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Original Article

Neuroprotective effect of Sanqi Tongshuan Tablets on sequelae post-stroke in rats

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ABSTRACT

Objective: To identify the therapeutic effect and possible mechanisms of Chinese medicine Sanqi Tongshuan Tablets (SQTS) on sequelae post-stroke in rats.

Methods: The rat cerebral ischemia sequelae post-stroke models were successfully induced by blocking the middle cerebral artery with electric coagulator after the seventh week and balance beam test ≤ 4. The rats were then received with SQTS (0.5, 1, and 2 g/kg) and Naodesheng (NDS, 1.24 g/kg), Vinpocetine (VP, 1.55 mg/kg) for 30 d. The beam-walking test and shuttle test were performed before and after 10, 20, and 30 d of administration. In addition, histopathology changes and GAP-43, GFAP were measured by H&E staining and immunohistochemisty.

Results: The model displayed signs of brain damage on motor function, learning and memory function and histopathology. After 30 d of treatment, SQTS at different doses (0.5, 1.0, and 2.0 g/kg) restored the beam-walking scores by 21.7% ($P > 0.05$), 30.4% ($P > 0.05$), and 39.1% ($P < 0.05$); Decreased electric shock by 35.0% ($P > 0.05$), 50.0% ($P > 0.05$), and 75.0% ($P < 0.05$), respectively. On the other hand, the histological changes were less severe and the GAP-43 expression increased in hippocampal CA1 and cortical region.

Conclusion: SQTS showed therapeutic benefits on sequelae post-stroke in rats, which might be through the pathway of regeneration or neuroplasticity.

1. Introduction

Sequelae post-stroke is generally from six months after the onset of cerebral infarction in human, despite achievements in early treatment, management and secondary prevention, a substantial proportion of stroke patients still experience severe consequences in terms of mortality and morbidity (Andersen, Andersen, & Olsen, 2011; Palnum et al., 2009), and early treatment is important for prognosis. Chinese herbal medicines have been used successfully for centuries to treat a wide variety of ailments and have attracted increasing attention from industry and academia (Liu et al., 2011; Shia et al, 2011; Wu et al., 2011). Sanqi Tongshuan Tablets (SQTS) is a Chinese herbal prescription derived from clinical experience, which was composed of *Panax pseudo-ginseng, Carthamus tinctorius, Moschus berezovskii, Pheretima, Salvia miltiorrhiza, Ligusticum wallichii*, etc, and intended for sequelae post-stroke with cerebral thrombosis. In our previous study, a rat model of $FeCl_3$ induced ischemic stroke recovery period was successfully established, SQTS could restore the beam-walking scores, and SQTS can be used as a therapeutic agent for stroke recovery period via alleviating inflammatory responses (Hao et al., 2017). The aim of this study was to evaluate the effect of SQTS on neural functional recovery and brain tissue remodeling in rat sequelae post-stroke, which could provide references and guidance for basic research and clinical treatment.

2. Materials and methods

2.1. Drugs, reagents, and devices

Sanqi Tongshuan Tablets (SQTS, batch number 130712) was purchased from Kunming Institute of Nephrology (Yunnan, China), a gram of powder was equivalent to 1.656 g of raw medicine. Naodesheng (NDS, batch number 20130801) was purchased from Harbin Huayu Pharmaceutical Group Co., Ltd. (Heilongjiang, China); Vinpocetine (VP, batch number 5131002) was purchased from Northeast Pharmaceutical Group Shenyang No.1 Pharmaceutical Co., Ltd. (Shenyang, China). Reagents including GAP-43 (batch

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number CJ36131) and GFAP (batch number CC36131) were purchased from Bioworld technology, Co., Ltd. (Nanjing, China); YLS-17B shuttle box, were purchased from Shandong Academy of Medical Sciences Jinan Yiyan Science and Technology Development Co., Ltd. (Shandong, China); Leika VT 1000S vibratome was purchased from Leica (Heiderberg, Germany).

2.2. Animals and experimental groups

Adult male Sprague Dawley rats weighing (276.6 ± 15.2) g [SCXK (JING) 2012-0001] were obtained from Vital River Laboratory Animal Technology Co., Ltd.

Sprague Dawley rats were anesthetized with chloral hydrate at a dose of 360 mg/kg by ip injection, the model was made as reported (Tamura, Graham, Mc Cullon, & Teasdale, 1981), the skin between right canthal and canal midpoint was dissected, after separation for the temporal muscle, separated the zygomatic arch and hinged off until the squamous part of the temporal bone was exposed. The trace of middle cerebral artery (MCA) was visualized after the squamous bone was removed using a high-speed drill, blocking up the middle cerebral artery by electric coagulator, then washed with normal salin and applied penicillin (1.6×10^5)/ U for 3 d.

