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Endogenous Neurogenesis and Chinese Medicine's Therapeutic Potential: A Potential Stroke Treatment Candidate

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Abstract

Stroke is the most common cause of adult morbidity and mortality worldwide. Numerous preclinical studies have demonstrated that neural-stem-cell-based stroke treatments have a significant therapeutic potential. A few investigations have affirmed that the compelling parts of conventional Chinese medication can secure and keep up with the endurance, multiplication, and separation of endogenous brain undifferentiated organisms through various targets and components. As a result, a potential treatment option for stroke patients is the use of Chinese medicines to activate and encourage endogenous nerve regeneration and repair. The current understanding of neural stem cell strategies for ischemic strokes and the potential effects of Chinese medicines on neuronal regeneration are summarized in this paper.

Keywords: Stroke • Chinese medication • Endogenous nerve regeneration • Neural stem cell • Neuronal regeneration

Introduction

Strokes are the main source of long haul incapacity and the subsequent driving reason for mortality and dismalness overall. Throughout the last ten years, numerous neuroprotective medication contenders for intense ischemic stroke that showed guarantee in exploratory creature stroke models have bombed in human clinical preliminaries. Two distinct FDA-approved treatments for acute ischemic strokes are thrombectomy and Recombinant Tissue Plasminogen Activator (rtPA). However, there are a few restrictions on these treatments. The use of rtPA is restricted due to the risk of hemorrhagic conversion and their limited temporal window (within 4.5 hours of stroke onset). According to statistics, only about 2–4% of stroke patients can benefit. Albeit current stroke therapy procedures in the subacute and persistent stages, for example, restoration, the drawn out administration of antithrombotic treatment (antiplatelet and anticoagulation), and the treatment of customary gamble factors, have shown wonderful adequacy, the general result stays poor. The molecular pathogenesis of neurological disorders is intricate, involving neuronal repair and irreversible brain injury. Neurogenesis is necessary for the growth of the brain and the repair of damage. Hypoxic Neural Stem Cells (NSCs) in vitro and ischemic brains in vivo, as well as neonatal mice, adult rats, and elderly humans, have all shown increased neurogenesis. However, because the majority of NSCs cannot survive tissue ischemia and reperfusion injury to induce differentiation, this type of spontaneous neurogenesis does not restore neurological function in ischemic stroke patients. There has been an ongoing search for more effective alternative therapies for neurogenesis. Due to its favorable preclinical and clinical outcomes, stem cell therapy has recently attracted a lot of interest as a regeneration therapy [1].

The transplantation of exogenous progenitor/stem cells and the activation/recruitment of endogenous NSCs are promising strategies for neuronal regeneration among all stroke treatments based on stem cells. However, the clinical application of NSC transplantation is hampered by a number of fundamental issues that remain unresolved. NSCs in the adult

brain, on the other hand, are induced to proliferate, migrate toward the damaged area, and differentiate into various cell types to help with functional repair, become functionally active and integrated into the surrounding tissue to help with neurological recovery in endogenous therapeutic strategies. Without the difficulties and difficulties of exogenous stem cell transplantation therapy, pharmacological interventions related to promoting adult endogenous neurogenesis may be a more practical strategy for treating stroke. Numerous foundational endlessly factors related with pathogenesis, like age, vascular gamble, span of treatment, and the site or degree of focal sensory system (CNS) harm, may influence the recuperation or fix of neurological shortfalls after a stroke. A complex sequence of coordinated neurodevelopmental events is necessary for the formation of brain circuits and the restoration of neurological function following a stroke. Neuronal migration, synaptic neogenesis, neural loop reconstruction, axonal regeneration, and neurovascular unit remodeling are all aspects of adult neurogenesis and neural regeneration following ischemic injury. These aspects are in addition to NPC proliferation. The complexity of the CNS response following a stroke, differences in synaptic plasticity, and limitations in axonal regeneration may be some of the factors that contribute to differences in the repair capacity of neurological functions in various forms of cerebral ischemic injury. The possibility of integrating newborn neurons into neural loops is determined by synaptic plasticity during the development of neural loops. The extent of neuronal impairment, myelin formation, synaptogenesis, astrocytic scars, and chondroitin sulfate proteoglycan levels all influence axonal regeneration, which is essential for the functional remodeling and restoration of the lost neural circuit. As a result, different types of stroke patients have different prognoses as a result of these differences [2].

