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Original Article

Network pharmacology of Huatan Tongluo decoction and clinical effects of its combination with acupuncture in the treatment of stroke

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Abstract: Objective: This study was carried out to probe the clinical effect and mechanism of Huatan Tongluo decoction combined with acupuncture in the treatment of patients with ischemic stroke. Methods: The clinical data of 100 patients with ischemic stroke were retrospectively collected. On the basis of treatment method, they were split into two groups, each with 50 cases: the conventional treatment group (acupuncture) and the combined treatment group (Huatan Tongluo decoction + acupuncture). After treatment, the neurological function and clinical therapeutic effects of the two groups were evaluated. The treatment of ischemic stroke with Huatan Tongluo decoction was studied by the method of traditional Chinese medicine (TCM) network pharmacology. Resources from databases such as GeneCards, TCMSP, PubChem, Swiss Target Prediction, String, and WebGestalt were integrated, in order to screen for targets of stroke treatment, the active compound composition of Huatan Tongluo decoction, and the targets of compound composition by the use of Cytoscape and R language software. Finally, from the perspective of a protein-protein interaction (PPI) co-expression network, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis, the significance of Huatan Tongluo decoction in the treatment of ischemic stroke was discussed. Results: The total effectiveness rate in the combined treatment group was superior to the conventional treatment group. The combined group had higher scores of neurological function, limb movement function, and ability to perform daily living tasks than the conventional treatment group (all $P < 0.05$). 368 pharmacological targets for Huatan Tongluo decoction and a total of 5690 ischemic stroke targets were retrieved from the database, and 215 intersection targets were found. The results of the PPI network indicated that 43 targets, including *EGFR* (epidermal growth factor receptor), *SRC* (proto-oncogene, non-receptor tyrosine kinase), *PTPN11* (protein tyrosine phosphatase non-receptor type 11), *PIK3CA* (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha), *AKT1* (serine/threonine kinase 1), *VEGFA* (vascular endothelial growth factor A), *STAT3* (signal transducer and activator of transcription 3), and *FYN* (FYN proto-oncogene, Src family tyrosine kinase), had the strongest interactions, so they could be used as targets for subsequent basic research verification. The results suggested that pathways such as vascular endothelial growth factor (VEGF) signaling pathway and other pathways were enriched. Conclusion: The combination of Huatan Tongluo decoction and acupuncture can help patients with sequelae of stroke promote the regaining of neurological function, thus improving their movement and enhancing their abilities to perform daily living. Huatan Tongluo decoction can mediate the VEGF signaling pathway and other pathways to treat ischemic stroke.

Keywords: Huatan Tongluo decoction, molecular mechanisms, acupuncture, stroke, clinical effect, network pharmacology

Introduction

Cerebral stroke is a disorder brought on by the sudden rupture of blood vessels in the brain or the inability of blood to flow to the brain owing to blocked blood vessels, causing brain tissue damage including ischemic and hemorrhagic stroke. Ischemic stroke has a higher incidence than hemorrhagic stroke, accounting for 87% of all strokess [1]. Stroke has a high mortality, disability rate, and recurrence rate. Research results show that about three-quarters of surviving stroke patients lose the ability to work to varying degrees [2]. Therefore, early effective promotion of neurological function recovery in stroke patients is essential to improving their

ability to labor and perform daily living, as well as reducing the recurrence rate. According to clinical investigations, traditional Chinese medicine (TCM) provides some benefit for increasing stroke patients' neurological functional recovery [3]. Acupuncture can regulate Qi and blood, warm meridians, and activate collaterals. Acupuncture therapy has a significant effect on stroke [4, 5]. Huatan Tongluo decoction is a TCM decoction including Danshen (Radix Salviae), Tianma (Gastrodia), Banxia (Pinelliae), Fuling (Poria), Baishu (Atractylodes), Xiangfu (Cyperi Rhizoma), Dahuang (Radix Rhei Et Rhizome), Dannanxing (Arisaema heterophyllum Blume), and Tianzhuhuang (Bambusa textilis McClure). Its main role is to remove dampness, phlegm, blood circulation, and collaterals [6]. According to our knowledge, the mechanism of Huatan Tongluo decoction in the treatment of stroke has not been clarified. Therefore, this study retrospectively analyzed the effect of Huatan Tongluo decoction and acupuncture on the repair of neurologic function in patients with sequelae of ischemic stroke. The goal of the current study was to screen for potential targets of ischemic stroke by a network pharmacology method, and to clarify the effect of Huatan Tongluo decoction in treating ischemic stroke, to provide a theoretical and practical foundation for preventing and treating stroke by the use of TCM.

