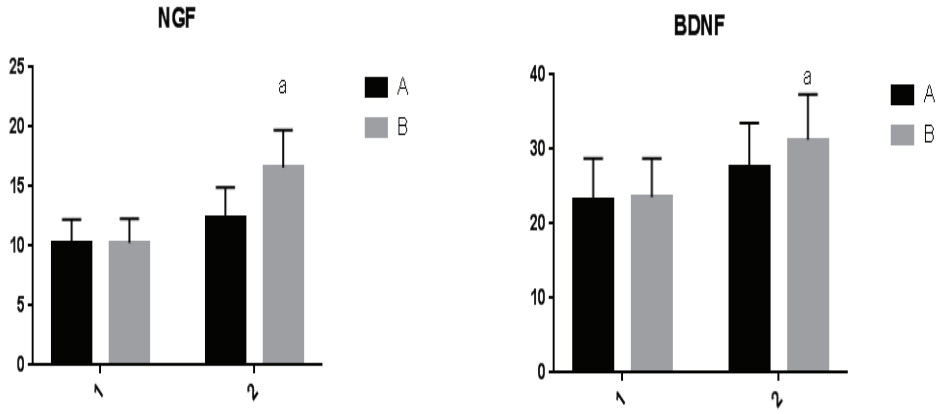

Fig. 2. Comparison of the levels of NGF and BDNF between two groups (ng/mL)
Note: Group A for the regular medication group, Group B for the gene-guided medication group, 1 for before treatment, 2 for after treatment; a for $p<0.05$.

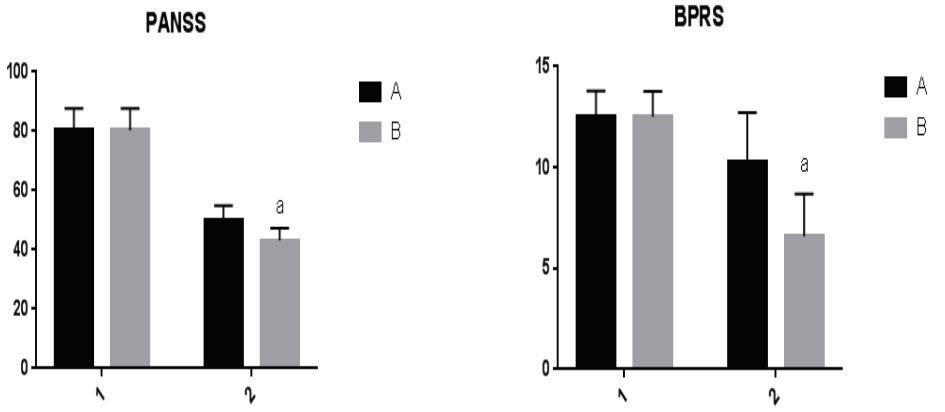

Fig. 3. Comparison of the Positive and Negative Syndrome Scale (PANSS) and the Brief Psychiatric Rating Scale (BPRS) scores between two groups (Points).
Note: Group A for the regular medication group, Group B for the gene-guided medication group, 1 for before treatment, 2 for after treatment; a for $p<0.05$.

of SSPI and ADL between the two groups (p >0.05); after treatment, significant increases were found in the scores of SSPI and ADL of both groups, while the increases in Group B were more noticeable (p<0.05, Fig. 4).

Comparison of the effectiveness rate between two groups

The total effectiveness rate in Group B was much higher than that in Group A (p< 0.05; Table 3).

Comparison of the rate of adverse events between two groups

As shown in Table 4, the rate of adverse events in patients of Group B was lower than that in Group A, although this difference had no statistical significance (p>0.05).