Mechanism for endogenous neurogenesis: a way to deal with reestablishing neurological capability

Necrosis of brain tissue, death of nerve cells, and disorder in the intricate wiring of neurons, glial cells, and the vascular system are all symptoms of stroke. Endogenous NSCs' survival, differentiation, and neurogenesis may be affected by catastrophic changes in the cellular microenvironment brought on by stroke-related injury to the blood–brain barrier, excitotoxicity, mitochondrial dysfunction, oxidative stress, and neuro inflammation. Expanding proof has upheld that ischemic stroke prompts neurogenesis in various cerebrum districts. In order for newborn neurons to play a functional role in recovery from a stroke, they must proliferate, migrate, differentiate, and integrate. The essential components hidden the neuro protective impacts of NSCs in strokes have been broadly illustrated, including dietary help, the constriction of provocative reactions, immune modulatory capabilities, the designated substitution of neurons, the re-formation of brain circuits, and the reclamation of brain tissues that were harmed . As a result, enhancing endogenous neurogenesis mechanisms to promote tissue repair and replace lost neurons in the Central Nervous System (CNS) has long been a promising therapeutic target for stroke. However, we must acknowledge that endogenous neurogenesis following a stroke is not a one-time event. A scope of moderate occasions includes the enactment and expansion of NSCs, the relocation of these cells to harmed regions, the separation of begetter cells into various heredities, and the coordination of neurological capabilities. The Wnt/-catenin, Notch, and other signaling pathways play a neuroprotective role in this process by influencing endogenous neurogenesis by regulating the expression of related proteins [3].

Activation and proliferation

NSC proliferation increases significantly in both the SVZ and SGZ two to five days after a stroke, reaches a peak seven to eight days after ischemia, and persists for approximately thirty days. It was also confirmed by examining brain samples taken from stroke patients that proliferating neoblasts or new neurons were found in the penumbra area of the ischemic cortex 30 days after the stroke. Some of these new neurons appeared to migrate. Although the proliferation period of SVZ cells appears to be brief and only a few can eventually become mature neurons, this process is essential for stroke recovery, which is a conclusive conclusion regarding endogenous poststroke neurogenesis . After

a stroke, the rate of neurogenesis, the stem cell bank's health, and the brain's neurogenic capacity all depend on how well NSCs balance quiescence, activation, and proliferation. This change between the calm and proliferative territories of NSCs is reversible and firmly controlled by numerous flagging pathways [4].

NSCs' quiescent, proliferative, or differentiated states are all determined by the Notch signaling pathway, which is a key modulator in their capacity to self-renew and maintain their undifferentiated state. Score receptors are trans membrane, single-channel, heterodimer proteins that go through conformational changes by associating with Score ligands in neighboring cells to deliver the Indent intracellular space (NICD). The NICD then moves to the nucleus, where it joins the transcriptional repressor Recombination Signal Sequence Binding Protein J (RBP-J) to form a complex. The NICD-RBP-Jκ complex capabilities as a transcriptional activator or inducer of record factor articulation, causing the statement of different objective qualities, for example, Hes family BHLH record factors 1 and 5 (Hes1 and Hes5), NeuroD, Mash1, Neurogenin1 (Ngn1), and Neurogenin2 (Ngn2) , and in this way impacting the enactment, multiplication, and separation of NSCs. The SVZ has Hes genes that are expressed, and the level of Hes1 protein expression fluctuates in active NSCs. This drives the cyclic expression of its target gene, Achaetescute homolog 1 (Ascl1), which causes cell proliferation to be activated [5].

