NEURAL REGENERATION RESEARCH
www.nrronline.org

Review

The role of exosomes in adult neurogenesis: implications for neurodegenerative diseases

Zhuoyang Yu[1, 2], Yan Teng[2], Jing Yang[1, 2], Lu Yang[1, 2, *]

https://doi.org/10.4103/1673-5374.379036

Date of submission: February 7, 2023

Date of decision: April 12, 2023

Date of acceptance: May 16, 2023

Date of web publication: July 7, 2023

From the Contents

Abstract

Exosomes are cup-shaped extracellular vesicles with a lipid bilayer that is approximately 30 to 200 nm in thickness. Exosomes are widely distributed in a range of body fluids, including urine, blood, milk, and saliva. Exosomes exert biological function by transporting factors between different cells and by regulating biological pathways in recipient cells. As an important form of intercellular communication, exosomes are increasingly being investigated due to their ability to transfer bioactive molecules such as lipids, proteins, mRNAs, and microRNAs between cells, and because they can regulate physiological and pathological processes in the central nervous system. Adult neurogenesis is a multistage process by which new neurons are generated and migrate to be integrated into existing neuronal circuits. In the adult brain, neurogenesis is mainly localized in two specialized niches: the subventricular zone adjacent to the lateral ventricles and the subgranular zone of the dentate gyrus. An increasing body of evidence indicates that adult neurogenesis is tightly controlled by environmental conditions with the niches. In recent studies, exosomes released from different sources of cells were shown to play an active role in regulating neurogenesis both *in vitro* and *in vivo*, thereby participating in the progression of neurodegenerative disorders in patients and in various disease models. Here, we provide a state-of-the-art synopsis of existing research that aimed to identify the diverse components of exosome cargoes and elucidate the therapeutic potential of exosomal contents in the regulation of neurogenesis in several neurodegenerative diseases. We emphasize that exosomal cargoes could serve as a potential biomarker to monitor functional neurogenesis in adults. In addition, exosomes can also be considered as a novel therapeutic approach to treat various neurodegenerative disorders by improving endogenous neurogenesis to mitigate neuronal loss in the central nervous system.
Key Words: adult neurogenesis; Alzheimer's disease; amyotrophic lateral sclerosis; exosome; Huntington's disease; neurodegenerative disease; neurogenic niches; Parkinson's disease

Introduction

Exosomes are tiny, single-membrane, organelles that are approximately 30 to 200 nm in size and are secreted as extracellular cup-shaped discoid vesicles with a lipid bilayer (Pegtel and Gould, 2019). Exosomes were first discovered in reticulocytes by Pan and Johnstone in 1983 (Pan and Johnstone, 1983). In terms of topological structure, exosomes are similar to cells and contain a variety of selected proteins, lipids, nucleic acids, and glycoconjugates; all of these can be delivered to cells (Salimi et al., 2020). Many studies have revealed that exosomes represent a novel mode of intercellular communication and participate in a wide range of physiological and pathological processes (Zhang et al., 2014, 2016b; Cano et al., 2023). A growing body of evidence suggests that exosomes also play critical roles in neurodegenerative diseases (D'Anca et al., 2019; Izco et al., 2022; Jiang et al., 2022). Exosomes and their cargoes may serve as biomarkers for disease progression. Exosomes could also be used as therapeutic targets to modulate neuroinflammation in the central nervous system (CNS). Recent studies have shown that exosomes also participate in crosstalk between cells in the neurogenic niche, thus modulating the process of neurogenesis in the adult brain (Bátiz et al., 2015; Egeland et al., 2015; Li and Guo, 2021). In this review, we summarized the bioactive cargoes of exosomes that have been identified to modulate the proliferation and fate of neural stem cells (NSCs) in the brain, and describe the underlying mechanisms of neurodegeneration and neuroinflammation that can be regulated by the cargo contained in exosomes. We also highlight the therapeutic potential of exosomes for neurodegenerative disorders via the improvement of neurogenesis in adults.