DISCUSSION

Schizophrenia represents a severe mental disease, and antipsychotics remain the predominant treatment for managing schizophrenia. However, about one-third of patients with schizophrenia respond poorly to these drugs [13]. Clinically, diagnosis or even treatment for schizophrenia mainly depends on the expertise of clinicians or the evaluation by scales [14]. Currently, the prevalence of schizophrenia remains high, and an available but simple medication that can perfect the precise treatment is an ideal strategy for schizophrenia treatment [15]. Continuous progress in pharmaceutics and pharmacogenomics enables the detection of drug-related genes to guide the clinical use of psychotropic drugs [16]. Gene tests before medication can clarify the patients' genotype, thus promoting rational, precise, and individualized medication [17].

The essential gene examined was CYP2D6, which encodes a critical enzyme involved in metabolizing many commonly used antipsychotics [18]. Patients received drug changes according to their CYP2D6 genotype to maximize efficacy and reduce adverse effects, as shown in Table 1. Poor metabolizers, possessing alleles leading to nonfunctional CYP2D6, were switched from Haloperidol and risperidone to alternative antipsychotics not extensively metabolized by this enzyme, like quetiapine [19]. This avoids drug accumulation and toxicity in these patients from impaired metabolism. In contrast, doses were increased for normal or ultra-rapid metabolizers to achieve adequate plasma concentrations.

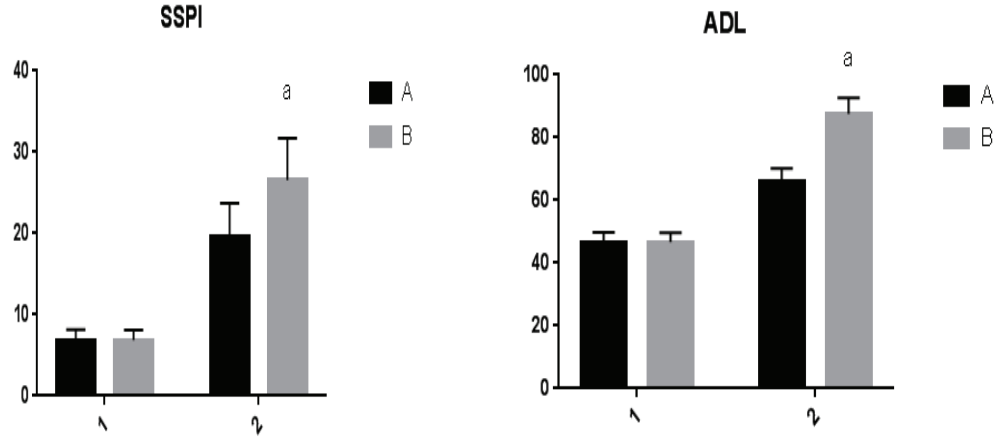

Fig. 4. Comparison of social function and activity of daily living between two groups (Points)
Note: Group A for the regular medication group, Group B for the gene-guided medication group, 1 for before treatment, 2 for after treatment; a for p<0.05.
-Social skills psychometric instruments (SSPI) and activities of daily living (ADL) scores.

Table 3
Comparison of the effectiveness rate between two groups

Group	Case (n)	Remarkable response	Response	Failure	Effectiveness rate*
Group A	55	25	20	10	47 (85.45)
Group B	55	28	25	2	53 (96.36)
c^2					5.986
P					0.014

*Values are expressed as n (%).

Table 4
Comparison of the rate of adverse events between two groups.

Group	Case (n)	Leukopenia	Constipation	Insomnia	Anomaly in blood glucose/lipid	Rate of adverse event*
Group A	55	1	1	2	1	5 (9.09)
Group B	55	0	2	0	1	3 (5.45)
c^2						0.539
P						0.462

*Values are expressed as n (%).