Materials and methods

General data of patients

In this retrospective study, 100 ischemic stroke patients who were hospitalized in Zhumadian Central Hospital between Jan. 2019 and Dec. 2020 were included. Diagnostic criteria for ischemic stroke: (1) Acute onset. (2) Local neurological deficits (weakness or numbness on one side of the face or limb, language disorder, etc.), a few cases have a comprehensive neurological function defect. (3) There is no limit to the duration of symptoms or signs (when imaging shows a responsible ischemic lesion) or for more than 24 h (when imaging shows a lack of a responsible lesion). (4) Non-vascular etiology is excluded. (5) Cerebral hemorrhage is excluded by brain CT/MRI.

Inclusion criteria: Patients suffering from ischemic stroke who received conventional treatment (conventional drugs + acupuncture) or combined treatment (conventional drugs + acupuncture + Huatan Tongluo decoction) and had complete clinical data were enrolled. Exclusion criteria: Patients with malignant tumor lesions and organic failure, mental disorders and cognitive impairment, abnormal expression ability, central neuropathy, or myocardial infarction were excluded. According to the treatment regimen, the patients were split into two groups, a conventional treatment group and a combined treatment group, with 50 cases in each group. There were 31 males and 19 females in the conventional treatment group with a mean age of 65.12±5.18 years (range, 54-76 years) and a mean course of disease of 3.56±1.41 months (range, 2-6 months). The combined treatment group consisted of 34 males and 16 females with a mean age of 64.06±5.30 years (range, 51-76 years) and a mean course of disease of 3.52±1.32 months (range, 2-6 months). There was no statistical difference in general data between the conventional group and the combined group ($P > 0.05$). The study was approved by the Ethics Committee of Zhumadian Central Hospital.

Therapeutic method

In the conventional treatment group, acupuncture was used on the basis of conventional drug treatment. The vasodilatation treatment, and acupuncture were used daily. The acupoints of Quchi, Hegu, and Zusanli were selected, and the needles were indwelled for 30 min after qi was obtained. The course of treatment lasted for 30 days, and the entire treatment lasted 90 days. Conventional drug treatment mainly included anticoagulation, blood pressure control, and coronary artery vasodilation treatment, with daily acupuncture.

The combined treatment group was treated with Huatan Tongluo Decoction in addition to conventional treatment (acupuncture + conventional drug treatment). The prescription composition of Huatan Tongluo decoction: Danshen 15 g, Tianma 10 g, Banxia 10 g, Fuling 10 g, Baishu 10 g, Xiangfu 10 g, Jiudahaung 6 g, Dannanxing 6 g, TianzhuHuang 6 g. The herbs were boiled with 1000 mL of water, and finally 200 mL of drug broth was obtained, which was taken orally in the morning (100 ml) and eve-

ning (100 ml) every day. 30 days of continuous medication was the course of treatment. After the end of the medication, the next course of treatment was given at an interval of 7 days, and the treatment lasted for 90 days.

Observational index

After the treatments were completed, the therapeutic outcome was assessed in light of the clinical treatment. The results were graded as follows: (1) After treatment, the clinical symptoms and indicators essentially vanished, the Neurological Deficit Scores (NDS) dropped by more than 90%, and the degree of disability was evaluated as 0, which was judged as *basically cured*. (2) After treatment, the NDS decreased by 46%-90%, significant improvements in the clinical symptoms and signs could be observed, and the severity of the disability was assessed as grade 1-3, which was judged as *significantly effective*. (3) After treatment, the NDS score decreased by 18%-45%, the clinical symptoms and signs were improved, and it was judged as *effective*. (4) Failure to meet the above criteria was judged as ineffective. Total effective rate = (basically cured + significantly effective + effective)/total amount of cases ×100%.

The clinical neurological deficit was evaluated by the Chinese Stroke Severity Scale (NDS) from 8 domains, namely consciousness, horizontal gaze function, facial paralysis, speech, upper limb strength, hand strength, lower limb strength and walking ability. The total score of 45 points is divided into mild (0-15), moderate (16-30), and severe (31-45).