It has been demonstrated that the levels of Notch signaling and its downstream transcriptional target, Hes1, rise in the SVZs of MCAO-treated rats four and twenty-four hours after ischemia. Mice's SVZ cell proliferation is reduced when Notch1 signaling is inhibited. In contrast, the administration of the Notch ligand resulted in an increase in the number of proliferative cells in the SVZ as well as new cells that expressed the immature neuronal marker Hu in the rat cerebral cortex. In neurosphere cultures from adult rats, the Notch signaling pathway is involved in the proliferation of SVZ progenitor cells. In addition, the activation of the Notch1 signaling pathway led to an increase in the proliferation of NPCs in aged, ischemia-induced rats, which reduced the volume of the infarct and improved motor deficits. Under physiological and ischemic conditions, these findings suggest that adult neurogenesis and neuronal proliferation in the SVZ are mediated by Notch signaling. Focusing on and balancing the Indent flagging pathway is practical for further developing neurogenesis after ischemic injury [6].

Shh is a pleiotropic flagging protein that regulates the enactment, multiplication, and relocation of NSCs. The Shh signaling pathway regulates self-renewal, which is essential for behavioral recovery following a stroke. This is accomplished by increasing the systemic division of NSCs. Shh protein levels significantly increased on day 7 after ischemia in mature hippocampal neurons, particularly in the CA3 and hilar regions. After a stroke, cell proliferation can be increased in the adult hippocampus by overexpressing Shh in neural progenitor cells within the DG through adenoviral transcription. In contrast, the proliferation of granule cells in the DG decreased when the Shh signaling inhibitor cyclopamine was injected into the adult hippocampus and lateral ventricle. These findings suggest that inhibition of Shh inhibits neuronal neurogenesis and proliferation, and that Shh expression is upregulated in neurons following stroke.The mechanism that controls NSC activation and proliferation also relies heavily on the PI3K-Akt pathway. FOXO3 is a key record factor that keeps up with the peaceful territory of NSCs. There are a few transcriptional target genes that FOXO3 and ASCL1 share. FOXO3 seriously stifles the outflow of the Ascl1 target qualities related with the cell cycle to actuate the resting state in NSCs. mTOR activation and FOXO3 phosphorylation and inactivation are two of the downstream AKT signaling mechanisms that encourage the activation or proliferation of NSCs. The AKT-mTOR1 flagging outpouring is a viable inducer of NSC actuation and is normally viewed as the flagging integrator of nerves. The AKT-mTOR1 signaling cascade is regulated by a number of growth factors, including members of the insulin family and the MFGE8/integrin/ILK pathway. Mfge8 can bind to Itgb and activate phosphatase and tensin homolog, a dominant negative regulatory factor for PI3K activation, thereby suppressing Akt mediated mTOR activation. Mfge8 is secreted by the NSCs and astrocytes in the SGZ. Consequently, Mfge8 restrains Akt intervened mTOR actuation, which is important for PI3K-Akt enactment to initiate NSC expansion [7].

Migration

It has been legitimate that after a stroke, separating neoblasts relocate from the SVZ into the ipsilateral striatum and periinfarct region. A crucial step in the cell-mediated restoration of homeostasis in areas of injury is the migration of NSCs to the areas of the CNS that are undergoing neurodegeneration and injury. These neoblasts may undergo remodeling and express Doublecortin (DCX) and polysialylated neural cell adhesion molecules during migration.