The improved outcomes with gene-guided treatment are biologically plausible based on the pharmacokinetics of antipsychotics. Variations in CYP2D6 polymorphisms can profoundly impact drug exposure by causing variations in metabolic capacity across different genotypes. CYP2D6 is an essential drug-metabolizing enzyme that contributes to the metabolism of 15-25% of all clinically used drugs. Genetic variations in the CYP2D6 gene can lead to considerable phenotypical interindividual differences in CYP2D6-dependent drug metabolism [20]. A study by Novalbos *et al* (2010), examining the relationship between the CYP2D6 genotype and the effects of risperidone found that individuals with different metabolizer phenotypes (ultrarapid metabolizers (UMs), extensive metabolizers (EMs), intermediate metabolizers (IMs), and poor metabolizers (PMs)) displayed distinct pharmacokinetic patterns. PMs and IMs exhibited higher levels and longer half-life of risperidone, while UMs and EMs had higher levels of 9-hydroxy risperidone [21]. Elmokadem *et al*. [22] conducted another study on aripiprazole, an antipsychotic, revealing significant time-to-effect differences between CYP2D6 EMs and PMs. This suggests a necessity for customized dosing strategies for PMs [22] and that tailoring medication and dosage based on CYP2D6 activity can optimize plasma levels, potentially reducing side effects in PMs and improving efficacy in rapid metabolizers

According to a current clinical study, schizophrenia is somehow related to the levels of inflammatory cytokines. For instance, TNF-α and IL-1β are clinically common inflammatory cytokines that can be used to evaluate the patients' inflammation state more accurately [23]. This study uncovered abnormal elevations in inflammatory cytokine levels among individuals with schizophrenia. With the aid of gene tests to inform individualized medication, the levels of TNF-α and IL-1β were reduced in patients. These results imply a direct association between inflammatory cytokines and schizophrenia, indicating that tailored medication can effectively mitigate inflammatory cytokine levels and enhance drug efficacy.

As a nerve growth factor, NGF can regulate the growth and development of neurons in the peripheral and central nervous system, maintain neurons' survival, promote synaptic growth, and restore nerve function[24,25]. BDNF, as a member of the family of neurotrophic factors, mainly distributes in the central nervous system and the endocrine system, restores the survival of damaged neurons and improves the functions in memory and learning [26,27]. In the present study, a decline in levels of NGF and BDNF was observed following the onset of schizophrenia. However, with the application of gene tests to guide individualized medication, it was observed that the levels of NGF and BDNF could be elevated in patients with schizophrenia. This finding indicates that personalized medication has the potential to facilitate the restoration of patients' learning and memory capacities, as well as promote the recovery of nerve function.

Since physicians may not provide the optimal choice in the efficacy and safety of antipsychotics according to their expertise or evaluation results, precise individualized medication is necessary for improving social function and activities of daily living [28,29]. The PANSS scale is a clinically established tool for assessing mental functioning, encompassing positive and negative symptom dimensions. The SSPI scale is applicable for gauging the social functionality of individuals with epilepsy-related mental disorders, whereas the ADL scale serves to evaluate the daily living activities of patients grappling with mental illnesses [30]. In the present study, we discovered that personalized medication, guided by genetic tests, has the potential to decrease PANSS scores while simultaneously elevating SSPI and ADL scores. These findings imply that this approach may effectively address mental symptoms and enhance the social functioning and daily activities of individuals dealing with schizophrenia.

In conclusion, the utilization of personalized medication guided by genetic testing has the potential to enhance the effectiveness of drugs. This improvement can enhance learning and memory capabilities in individuals with schizophrenia, facilitating the restoration of neural function and bolstering social engagement and daily activities. Ultimately, this approach aids patients in transitioning back to their daily lives. Furthermore, this strategy holds the promise of refining drug selection and dosages and providing guidance for developing treatment protocols. As a result, it enables the realization of precise treatment using psychotropic medications.

Conflict of competence

The authors declare no conflict of interest.

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Authors' contribution

The present study involved a collaborative effort where S.Z. provided expertise in gene-based medication, conducted data analysis, and contributed to result interpretation; GZ coordinated the study, collected and organized data, and drafted the manuscript; ZW contributed expertise in gene-based medication, assisted in data interpretation, and critically reviewed the manuscript; LW contributed to the litera-

ture review, performed statistical analysis, and assisted in manuscript revisions; M.Z assisted in data collection and participated in data analysis and J.H supervised the study, contributed to data analysis and interpretation, and provided overall guidance in manuscript preparation.

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