Literature Retrieval Strategy

We used the Web of Science and PubMed databases to collate relevant full-text articles published from inception to January 31, 2023 and written in English. The literature search was conducted by combining a range of key words, including "adult neurogenesis", "exosome", "extracellular vesicles", "neurodegenerative disorders", "Parkinson's disease", "Alzheimer's disease", "Huntington's disease" and/or," amyotrophic lateral sclerosis" to limit the topics and maximize the specificity and sensitivity of the references identified. After acquiring the selected reference list, we screened the titles and abstracts to identify potentially useful studies. We also used the Web of Science database to identify the citation status of each reference and by determining how many times each reference had been cited, we were able to identify high-impact papers. Next, we used the PubMed database to access the full texts of useful studies. In particular, we included two aspects of studies in each category of neurodegenerative diseases; we included studies that focused on the relationship between exosome cargoes and neurogenesis, and studies that were related to exosomes derived from neural stem cells. For example, when considering the "Regulation of neurogenesis by exosomes in PD", we collated studies that investigated the relationship between neurogenesis and exosomes in PD. However, we also included studies that focused on exosomes derived from other cell types and used to modulate neurogenesis for the treatment of animal model of PD.

Exosome Biogenesis

Exosomes were initially thought to be extracellular debris secreted by the reticulocyte substances that were destroyed by lysosomes (Kruh-Garcia et al., 2015). However, more recent studies have demonstrated that exosomes originate from the endocytic pathway (Lässer, 2015; Hessvik and Llorente, 2018) and that the typical process of exosomal biogenesis includes the formation of intraluminal vesicles and multi-vesicular bodies before extracellular release (Alenquer and Amorim, 2015; Yue et al., 2020). There are three main mechanisms involved in the formation of exosomes (DM and SJ, 2019): (1) vesicles bud into discrete endosomes that mature into multivesicular bodies and release exosomes as the plasma membranes undergo fusion; (2) immediate release from the plasma membrane by direct vesicle budding, and (3) delayed release by budding in the intracellular plasma membrane-connected compartment (IPMC) followed by contraction of the IPMC neck.

[1]Institute of Neurology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, Sichuan Province, China; [2]Laboratory of Aging Research, School of Medicine, University of Electronic Science and Technology of China, Chengdu, Sichuan Province, China
*Correspondence to: Lu Yang, PhD, lyang@uestc.edu.cn.
https://orcid.org/0000-0001-9144-3234 (Lu Yang)

Funding: *This work was supported by grants from the Department of Science and Technology of Sichuan Province, Nos. 2021ZYD0093 (to LY), 2022YFS0597 (to LY), 2021YJ0480 (to YT), and 2022ZYD0076 (to JY).*
How to cite this article: *Yu Z, Teng Y, Yang J, Yang L (2024) The role of exosomes in adult neurogenesis: implications for neurodegenerative diseases. Neural Regen Res 19(2):282-288.*

During the process of biogenesis, many types of proteins are loaded into exosomes, including membrane transporters and heat shock proteins (Jones et al., 2018). In addition, exosomes also contain a multitude of non-coding RNAs, including long non-coding RNAs (lncRNAs), microRNAs (miRNAs) and circular RNAs (circRNAs) (Li et al., 2021). Exosomes are enriched in body fluids, including urine, blood, milk, and saliva (Qin and Xu, 2014; Sun et al., 2018), and are frequently transported in the body via the blood circulation to exert their biological effects. As with the pathways by which viral particles are transported in target cells, exosomes are taken up by multiple processes, including macropinocytosis, phagocytosis, clathrin-dependent endocytosis, and clathrin-independent endocytosis (van Dongen et al., 2016). Target cells usually recognize and capture exosomes in three ways: (1) exosomes or their released substances bind to ligands on the surface of cell membranes; (2) exosomes are endocytosed by recipient cells, and (3) exosomes fuse with the membranes of target cells. Therefore, as shown in **Figure 1**, exosomes exert biological effects mainly by transporting bioactive materials such as proteins and miRNAs between cells.