Tropism is the natural tendency of NSCs to concentrate on the injury site, which is partly mediated by their chemokine receptors. The most common mechanisms that control migration include the chemokine SDF-1 and the CXCR4 receptor for it. After an ischemic stroke, it was found that the SDF-1 receptor, CXCR4, was communicated in brain forebears and stroke-created neuroblasts and that the statement of SDF-1 was expanded in responsive astrocytes and enacted microglia in the harmed region and stroke side of the equator. Two examples of cells that are influenced to migrate in a particular direction by the chemokine SDF-1 and its corresponding receptor, CXCR-4, are hippocampal dentate granule cells and cortical interneurons. Notwithstanding, the restraint of CXCR4 articulation incredibly lessens neuroblast relocation, proposing that SDF-1/CXCR-4 flagging advances the movement of neuroblasts to harmed regions. SDF-1 restricting to CXCR4 can actuate different flagging pathways, for example, p38 MAPK, PI3K/Akt, c-Jun N-Terminal Kinase (JNK), and ERK1/2, to upgrade foundational microorganism relocation. Osteopontin is a constitutive phosphoglycoprotein that is expressed in the brain. It is important for the homeostasis of tissues and may have therapeutic effects by increasing CXCR4 expression and encouraging the migration of NSCs. Additionally, one of the most widely used chemokines expressed during ischemia is CC motif Chemokine Ligand 2 (CCL2). Studies have demonstrated that an enhanced interaction between CCL2 and the CCL2 receptor (CCR2) is responsible for the migration of NSCs to the infarct area and subsequent neural repair [7].

Another crucial factor in neuroblast migration following a stroke is Monocyte Chemoattractant Protein-1 (MCP-1). After a stroke, MCP-1 is upregulated in responsive astrocytes and microglia in the cortex and striatum, and the MCP-1 receptor, CCR2, is communicated in new neuroblasts. Additionally, neuroblast migration is linked to a number of ECM proteins. After brain damage, Matrix Metalloproteinases (MMPs), a protease family involved in ECM remodeling, is upregulated and participate in neuroblast migration. In mice that had strokes, MMP-9 in the SVZ and striatum colocalized with the neuroblast marker DCX. The use of a MMP inhibitor fundamentally restrained the relocation of neuroblasts. DCX-positive neuroblasts migrating in another stroke mouse model expressed MMP-3. Using an in vitro assay system and specific siRNAs, it was discovered that chemokine migration was aided by endogenous MMP-3 and MMP-9 [6].

Differentiation

The completion of network reconstruction marks neural function recovery following brain injury. The brain's reconstruction of neural networks is supported anatomically by the functional differentiation of neurons. The separation of NSCs is managed by various sign co operations and is impacted by development factors, cytokines, bond particles, the extracellular network, and the cell microenvironment after a stroke. Ongoing examination recommends that FGF2 is a significant administrative variable for neurogenesis in the cerebrum, and the infusion of FGF2 into the parallel ventricle can build the quantity of new cells shaped in the hippocampal tissue of the grown-up mind. In addition, neuronal progenitor cell proliferation and disruptions in the generation of new neurons in the DG region were observed in conditional FGFR1-deficient mice. In neonatal rats with bilateral common carotid artery occlusion, FGF-2 treatment accelerates the differentiation of these cells into neurons, astrocytes, and oligodendrocytes in the SVZ. IGF-1 is a promitotic factor with multiple functions that plays a role in adult brain development. Through MAPK kinase, IGF-1 can directly stimulate hippocampal progenitor proliferation in adult brain. IGF-1 suppresses BMP signal transduction to promote the differentiation of adult hippocampal progenitor cells into oligodendroglial cells in vitro and in vivo in tandem with promoting

adult neurogenesis. After a stroke, Vascular Endothelial Growth Factor (VEGF) has a lot of neurogenic activity. After a stroke, the SVZ's levels of VEGF-A and VEGF receptor-1 increased. By increasing angiogenesis and neurogenesis, a short-term injection of VEGF-A into the ventricles is important for functional recovery after a stroke because it increases cell proliferation in the SVZ and DG 28 days after the stroke. Through a Flk-1-dependent mechanism, VEGF can directly induce mitosis in neuron progenitor cells. In addition, the SVZ's neuroglial progenitor cell differentiation into astrocytes is enhanced by VEGF-A. BDNF has a place with the neurotrophic factor family, which increments neurogenesis and the movement of brain begetter cells from the SVZ, in this way working on the recuperation of sensorimotor capability after a stroke. The sign transduction of BDNF and its TrkB receptor can advance neuronal endurance, dendritic arborization, and neurotransmitter arrangement to improve neurogenesis. BDNF likewise advances gamma-aminobutyric corrosive delivery, which is significant for advancing NSC separation and neurotransmitter development [8].