The Barthel Index (BI) scoring scale was used to score the ability to perform daily living. The full score was 100. 100: Self-care; 61-99: Mild dysfunction; 41-60: Moderate dysfunction; ≤40: Severe dysfunction.

Functional Comprehensive Assessment (FCA) was used to score cognitive function and motor function, and the total score was 108, 108: normal comprehensive function; 107-90: basically normal function; 89-72: mild dysfunction; 71-54 points: moderate dysfunction; 53-36: severe dysfunction; 35-19: very severe dysfunction; and 18 points or below: complete dysfunction.

Screening of disease targets for ischemic stroke

By the use of "Cerebral ischemic stroke" as the search term, ischemic stroke disease-related targets were searched in GeneCards database (https://www.genecards.org/).

Screening of possible drug targets of Huatan Tongluo decoction

The active ingredients and structural formula of Huatan Tongluo decoction were collected in two ways. First, based on data of Traditional Chinese Medicine Systems Pharmacology (TCMSP) database [7] (https://old.tcmsp-e.com/tcmsp.php) as well as with oral bioavailability (OB) ≥ 30% and drug likeness (DL) ≥ 0.18 [8] from pharmacokinetics parameters as conditions, 10 active compound composition of TCM including Danshen, Tianma, Banxia, Fuling, Baishu, Xiangfu, Jiudahaung, Dannanxing, TianzhuHuang were obtained. Second, The PubChem database [9] (https://pub-chem.ncbi.nlm.nih.gov/) was used to collect the SDF structure of each active compound composition. Active compound composition was structured to import into SwissTargetPrediction database [10] (http://www.swisstargetprediction.ch/), in order to get Huatan Tongluo decoction potential drug targets.

Screening of common targets and creating of PPI network

The "intersect" package of R 4.2.1 software was used to intersect the disease targets of ischemic stroke and the potential drug targets of Huatan Tongluo decoction, and the "VennDiagram" package was used to draw the Venn diagram to obtain the common targets of Huatan Tongluo decoction in treating the ischemic stroke.

Common targets were put into String database [11], where "minimum required interaction score" was set to "highest confidence (0.700)". Finally, the PPI-related information (files with tsv suffix) was exported, and then these files were put into the Cytoscape 3.9.1 software to visualize the results. Based on cytoHubba plugin, the genes were sorted according to "Maximal Clique Centrality (MCC)" score and "Degree" to determine the top 30 targets, and these key

Table 1. General data of the two groups

Group	n	Male/Female	Age (years)	Duration of disease (months)
Conventional treatment	50	31/19	65.12±5.18	3.56±1.41
Combined treatment	50	34/16	64.06±5.30	3.52±1.32
χ^2/t		0.396	1.011	0.146
P		0.529	0.314	0.884

Table 2. Treatment effects of the two groups were compared (n%)

Group	n	Basically cured	Significantly effective	Effective	Invalid	Total effective rate
Conventional treatment	50	3 (6.0)	8 (16.0)	14 (28.0)	25 (50.0)	25 (50.0)
Combined treatment	50	8 (16.0)	13 (26.0)	19 (38.0)	10 (20.0)	40 (80.0)
Z				-3.266		
P				0.001		

Table 3. Functional scores of the two groups were compared (x ± s)

Group	n	NDS		BI		FCA	
		Before	After	Before	After	Before	After
Conventional treatment	50	25.76±4.60	18.98±4.66	49.80±4.82	65.16±5.64	31.80±3.46	45.12±5.84
Combined treatment	50	25.84±4.33	14.96±5.66	50.82±5.73	80.72±7.15	32.16±3.76	64.80±6.87
t		0.089	3.876	0.963	12.080	0.498	15.434
P		0.929	< 0.001	0.338	< 0.001	0.620	< 0.001

Notes: NDS, Neurological Deficit Scores; BI, Barthel Index; FCA, Functional Comprehensive Assessment.

targets were integrated for subsequent analysis.

GO and KEGG enrichment analysis

Key targets were imported into WebGestalt database [12] (http://www.webgestalt.org/) with options of "Over Representation (ORA)" in the "Method of interests", and "BH" Method in the "Multiple Test Adjustment", and false discovery rate (FDR) ≤ 0.05. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were performed. The data of Biological Process (BP), Cellular Component (CC), Molecular Function (MF) and KEGG enrichment analysis were collected, and a bar chart was drawn.