The cerebral ischemia model was successfully established when balance beam test ≤ 4 after the seventh week, which were randomly divided into six groups: A, model (saline solution); B, SQTS (0.5 g/kg); C, SQTS (1.0 g/kg); D, SQTS (2.0 g/kg); E, NDS (1.24 g/kg, clinical equivalent dose); F, VP (1.55 mg/kg, clinical equivalent dose). In addition, the rats in the sham group (without electric coagulation) were also given with 0.5% Carboxymethylcellulose (CMC). Ten rats in each group were treated orally everyday from the seventh week and lasting 30 d with the volume of 10 mL/kg.

2.3. Beam-walking test

The motor function was evaluated using a modified scale of beam-walking test (Abo, Yamauchi, Suzuki, Sakuma, & Urashima, 2006; Feeney, Gonzalez, & Law, 1982; Ohwatashi, Ikeda, Harada, Kamikawa, & Yoshida, 2013) before and after 10, 20, and 30 d of administration. An elevated narrow beam (122 cm × 2.5 cm) was used, one side of which was strong and noise stimulation, the contralateral side was a black cage. Score 7, the rats traversed the beam with no foot slip; Score 6, the rats traversed while grasping the lateral side of the beam; Score 5, the rats showed walking disability on the beam but they could traverse it; Score 4, the rats took a considerable amount of time to traverse the beam due to difficulty walking; Score 3, the rats were unable to traverse the beam; Score 2, the rats displayed difficulty in moving the body or any limb on the beam; Score 1, the rats were unable to stay on the beam for 10 s.

2.4. Learning and memory function test

The shuttle test was made by YLS-13A shuttle box (Lalanza et al., 2015) before and after 10, 20, and 30 d of treatment. Each shuttle box was divided into two equally sized compartments (25 cm × 25 cm × 25 cm), both sound-attenuated, connected by an opening door (8 cm and 10 cm). Each trial consisted of 10 s of conditioned stimulus (light of 7 W and sound of 2400 Hz at 40 dB, presented simultaneously), immediately followed by a 20 s of scrambled electric shock (unconditioned stimulus, UCS, 60 V, 0.9 mA) administered through the metal grid floor of the box. The conditioned stimulus was terminated when the rats crossed from one side to the other compartment. The numbers of electric shock within 5 min were recorded.

2.5. Histopathology and GAP-43, GFAP expression

At the end of experiment, the brains of rats were removed, fixed in 10% formaldehyde for 24 h and then embedded in paraffin. Blocks were obtained from cutting through the whole globe coronally with Leika VT 1000S vibratome. Five-μm-thick sections were stained with Hematolxylin and Eosin (H&E) for light microscopic examination at ×200 magnification in the hippocampus CA1 and cortical region. The number of surviving neurons was recorded.

Brain sections were also treated with 3% H_2O_2 for 15 min and then blocked with 10% normal goat serum for 1 h at room temperature. Then, the sections were reacted with primary antibodies, including anti-GAP-43 (1:100), anti-GFAP (1:100) overnight at 4 °C. Subsequently, the sections were incubated with anti-rabbit secondary antibody for 15 min at room temperature. The primary antibodies were replaced with PBS in the negative control analyses. After exposed to 3,30-diaminobenzidine tetrahydrochloride (DAB) reagent and counter-stained with hematoxylin, the numbers of positive neurons were counted at ×200 magnification in the hippocampus CA1 and cortical region (Fang et al., 2016).

2.6. Statistical analysis

All results were expressed as mean ± SD. Comparison among multiple groups was performed with one-way analysis of variance (ANOVA). Differences were considered statistically significant at a value of $P < 0.05$.

3. Results

3.1. Effect of SQTS on motor function

Compared with the sham group, the motor function decreased significantly ($P < 0.001$) in model group. SQTS (0.5, 1.0, and 2.0 g/kg) restored the scores by 24.0% ($P > 0.05$), 36.0% ($P > 0.05$), and 40.0% ($P < 0.05$) after 20 d treatment; 21.7% ($P > 0.05$), 30.4% ($P > 0.05$) and 39.1% ($P < 0.05$) after 30 d treatment. The positive control of NDS (1.24 g /kg) decreased by 36.0% ($P < 0.05$) and 39.1% ($P < 0.05$); VP (1.55 mg/kg) decreased by 48.0% ($P < 0.05$) and 47.8% ($P < 0.01$) after the treatment of 20 d and 30 d, respectively (Table 1).