In adult brain and ischemic mouse models, recent evidence suggests that the Wnt/-catenin pathway is involved in the proliferation and differentiation of NSCs. Wnt proteins are principally emitted by NSCs and astrocytes in neurogenic specialties. The primary pathways involved in NSC differentiation are Wnt/-catenin and Wnt/planar cell polarity. The qualities, which code for Wnt (particularly Wnt1 and Wnt3), have been demonstrated to be upregulated in late ischemic strokes and are hence engaged with recuperation after ischemic injury. Wnt3 can bind to and activate target cells' transmembrane frizzled and low-density lipoprotein receptor-related protein 5/6 receptors because it is highly expressed in hippocampal DG cells. Consequently, the initiated receptor complex represses the enactment of glycogen synthase kinase-3 (GSK-3β), balancing out β-catenin inside the cell, moving it to the core, and consolidating it with the lymphoid enhancer factor/Lymphocyte factor (TCF). While Wnt ligands are missing, GSK-3β is actuated, prompting the intracellular corruption of β-catenin and the advancement of target quality record. Pax6, distal-less homeobox 2, and octamer-binding transcription factor 4 are among the target genes that are influenced by the Wnt signaling pathway and are associated with neurogenesis. It has been shown that after cerebral ischemia, Wnt3a for the most part improves the articulation levels of β-catenin and TCF-4 and the downstream enactment of the record factors Pax6 and Neurogenin2 in SD rodents. It has been demonstrated that Pax6, which is expressed in the SVZ and OB, regulates the proliferation and differentiation of NSCs both in vivo and in vitro. In the wake of prompting central cerebral ischemia in mice utilizing a nearby infusion of a lentivirus communicating Wnt3a-HA into the striatum or SVZ district, an emotional expansion in the quantity of separated BrdU-positive cells in the striatum into full grown and youthful neurons in the SVZ was noticed. Also, following 7 days of intranasal treatment with Wnt3a, BDNF articulation levels were upregulated in grown-up mice exposed to MCAO/R [8].

Effect of Chinese medicine in neurogenesis

NSCs have been demonstrated to be a likely wellspring of substitution for deteriorated neurons in CNS sicknesses. Utilizing little particles to prompt endogenous NSC neurogenesis is a possible methodology for producing the ideal cell types en masse. As a result, the applications of TCM's effects on NSCs are extremely promising. Because of its multicomponent and multitarget properties, it plays a significant role in NSCs' activation, proliferation, migration, differentiation, repair of neuronal loss, and functional injury [8].

Momordica charantia, also known as bitter melon, is a traditional fruit that is frequently used as an additional treatment for diabetes and cardiovascular disease. M Charantia Polysaccharides (MCPs) are significant bioactive parts with hypoglycemic, cholesterol-lessening, cancer prevention agent, and against corpulence properties. MCPs have been shown to restore memory and learning ability in MCAO rats and increase NSC proliferation in the SVZ and SGZ. Moreover, it advanced C17.2 cell expansion because of OGD injury. The potential instrument depends on the upregulation of SIRT1 movement and cytoplasmic β-catenin deacetylation, which advance β-catenin atomic movement to actuate NSC

multiplication [8].

Panax pseudoginseng ssp. leaves contain a saponin known as Pseudodoginsenoside-F11 (PF11). PF11 significantly reduced cognitive impairment, sensory dysfunction, infarction, mortality, and hippocampal atrophy in tMCAO mice. It also increased neuroblast migration and newborn neuron survival in the ipsilateral striatum and DG, primarily through activation of the BDNF/TrkB pathway. These effects improved long-term nerve damage and increased neurogenesis following a stroke, suggesting that it may play a role in the treatment of ischemic strokes in the post-stroke period [9].