Statistical analysis

With the help of SPSS 23.0 software, data were analyzed and processed. Quantitative data were denoted by ($\overline{x}$ ± s), and t-test was applied for comparison between the two groups. Qualitative data were denoted by n (%), and X^2 test was applied to compare the two groups. Ordinal data were expressed by rank sum test. $P < 0.05$ was considered significant.

Results

Clinical performance of Huatan Tongluo decoction combined with acupuncture on ischemic stroke

There was no significant difference in the general information (gender, age, and disease duration) between the two groups ($P > 0.05$, as shown in **Table 1**). After treatment, the total effective rate of the combined treatment group was noticeably higher than that of the conventional treatment group ($P < 0.05$, **Table 2**). The combined treatment group had a lower NDS score than the conventional treatment group ($P < 0.05$). Furthermore, the combined treatment group also had higher scores of BI and FCA than the conventional treatment group (all $P < 0.05$, **Table 3**).

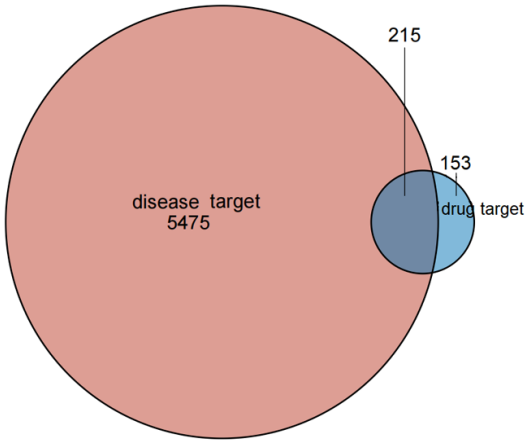

Figure 1. Venn diagram shows 215 intersections between 5690 ischemic stroke disease targets and 1193 Huatan Tongluo decoction drug targets.

Targets of ischemic stroke and potential drug targets of Huatan Tongluo decoction

The GeneCards database showed 5690 ischemic stroke-related targets in total after searching. Ten active compound components of TCM were obtained from the TCMSP database, including 15 active compounds of Fuling, 13 active compounds of Banxia, seven active compounds of Baishu, 65 active compounds of Danshen, 18 active compounds of Xiangfu, 16 active compounds of Dahuang, and eight active compounds of Sanqi. The effective compounds of Tianma, Dannnaxing and Tianzhuhuang were not screened out. The sdf structure of the active compounds described above was collected using the PubChem database. The probable drug targets of Huatan Tongluo decoction were predicted using the SwissTargetPrediction website. After removing repeated values and retaining unique values, Huatan Tongluo decoction was found to have 368 total drug targets.

Screening results of common targets and construction of PPI network

The intersection analysis of 5690 targets of ischemic stroke and 368 drug targets of Huatan Tongluo decoction yielded 215 common targets (**Figure 1**). To get information related to PPI, 215 common targets were put into the String database (**Figure 2A**). There were 193 nodes and 621 edges in the PPI network, with an average number of neighbors of 6.553. Cytoscape software was used to visualize PPI network information, and the top 30 key targets were determined according to MCC score and Degree (**Figure 2B**, **2C**). The ranking of the scores of the targets is shown in **Table 4**. The "MCC" and "Degree" screening results were integrated to finally obtain a total of 43 key targets.

GO and KEGG pathway analysis of key targets

KEGG results showed that altogether 51 signaling pathways were enriched (enrichment significance FDR < 0.05), mainly including VEGF signaling pathway, EGFR tyrosine kinase inhibitor resistance, non-small cell lung cancer, linoleic acid metabolism, HIF-1 signaling pathway, etc. (**Figure 3A**). Results of BP showed a total of 248 biological processes, which were mainly enriched in Response to insulin, Response to peptide hormone, Response to peptide, Cellular response to hormone stimulus, Response to hormone, etc. (**Figure 3B**). The results of CC showed a total of five cellular components that were mainly enriched in Perinuclear region of cytoplasm, Membrane region, and Vesicle lumen (**Figure 3C**). The results of MF showed that a total of 55 molecular functions, mainly enriched in Insulin receptor substrate binding, nuclear receptor activity, Transcription factor activity, Direct ligand regulated sequence-specific DNA binding, Phosphatidylinositol-4,5-bisphosphate 3-kinase activity, etc. (**Figure 3D**).