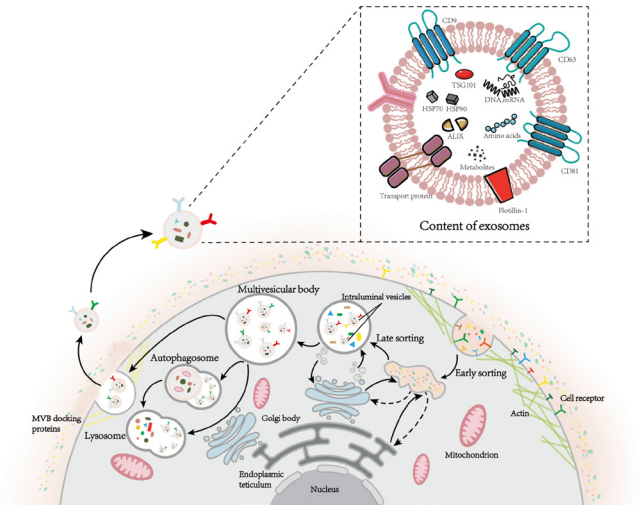

Figure 1 | **Exosomal cargoes.**
Exosomes bud from the endosomes and plasma membranes of cells and are mostly made up of genomic cargoes and non-genomic cargoes. There are two main protein components: one of these is essential for exosomal production and the other is unique to cell derivation. The majority of proteins involved in the synthesis of poly-vesicular endosomes are ALG-2-interacting protein X (Alix), tumor susceptibility gene 101 (TSG101), chaperone heat shock proteins (HSP70, HSP90, and HSP60), the tetraspanin superfamily (CD9, CD63, CD81, and CD82), RAS-related protein (Rab), and lipid raft marker protein (Yoshioka et al., 2013). Cholesterol, sphingolipids, and ceramides are all examples of lipid components. In addition, DNA, mRNAs, microRNAs (miRNAs), circular RNAs (circRNAs), and long non-coding RNAs are abundant in exosomes. Created using Adobe Illustrator.

The Relationship between Exosomes and Adult Neurogenesis

It is widely acknowledged that NSCs are present in certain regions of the adult mammalian brain where they proliferate to produce new neurons, a process known as adult neurogenesis (Matsubara et al., 2021). It is estimated that 9000 new cells are generated every 25 hours in the rat hippocampus (Cameron and McKay, 2001). In humans, direct evidence of adult neurogenesis was first obtained by the analysis of post-mortem brain tissue from cancer patients treated with the thymidine analog bromodeoxyuridine (BrdU, 5-bromo-2′-deoxyuridine) (Eriksson et al., 1998). The regulation of adult neurogenesis is a complex process that involves extracellular factors and intracellular mechanisms in the brain; this is a complex topic and has become a significant hotspot in research. Most regions of the mammalian brain acquire intact neurons before birth, and each neuronal population is added during a specific developmental stage (Cameron and Glover, 2015). In the mammalian brain, new neurons arise predominantly in the subventricular zone (SVZ) of the ventricular lateral zone (Bonaguidi et al., 2011) and the subgranular zone (SGZ) of the hippocampal dentate gyrus (DG) (Seri et al., 2001). Two significant properties of NSCs are cell proliferation and the production of three differentiated neural lineages: neurons, astrocytes, and oligodendrocytes (Gonçalves et al., 2016). NSCs can divide symmetrically or asymmetrically although the latter process is more dominant. Research has shown that the symmetrical division of a single NSC produces offspring and an immature neuron (Bonaguidi et al., 2011). These immature neurons migrate to the DG or olfactory bulb (OB) to further differentiate and mature into corresponding neural cells (Cope and Gould, 2019).

Many studies have demonstrated that the regulation of neurogenesis is dependent on the microenvironment (the neurogenic niche) of NSCs in the brain (Lepousez et al., 2013; Toda et al., 2019; Li and Guo, 2021). A distinct and specialized microenvironment known as the neurogenic niche encourages the proliferation and differentiation of NSCs toward the neuronal lineage and glia cells (Shin et al., 2014). As indicated in **Figure 2**, the neurogenic niche is known to be made up of a variety of cell types, including astrocytes, neurons, axon projections, and structures such as blood vessels. One of the key roles of the niche is to create an environment that will maintain most stem cells in a dormant and undifferentiated state. Signals from different cellular components within the niche also play a role in regulating the self-renewal and multipotent properties of NSCs (Liu et al., 2017).