3.2. Effect of SQTS on learning and memory function

The numbers of electric shock in model group were increased ($P < 0.05$, $P < 0.001$). SQTS (0.5, 1.0, and 2.0 g/kg) decreased electric shock by 26.9% ($P > 0.05$), 30.8% ($P > 0.05$), and 34.6% ($P < 0.05$) after 20 d treatment; 35.0% ($P > 0.05$), 50.0% ($P > 0.05$) and 75.0% ($P < 0.05$) after 30 d treatment. The positive control of NDS (1.24 g/kg) decreased by 19.2% ($P > 0.05$) and 55.0% ($P < 0.05$); VP (1.55 mg/kg) decreased by 46.2% ($P < 0.05$) and 85.0% ($P < 0.05$) in the treatment of 20 and 30 d, respectively. SQTS (1.0 g/kg) was the same as NDS (50.0% *vs* 55.0%), weaker than VP (50.0% *vs* 85.0%) (Table 2).

3.3. Effect of SQTS on pathohistology and numbers of neurons

The optical microscopic examination of the impact areas demonstrated that there were no morphology changes in the sham group, nuclear membrane and clear nucleolus were integrated. In the model group, significant neuronal damage in the pyramidal cell layer of the hippocampal CA1 region was found, including the loose neurons arrangement, smaller number and volume, deepened dyeing cytoplasm and nuclear pyknosis. Cortical region cells were arranged in irregular and sparse, cytoplasm's stain was dark, karyopyknosis were observed, and the cytoplasm was eosinophilic.

Table 1
Effects of SQTS on motor function of rats in sequelae post-stroke (mean ± SD, $n = 10$)

Groups	Dose / ($g \cdot kg^{-1}$)	Scores (Before treatment)	Scores (After treatment)		
			10 d	20 d	30 d
Sham	-	5.9 ± 1.0	6.7 ± 0.7 (0.8 ± 0.9)	6.6 ± 0.8 (0.7 ± 0.9)	6.7 ± 0.7 (0.8 ± 0.9)
Model	-	3.0 ± 0.8$^{\Delta\Delta\Delta}$	4.0 ± 1.1$^{\Delta\Delta\Delta}$ (1.0 ± 0.8)	4.1 ± 1.2$^{\Delta\Delta\Delta}$ (1.1 ± 0.9)	4.4 ± 1.0$^{\Delta\Delta\Delta}$ (1.4 ± 0.8)
SQTS	0.5	3.0 ± 0.8	3.9 ± 1.5 (0.9 ± 1.4)	4.7 ± 1.1 (1.7 ± 0.9)	4.9 ± 1.2 (1.9 ± 1.3)
	1.0	3.0 ± 0.8	3.8 ± 1.4 (0.8 ± 1.5)	5.0 ± 1.2 (2.0 ± 1.2)	5.1 ± 1.2 (2.1 ± 0.9)
	2.0	3.0 ± 0.8	4.4 ± 1.3 (1.4 ± 1.3)	5.1 ± 1.3 (2.1 ± 1.1*)	5.3 ± 0.9 (2.3 ± 0.8*)
NDS	1.24	3.0 ± 0.8	4.3 ± 1.6 (1.3 ± 1.3)	5.0 ± 1.3 (2.0 ± 0.9*)	5.3 ± 0.7 (2.3 ± 1.1*)
VP	1.55×10^{-3}	3.0 ± 0.7	4.7 ± 1.3 (1.7 ± 1.3)	5.3 ± 0.9 (2.3 ± 1.2*)	5.5 ± 0.7 (2.5 ± 0.8**)

Difference before and after treatment were available in brackets.
Note:
$^{\Delta\Delta\Delta}$ $P < 0.001$ *vs* sham group.
* $P < 0.05$,
** $P < 0.01$ *vs* model group.

Table 2
Effect of SQTS on learning and memory function of rats in sequelae post-stroke (mean ± SD, $n = 10$).

Groups	Dose / ($g \cdot kg^{-1}$)	Numbers (Before treatment)	Numbers (After treatment)		
			10 d	20 d	30 d
Sham	-	4.2 ± 1.8	4.3 ± 1.4 (0.1 ± 1.3)	4.2 ± 1.5 (0.0 ± 2.1)	4.7 ± 2.2 (0.5 ± 2.4)
Model	-	7.0 ± 1.2$^{\Delta\Delta\Delta}$	6.3 ± 2.1$^{\Delta}$ (−0.7 ± 2.3)	6.8 ± 1.5$^{\Delta\Delta\Delta}$ (−0.2 ± 1.6)	6.7 ± 1.3$^{\Delta}$ (−0.3 ± 1.9)
SQTS	0.5	7.1 ± 1.2	6.4 ± 1.2 (−0.7 ± 1.9)	6.1 ± 1.4 (−1.0 ± 2.0)	6.0 ± 1.1 (−1.1 ± 1.4)
	1.0	7.2 ± 0.8	6.1 ± 1.4 (−1.1 ± 1.2)	6.0 ± 1.3 (−1.2 ± 1)	5.7 ± 0.9 (−1.5 ± 1.3)
	2.0	7.5 ± 1.3	6.0 ± 1.4 (−1.5 ± 0.8)	5.9 ± 1.1 (−1.6 ± 0.8*)	5.2 ± 1.4 (−2.3 ± 1.2*)
NDS	1.24	7.5 ± 0.8	6.2 ± 1.0 (−1.3 ± 1.2)	6.3 ± 1.3 (−1.2 ± 1.2)	5.6 ± 1.0 (−1.9 ± 0.9*)
VP	1.55×10^{-3}	7.3 ± 1.3	5.9 ± 1.2 (−1.4 ± 0.7)	5.6 ± 1.2 (−1.7 ± 0.7*)	5.0 ± 1.3 (−2.3 ± 1.3*)