Discussion

In traditional Chinese medicine (TCM), the onset of stroke is related to Qi, deficiency, wind, fire, blood stasis and other factors. Damage to the brain and medulla nerves can cause disorders of liver tendons, insufficiency of liver Qi and blood, insufficiency of tendons and veins, and sequelae of stroke. Acupuncture and moxibustion can improve Qi and blood, channel meridians, benefit joints, relax tendons and activate collaterals, activate blood circulation and remove blood stasis, promote central nervous excitability and limb movement ability in stroke patients [13]. Acupuncture and moxibustion are commonly used adjuvant treatments for stroke patients. The possible mechanisms of its effect on nervous system diseases include stimulating neuronal cell proliferation,

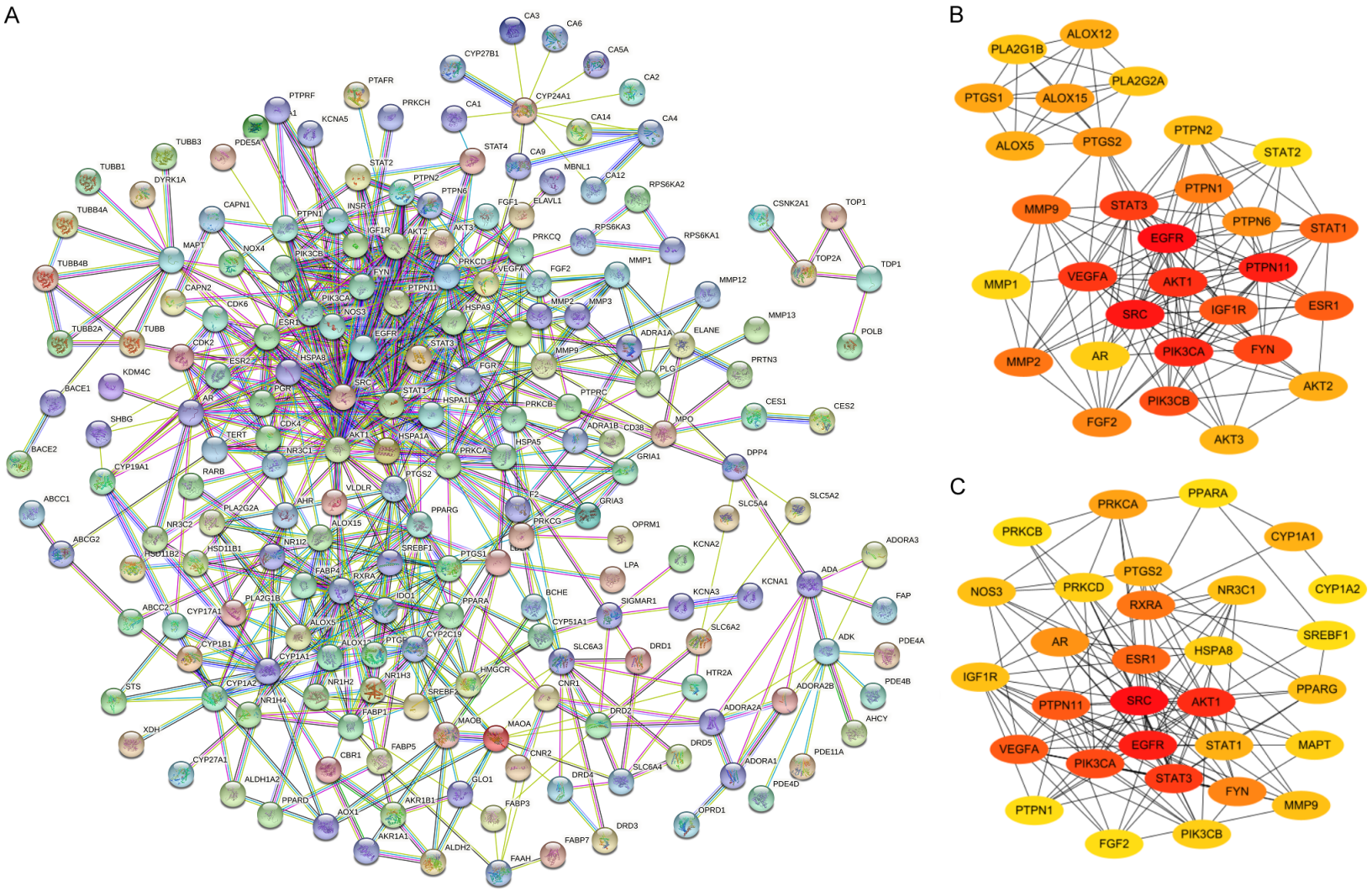

Figure 2. String and Cytoscape were used to screen the key targets. A: Protein-protein interaction (PPI) network diagram; B: Network of the top 30 targets screened according to Maximal Clique Centrality (MCC) score; C: Network of the top 30 targets screened according to degree; the redder the color, the higher the score.

Table 4. Analysis results of Maximal Clique Centrality (MCC) and Degree algorithms (top 30)

Gene symbol	MCC	Gene symbol	Degree
EGFR	20060	*SRC*	40
SRC	19638	*EGFR*	35
PTPN11	17851	*AKT1*	32
PIK3CA	16776	*STAT3*	31
AKT1	15848	*PIK3CA*	23
VEGFA	14721	*PTPN11*	21
STAT3	13431	*VEGFA*	21
FYN	12686	*ESR1*	20
PIK3CB	6624	*RXRA*	19
IGF1R	3222	*FYN*	18
ESR1	2495	*AR*	17
STAT1	2148	*PRKCA*	16
MMP9	1974	*STAT1*	15
MMP2	1584	*PTGS2*	15
PTPN1	1526	*CYP1A1*	15
FGF2	1328	*IGF1R*	14
PTPN6	1236	*MMP9*	14
PTGS2	976	*NOS3*	14
ALOX15	845	*NR3C1*	14
PTGS1	843	*PPARG*	14
AKT2	840	*PIK3CB*	13
ALOX12	840	*PRKCD*	13
ALOX5	840	*HSPA8*	13
AKT3	768	*MAPT*	13
PTPN2	750	*PTPN1*	12
PLA2G1B	720	*FGF2*	12
PLA2G2A	720	*PRKCB*	12
AR	317	*PPARA*	12
MMP1	290	*CYP1A2*	12
STAT2	288	*SREBF1*	12