Inhibiting oxidative stress, glutamate neurotoxicity, and apoptosis, ginsenoside, the primary active ingredient in ginseng, improves mitochondrial dysfunction and is widely used to treat acute ischemic strokes. NSC differentiation and proliferation are also aided by ginsenosides. Ginsenoside's ability to increase optical density and area density, the number of cells that are positive for nestin/BrdU, nestin/vimentin, and nestin/tuj-1, as well as the expression levels of BrdU, tuj-1, and vimentin, suggests that it may help NSCs in neurons and astrocytes grow and develop. Ginsenosides can also make HIF-1 and VEGF proteins express themselves, which suggests that neurogenesis is linked to the HIF-1-VEGF pathway being activated. Ginsenoside Rb1 improved stroke-related cortical axon regeneration and long-term motor function recovery, according to a recent study. Numerous signaling pathways, including cAMP, calmodulin, and NMDA receptors, phosphorylate CREB, a crucial transcription factor for cell growth and development. Cerebral ischemia incites a gigantic arrival of glutamic corrosive, which initiates the CREB pathway by collaborating with NMDA receptors, in this way prompting the declaration of Bcl-2 and BDNF. Research proposes that cAMP-intervened CREB phosphorylation advances NSC expansion and neuronal endurance in the grown-up hippocampus. In addition, the differentiation and maturation of newly formed hippocampal granule cells may be hindered by the spontaneous knockdown of CREB in mouse hippocampal cells. CREB flagging is fundamental for directing the endurance, relocation, and morphological separation of neuroblastomas in the SVZ. Pax6 may be regulating the effects of CREB signal transduction on the survival of immature neurons in the RMS, as evidenced by the fact that CREB deletion increases Pax6 expression. Following 14 days of mediation, ginsenoside Rb1 expanded GAP43 and BDA articulation in the ipsilateral and contralateral cortices of mice with distal center cerebral conduit impediment and worked on engine capability, which might have been because of the guideline of the cAMP/PKA/CREB flagging pathway [9].

The Buyang Huanwu decoction is made with Astragali Radix (AR), a popular TCM herb that is used to treat strokes. In a variety of experimental animal models of stroke, numerous active ingredients extracted and isolated from AR have demonstrated significant neuroprotective effects, including AS-VI's promotion of neurogenesis. By inducing neurogenesis and astrogenesis in the DG, SVZ, and cortex, AS-VI (2 g/kg) treated transiently ischemic rats for seven days improved spatial learning, memory, and motor function. Also, it improved the self-recharging and expansion of NSCs in vitro. Grown-up NPCs express the EGF receptor (EGFR), which is upregulated under ischemic circumstances to improve their weakness to EGF or other EGFR ligands in light of ischemia. EGF mediation advances neuronal separation in the corpus striatum after the beginning of ischemia in recently framed parvalbumin neurons. Neurosphere size and expression of nestin, p-EGFR, and p-MAPK proteins are increased by AS-VI treatment; however, this effect is reversed when gefitinib, an EGF receptor inhibitor, and PD98059, an ERK inhibitor, are administered together. After stroke treatment, AS-VI may be a therapeutic option for adult neurogenesis and brain repair by targeting the EGFR/MAPK signaling pathway.

A highly effective treatment for malaria is Artesunate (ART), a derivative of artemisinin. In a previous study, damage to the blood brain barrier in mice with subarachnoid hemorrhage was reduced by ART, primarily through mediation of the S1pR/PI3K signaling pathway. In addition, studies have uncovered that Workmanship lessens ischemic mind volume and white matter sores in MCAO mice and expands the extent of BrdU-positive endogenous NSPCs in the ipsilateral SVZ and periinfarct cortex. However,

FOXO3a overexpression counteracted the neurorestorative effects of ART, indicating that ART can promote endogenous NSPC neurogenesis and proliferation via the FOXO3a/p27Kip1 pathway to alleviate ischemia/reperfusion damage [9].