Difference before and after treatment were available in brackets.
Note: $^{\Delta}P < 0.05$,
$^{\Delta\Delta\Delta}$ $P < 0.001$ *vs* sham group.
* $P < 0.05$ *vs* model group.

In each treatment group, these histological changes were less severe, differing in extent according to the dose of SQTS administrated (Fig. 1).

The number of neurons in hippocampal CA1 and cortical region of model group was decreased significantly compared with the sham group ($P < 0.001$). SQTS (0.5, 1.0, and 2.0 g/kg) increased neurons by 7.3% ($P > 0.05$), 26.7% ($P > 0.05$), and 68.5% ($P < 0.01$) in hippocampal CA1 region; 31.7% ($P > 0.05$), 37.4% ($P < 0.05$), and 57.6% ($P < 0.01$) in cortical motor region. The positive control of NDS and VP also increased neurons (Table 3).

3.4. Effect of SQTS on GAP-43 and GFAP expression

GAP-43 has been shown to be expressed as brownish yellow in neurons at a low level, and a slight increase in the model group was observed. GAP-43 staining was much stronger in the SQTS groups, GAP-43 in the NDS and VP group was expressed similarly as model group (Fig. 2).

The expression of GAP-43 and GFAP in hippocampal CA1 and cortical region of model group was increased significantly when compared with sham group ($P < 0.05$, $P < 0.01$). SQTS (0.5, 1.0, and 2.0 g/kg) increased GAP-43 by 17.3% ($P > 0.05$), 20.5% ($P > 0.05$) and 27.6% ($P < 0.05$) in hippocampal CA1 region; 9.0% ($P > 0.05$), 18.8% ($P > 0.05$), and 30.6% ($P < 0.05$) in cortical motor region. The positive control of NDS and VP did not increase GAP-43 (Table 4).

GFAP was differentially expressed in sham rats and rats in sequelae post-stroke, more expression of GFAP was observed in model group, GFAP levels were similar between model and SQTS groups (Fig. 3), and there was no influence of SQTS (0.5, 1.0, 2.0 g/kg) on GFAP (Table 5).

4. Discussion

Stroke is a major cause of disability and death worldwide (Mozaffarian et al, 2016), and known to produce brain damage and related behavioural deficits, including memory deficits and motor disorders (Xu et al., 2013). People with such disabilities often require extensive long-term care by health care professionals and family (Li et al., 2009). Therefore, new strategies should be developed for this serious disease (Fisher et al, 2006; Lu et al., 2002). The use of herbal medicines for the treatment of cerebral ischemia has a long history in China.

SQTS was designed for sequelae post-stroke with cerebral thrombosis with four tablets each time for three times per day. SQTS mainly composed with medicinal plant including *Panax pseudo-ginseng, Carthamus tinctorius, Moschus berezovskii, Phere-*