promoting neural plasticity, reducing the inflammatory response after ischemia, and preventing neuronal apoptosis [14]. According to TCM, phlegm and blood stasis block collaterals in the process of stroke, so the treatment of acute stroke should focus on eliminating phlegm and removing blood stasis and dredging collaterals. In the formula of Huatan Tongluo decoction, Banxia, Baishu and Fuling have the effects of invigorating the spleen, removing dampness and eliminating phlegm. Dahuang can activate blood circulation and remove blood stasis; Xiangfu con soothe the liver and relieve depression; Dannanxing and Tianzhuhuang can clear away heat and phlegm; Tianma has the effect of dispelling wind and dredging collaterals; Danshen has the effect of activating blood circulation and removing blood stasis; Sanqi can stop bleeding, break blood stasis, relieve inflammation, relieve pain and nourish. All kinds of drugs can be used together to channel the vein, disperse congestion, phlegm turbidity [15-20]. Modern studies have confirmed [21, 22] that Huatan Tongluo decoction can inhibit apoptosis, promote functional repair of nerve tissue, and improve hemorheology. Huatan Tongluo decoction combined with acupuncture can help promote blood circulation, eliminate blood stasis, and unchoke meridians and collaterals, so as to accelerate the recovery of nerve function. Similarly, it can be observed from this study that the therapeutic effect of Huatan Tongluo decoction and acupuncture was 80%, which was muchhigher than the control group. After treatment, the neurological function score, limb motor function, and daily living ability score of patients in the combined treatment group was higher than those of the control group. This indicates that the application of Huatan Tongluo decoction and acupuncture in the treatment of stroke sequelae can enhance the therapeutic effect, improve the motor ability and daily living ability, as well as accelerate the recovery of neurological function.