Osthole (Ost), a characteristic coumarin subsidiary separated from Cnidium monnieri (L.) Cusson, shows mitigating, antiapoptotic, antioxidative, and neurotrophic properties. Ost has been shown to improve neurogenesis in the hippocampus of APP/PS-1 double transgenic mice and to promote the proliferation of NSCs in vitro. In addition, it improved MBI mice's learning and memory function, increased the proliferation of endogenous NSCs, and enhanced neuronal restoration in areas of brain injury and the hippocampal DG and CA3. The fact that the c-secretase inhibitor DAPT inhibited Ost's upregulation of Notch1 and Hes1 gene expression as well as NICD and Hes1 protein expression suggests that Ost's neuroprotective effects are partially responsible for activating the Notch signaling pathway [10].

A perennial iris crocus (*Crocus sativus L.*) with a dry stigma yields crocin, a series of ester glycosides made by combining crocin acid and various sugars. Crocin hinders the Bax/Bcl-2 proportion in endogenous NSCs, lessens fiery variable delivery, and improves Notch1 articulation after cerebral ischemia reperfusion in the rodent mind. By mediating the Notch signaling pathway in a hypoglycemic/reoxygenation model, crocin's neuroprotective effects on NSC proliferation and migration were also demonstrated [10].

In traditional Chinese medicine, Elagic Acid (EA), a pomegranate derived antioxidant, is used to alleviate muscle spasms and neuropathic pain. EA has also been suggested as a possible treatment for a number of CNS conditions, like stroke and dementia. In rat ischemic penumbra, the administration of EA decreased infarct volume, enhanced neurological function, and raised nestin protein levels. Primary cultured NSCs also showed increased cell proliferation and upregulation of the catenin and cyclin D1 genes, indicating that EA can promote NSC proliferation and ameliorate brain injury via the Wnt/-catenin signaling pathway [10].

Conclusion

TCM's safety has been demonstrated through long-term clinical use, and it has been a popular research topic for the prevention and treatment of CNS diseases. The holistic regulation and comprehensive treatment of incurable neurological diseases like strokes that Chinese medicine offers are two of its advantages. Endogenous neurogenesis and repair are severely hindered in the pathological environment created by cerebral ischemic injury, as is well known. After a stroke, Chinese medicine may be an effective treatment option for promoting neuroprotection, ant apoptotic differentiation, and proliferation of NSCs, enhancing the brain's microenvironment, and decreasing neuroinflammation. Chinese medicine has been shown in a number of meta-analyses to significantly improve neurological deficits and clinical recovery in stroke patients, thereby enhancing their quality of life and overall therapeutic efficacy. Chinese medicines that regulate endogenous neurogenesis following a stroke and their related mechanisms are summarized in this review. However, we also noted that only a few of these studies were of high quality, that the majority of the data were generated in cell culture models with short-term outcomes, that there were few supportive, robust *in vivo* experiments, and that human clinical trials and epidemiologic data were relatively insufficient. These findings should be taken into consideration by researchers conducting follow-up studies. Besides, issues with fix/recovery in the CNS are not novel; instead, the majority of terminally differentiated organs and tissues share these characteristics. It would be interesting to find out if Chinese herbal medicines have the ability to repair and regenerate these organs and tissues. Due to the diversity of Chinese herbal medicines' active ingredients, it is difficult to establish a connection between herbs, ingredients, targets, and diseases, which results in a lack of relevant research. To fully analyze network relationships and integrate regulatory processes between the signaling pathways regulated by Chinese medicine, it is necessary to strengthen the application of technologies like high-throughput screening, small-molecule probes, label-free detection, and target identification and validation. Since no single compound will really treat

or fix stroke, a method for coordinating the utilization of individual substances or spices to deliver comprehensive treatment and show the system is as yet a test.

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