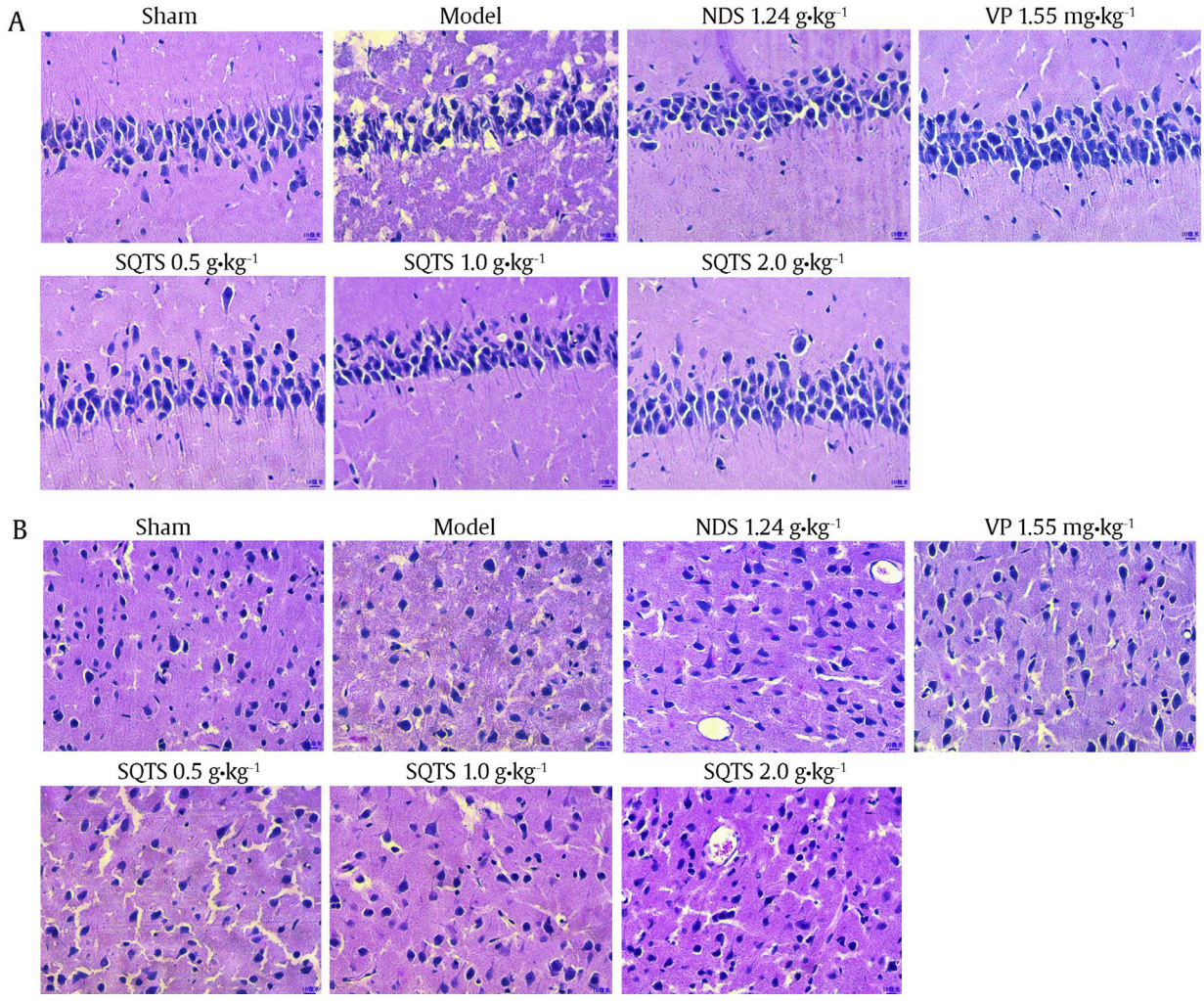

Fig. 1. Effects of SQTS on neurons numbers in hippocampal CA1 region (A) and cortical region (B) (×200, Scale bar 10 μm).

Table 3
Effects of SQTS on neurons numbers of rats in sequelae post-stroke (mean ± SD, $n = 10$).

Groups	Doses /(g•kg^{-1})	Numbers	
		Hippocampal CA1 region	Cortical region
Sham	-	96.2 ± 10.8	93.8 ± 10.4
Model	-	73.0 ± 12.1$^{\Delta\Delta\Delta}$	67.6 ± 10.6$^{\Delta\Delta\Delta}$
SQTS	0.5	74.7 ± 10.0	75.9 ± 7.5
SQTS	1.0	79.2 ± 12.7	77.4 ± 6.3*
SQTS	2.0	88.9 ± 8.5**	82.7 ± 7.9**
NDS	1.24	85.5 ± 7.6*	83.8 ± 14.5*
VP	1.55×10^{-3}	89.9 ± 5.0***	85.0 ± 12.2**

Note:
$^{\Delta\Delta\Delta}$ $P < 0.001$ *vs* sham group;
* $P < 0.05$,
** $P < 0.01$,
*** $P < 0.001$ *vs* model group.