To determine the mechanism of Huatan Tongluo decoction, this study collected the disease targets of ischemic stroke, and targets of TCM active component in Huatan Tongluo decoction from GeneCards, TCMSP, PubChem, and Swiss Target Prediction databases by the network pharmacology method. There were 215 common targets of disease and drugs. PPI network analysis of these 215 targets showed that *EGFR* (epidermal growth factor receptor), *SRC* (proto-oncogene, non-receptor tyrosine kinase), *PTPN11* (protein tyrosine phosphatase non-receptor type 11), *PIK3CA* (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha), *AKT1* (serine/threonine kinase 1), *VEGFA* (vascular endothelial growth factor A), *STAT3* (signal transducer and activator of transcription 3), *FYN* (FYN proto-oncogene, Src family tyrosine kinase) and other 43 targets had the strongest interaction. Studies revealed that the expression of Transforming growth factor alpha-Epidermal growth factor receptor

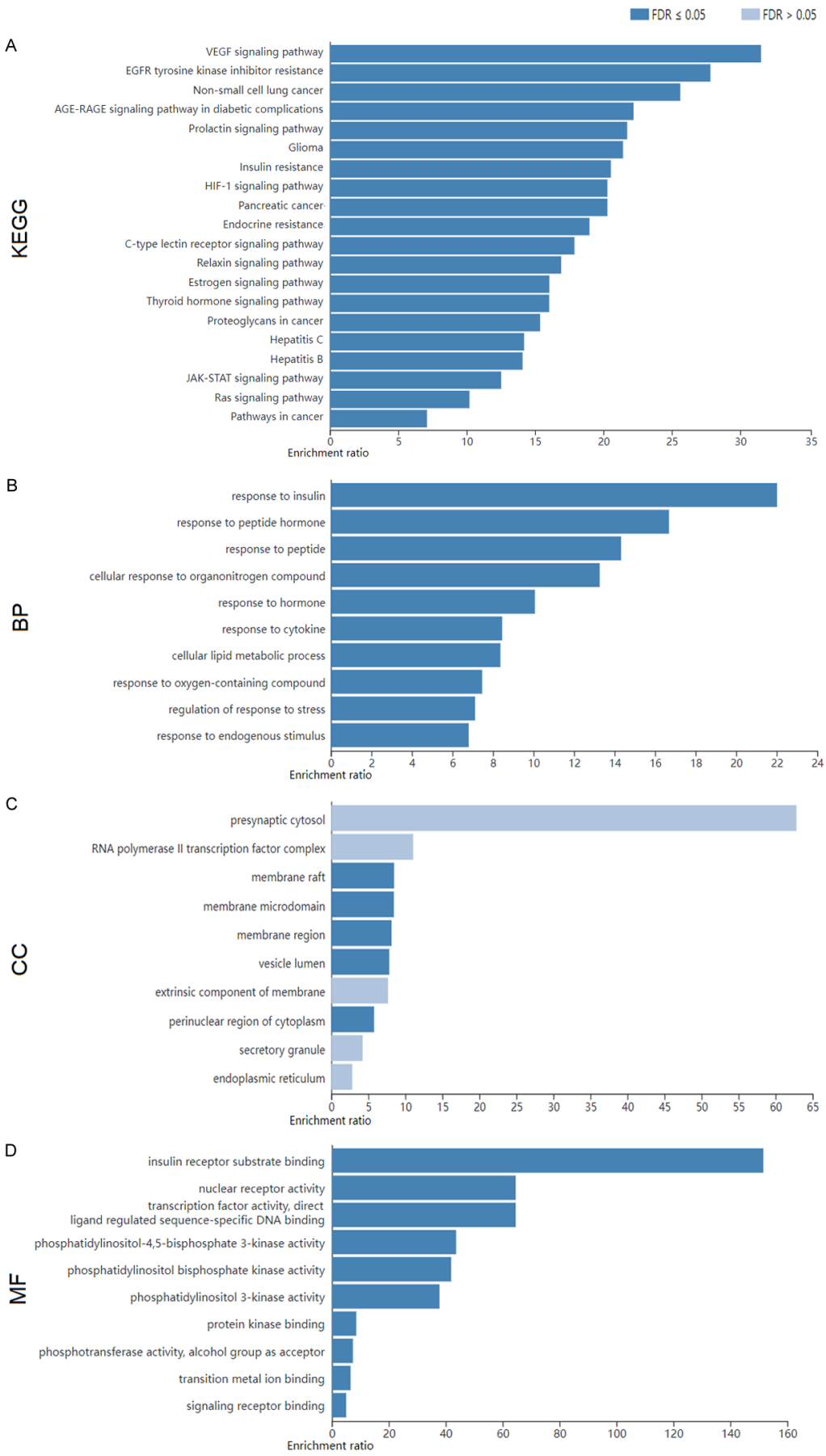
FDR ≤ 0.05
FDR > 0.05
A
KEGG
VEGF signaling pathway
EGFR tyrosine kinase inhibitor resistance
Non-small cell lung cancer
AGE-RAGE signaling pathway in diabetic complications
Prolactin signaling pathway
Glioma
Insulin resistance
HIF-1 signaling pathway
Pancreatic cancer
Endocrine resistance
C-type lectin receptor signaling pathway
Relaxin signaling pathway
Estrogen signaling pathway
Thyroid hormone signaling pathway
Proteoglycans in cancer
Hepatitis C
Hepatitis B
JAK-STAT signaling pathway
Ras signaling pathway
Pathways in cancer
0 5 10 15 20 25 30 35
Enrichment ratio
B
BP
response to insulin
response to peptide hormone
response to peptide
cellular response to organonitrogen compound
response to hormone
response to cytokine
cellular lipid metabolic process
response to oxygen-containing compound
regulation of response to stress
response to endogenous stimulus
0 2 4 6 8 10 12 14 16 18 20 22 24
Enrichment ratio
C
CC
presynaptic cytosol
RNA polymerase II transcription factor complex
membrane raft
membrane microdomain
membrane region
vesicle lumen
extrinsic component of membrane
perinuclear region of cytoplasm
secretory granule
endoplasmic reticulum
0 5 10 15 20 25 30 35 40 45 50 55 60 65
Enrichment ratio
D
MF
insulin receptor substrate binding
nuclear receptor activity
transcription factor activity, direct ligand regulated sequence-specific DNA binding
phosphatidylinositol-4,5-bisphosphate 3-kinase activity
phosphatidylinositol bisphosphate kinase activity
phosphatidylinositol 3-kinase activity
protein kinase binding
phosphotransferase activity, alcohol group as acceptor
transition metal ion binding
signaling receptor binding
0 20 40 60 80 100 120 140 160
Enrichment ratio