*tima, Salvia miltiorrhiza, Ligusticum wallich*ii, etc, and the various composition of materials in the prescription is the basis for exerting pharmacological action. Present study verified the efficiency of 50 mg/L of *Panax notoginseng* saponin exposure following hypoxia-reoxygenation injury in fetal rat cortical neurons (Yan et al., 2012). In addition, *in vivo* and *in vitro* neuroprotective effects of *Carthamus tinctorius* extract on cerebral ischemic injury were reported that reduced neurological deficit scores in a rat infarction model (Wei et al, 2005; Zhu et al., 2005). Moschus has been shown to contribute to bidirectional central nervous system modulation: low dose moschus excites the center, and high doses inhibit the center (Sun, Wang, & Yu, 2005). Curative effect of *Pheretima aspergillum* (earthworm, PA) on rats with middle cerebral artery occlusion (MCAO) was reported, the results showed that oral administration of PA for two weeks to rats with MCAO successfully reduced cerebral infarction areas in the cortex and striatum, and also reduced scores of neurological deficit (Liu et al., 2012). *Salvia miltiorrhiza* Bge. plus *Carthamus tinctorius* L. could achieve remarkable synergistic neuroprotective effects on ischemia/reperfusion (I/R) injury, which is related to the anti-inflammatory and antioxidant pathways (Xu et al., 2017). The main constituent of *Ligusticum wallichii* (Ligustrazine) can reduce blood-brain barrier permeability as well as neuronal damage in focal cerebral I/R injury in rats (Tan, Fu, Cheng, Meng, & Gu, 2015).

In this study, we evaluated the effect of SQTS on sequelae post-stroke in rats. In order to guarantee the success of rat cerebral ischemia model, the neurological deficit of the balance beam test was measured after the seventh week of surgical work, and score ≤4 as a successful model. The motor function, learning and memory function were also decreased followed with neuronal damage in the pyramidal cell layer of the hippocampal CA1 region and the cortical region. As the literature reports, during ischemia of stroke, deprivation of oxygen and glucose can induce immediate, localized

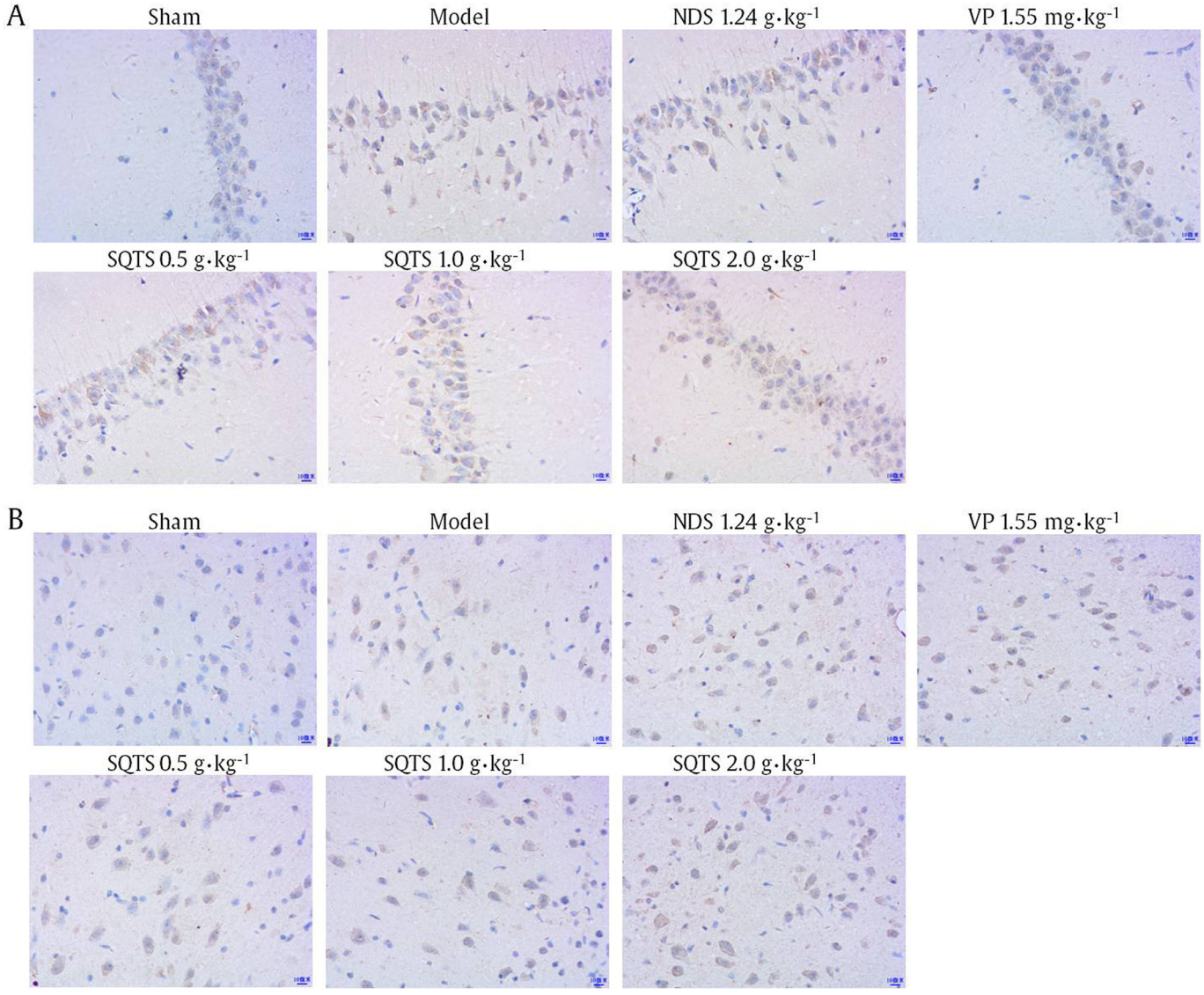

Fig. 2. Effects of SQTS on GAP-43 expression in hippocampal CA1 region (A) and cortical region (B) (×200, Scale bar 10 μm).

Table 4
Effect of SQTS on GAP-43 positive numbers of rats in sequelae post-stroke (mean ± SD, $n = 10$).

Groups	Doses / ($g \cdot kg^{-1}$)	Numbers	
		Hippocampal CA1 region	Cortical region
Sham	-	13.3 ± 5.1	9.3 ± 3.0
Model	-	18.5 ± 4.3$^{\Delta}$	14.4 ± 3.4$^{\Delta\Delta}$
SQTS	0.5	21.7 ± 9.0	15.7 ± 4.9
	1.0	22.3 ± 6.1	17.1 ± 5.7
	2.0	23.6 ± 5.7*	18.8 ± 5.2*
NDS	1.24	21.9 ± 4.0	17.8 ± 5.5
VP	1.55×10^{-3}	21.7 ± 3.9	18.1 ± 5.3

Note:
$^{\Delta}$ $P < 0.05$,
$^{\Delta\Delta}$ $P < 0.01$ *vs* sham group;
* $P < 0.05$ *vs* model group.

neuronal cell death at the ischemic core via excitotoxic activity (Lai, Zhang, & Wang, 2014).

In this study, it demonstrated that SQTS treatment attenuated the cerebral injury as evidenced by the improvement of motor function, learning and memory function. Moreover, the histological changes were less severe, differing in extent according to the dose of SQTS administrated.

Overwhelming evidence has accumulated that immune responses against glial fibrillary acidic protein (GFAP) have been associated with larger cerebral infarctions and increased the likelihood of worse outcome in stroke patients (Becker et al., 2011; Planas et al, 2012). The GFAP expression in hippocampal CA1 and cortical region of model group was increased significantly in our experiment, but we did not find the effect of SQTS on GFAP. To further evaluate the role of neuroplasticity, cellular localization of GAP-43 was assessed. GAP-43 (Raghanti et al., 2008) is a calmodulin-binding phosphoprotein found in growing axons and growth cones of developing neurons and also in regenerating axons, considered to be a useful marker of developing neural connections and neuroplasticity or regenerating nerve fibres (Gil-Loyzaga et al., 2010). The results of this study verified that SQTS led to an increase in GAP-43 expression, which might indicate the existence of a regeneration or neuroplasticity process.

Chinese herbal medicine NDS and pharmaceutical chemical VP were used as the positive control. NDS ameliorates cerebral arteriosclerosis, ischemic stroke, and sequela of ischemic cerebrovascular disease. VP is a cerebral vasodilator that improves brain blood flow, and a cerebral metabolic enhancer by enhancing oxygen and