Figure 3. Results of functional enrichment analysis. A: Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis (top 20); B: Biological Process (BP) analysis (top 10); C: Cellular Component (CC) analysis (top 10); D: Molecular Function (MF) analysis (top 10).

(TGFα-EGFR) receptor was increased in glial cells after ischemia, which can improve neurological recovery after stroke [23]. Chen et al. [24] showed that activation of the EGFR/MAPK signaling cascade promoted the proliferation of neural stem cells and enhanced the recovery of neurological function after transient cerebral ischemic injury. Moreover, Tian et al. [25] indicated that the non-receptor tyrosine kinase SRC increased the number of nascent neuronal cells in the dentate gyrus through the activation of the Raf/ERK/CREB signaling cascade after cerebral ischemia. According to related studies, activation of STAT3 and ERK1/2 pathways can promote nerve regeneration activity [26]. It is suggested that Huatan Tongluo decoction and its active components may affect the expression of ischemia-related proteins (such as *EGFR*, *SRC*, *PTPN11*, *PIK3CA*, *AKT1*, *VEGFA*, and *STAT3*) in the form of a co-expression network mainly through PPI, so as to play a brain protective effect.

Further analysis of the main pathways involved in the 43 targets showed that Huatan Tongluo decoction could treat stroke with multiple targets, multiple components, and multiple pathways. The decoction mediates the VEGF signaling pathway and other pathways to play a role in improving the symptoms of ischemic stroke. VEGF signaling pathway exerts an essential effect on ischemic stroke. Research has indicated that Catalpol can significantly improve the damaged neurovascular units in the ischemic area by protecting the structure and morphology of blood vessels, neurons, and astrocytes, promoting angiogenesis and nerve regeneration to replenish lost blood vessels and neurons [27]. Limitations of this study: due to limited funding, no specific molecular or protein experiments were performed to verify the correctness of the network pharmacological targets, which will be refined in our future experiments.

Conclusion

Huatan Tongluo decoction and acupuncture can promote the recovery of neurological function, and improve limb motor function and daily living ability of patients with sequelae of stroke. Huatan Tongluo decoction can mediate VEGF signaling pathway and other pathways in the form of multi-component and multi-function to play a role in stroke.

Disclosure of conflict of interest

None.

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