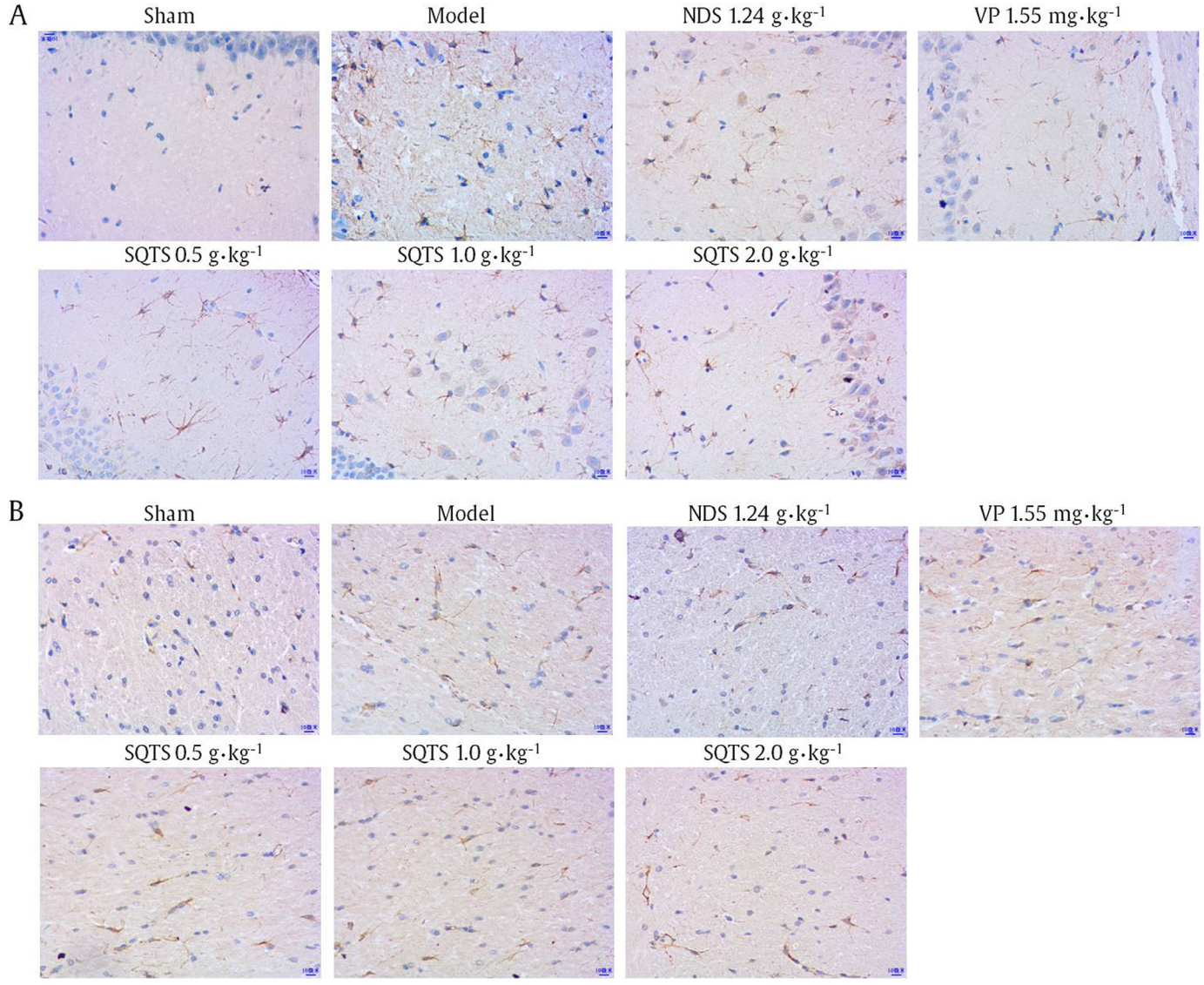

Fig. 3. Effects of SQTS on GFAP expression in hippocampal CA1 region (A) and cortical region (B) (×200, Scale bar 10 μm).

Table 5
Effect of SQTS on GFAP positive numbers of rats in sequelae post-stroke (mean ± SD, $n = 10$).

Groups	Doses / (g•kg^{-1})	Numbers	
		Hippocampal CA1 region	Cortical region
Sham	-	15.0 ± 2.7	13.7 ± 2.5
Model	-	25.0 ± 8.3$^{\Delta\Delta}$	21.8 ± 6.1$^{\Delta\Delta}$
SQTS	0.5	23.9 ± 7.1	19.9 ± 3.9
	1.0	24.2 ± 5.9	20.6 ± 3.6
	2.0	20.3 ± 6.1	22.4 ± 7.0
NDS	1.24	20.6 ± 2.9	20.8 ± 3.2
VP	1.55×10^{-3}	20.2 ± 5.5	20.5 ± 4.5

Note:
$^{\Delta\Delta}$ $P < 0.01$ *vs* sham group.

glucose uptake and increasing neuronal ATP production, which has been widely used in many countries for the prevention of cerebrovascular disorders and cognitive impairment, including stroke, senile dementia, and memory disturbances (Bagoly, Fehér, & Szapáry, 2007). Our experiment confirmed that SQTS could exert the same effect in ameliorating motor function as NDS at a dose of 2.0 g /kg after 30 d treatment, and showed the same effect as NDS on learning and memory function at a dose of 1.0 g/kg after 30 d treatment. SQTS may be superior to NDS on effect of GAP-43 positive numbers, NDS did not increase GAP-43, but SQTS 2.0 g/kg increased GAP-43 by 27.6% ($P < 0.05$) in hippocampal CA1 region and 30.6% ($P < 0.05$) in the cortical motor region, respectively.

5. Conclusion

In summary, SQTS shows robust neuroprotective effects in rats exposed to ischemic sequelae post-stroke. Such protective mechanisms may be involved via regeneration as activation of GAP-43 pathways.

Conflict of interest

The authors declare that they have no competing interests.

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