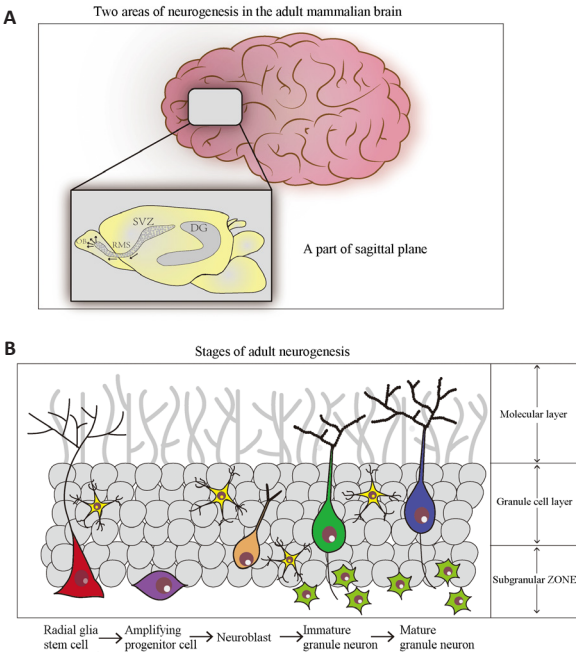

Figure 2 | **Neural stem cells in the neurogenic niche.**
Neural stem cells are mainly found in the subventricular zone (SVZ) region of the lateral ventricle and the subgranular zone (SGZ) region of the dentate gyrus of the hippocampus in the adult mammalian brain under physiological conditions. In the process of neurogenesis, neuroblasts in the SGZ and SVZ migrate to the dentate gyrus (DG) and olfactory bulb (OB) regions in a short or long migrational manner, respectively, following early differentiation to further differentiate and mature into corresponding neural cells into related circuits. Neural stem cells, neural progenitor cells, neuroblasts, immature neurons, and mature neurons are successively produced. Created using Adobe Illustrator. RMS: Rostral migratory stream.

The Transmission of Exosomes in Neurogenic Niches

Intercellular communication in the neurogenic niche is crucial for dynamic balance and the regulation of adult neurogenesis, especially with regards to signaling molecules such as cytokines, neurotransmitters, and hormones. Since exosomes serve as a tool for epigenetic regulation and the delivery of bioactive proteins for intercellular communication (Li et al., 2022a), they may also provide a microenvironment that facilitates disease progression in the brain. For example, it has been shown that in the animal model of Alzheimer's disease (AD), exosomes loaded with tau and α-synuclein (α-syn) were transported between neurons that were connected by synapses. The intracerebral injection of pathological tau from AD brains induces the seeding of normal tau in mouse brain (de Fisenne et al., 2022). In addition, researchers analyzed samples from the niches of adult amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), Parkinson's disease (PD), Lewy body dementia, and frontotemporal dementia (Terreros-Roncal et al., 2021) and identified alterations in the ratio of quiescent to proliferating hippocampal NSCs along with alterations in homeostasis within the neurogenic niche. Studies have also demonstrated that aging and neurodegenerative processes can reduce the phagocytic capacity of microglia (Yanguas-Casás et al., 2020), trigger astrogliosis, and alter the microvasculature of the dentate gyrus. It is known that signal transmission between diverse glial cells and neurons in neurogenic niches is particularly critical for maintaining the dynamic balance of adult neurogenesis and the active regulation of neural plasticity (Terreros-Roncal et al., 2021). Many cytokines, neurotransmitters and hormones play a significant role in this process. Different cell types, including NSCs, neurons and glia, have all been shown to release exosomes in the niche and, in turn, exert impact upon complex niche environments (Pardal and Lopez Barneo, 2016; Men et al., 2019; Rong et al., 2019). An elegant review previously summarized our current knowledge of the physiological role of exosomes within the neurogenic niche and how they can modulate neurogenesis (Losurdo and Grilli, 2020). An increasing body of evidence also indicates that exosomes and their contents are also involved in the onset and progression of neurodegenerative diseases by modulating the microenvironment of the niche.

Conversely, recent studies have demonstrated that the non-niche cells derived exosomes also participate in the regulation of neuroinflammation; this can benefit the environment supporting the neurogenic niche, enhance neurogenesis, and may even have potential therapeutic applications for several neurological diseases (Luarte et al., 2016; Yang et al., 2017; Nasirishargh et al., 2021). For example, exosomes secreted by somatic cell-induced NPCs and normal NPCs have been shown to regulate neuronal differentiation and promote neural regeneration via miR-21a (Ma et al., 2019). Another study found that multiple miRNAs (miR-125, miR-145, miR-18, and miR-21) are closely related to the process of adult neurogenesis in human mesenchymal stem cell-derived exosomes (Lojewski et al., 2014). These authors investigated the potential effects of these exosomes on the differentiation of multipotent NSCs and found that the mRNA levels of the NPC marker nestin were elevated in NSCs exposed to exosomes from all sources of human mesenchymal stem cells. Based on these properties, these exosomes also have significant therapeutic potential for various neurological diseases.

The Role of Exosomes in the Regulation of Neurogenesis in Neurodegenerative Disorders

The regulation of neurogenesis by exosomes in PD

PD, the second most common neurodegenerative condition after Alzheimer's disease, is clinically characterized by tremor, rigidity, bradykinesia and postural instability. The pathological characteristics of PD include the loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), severe misfolding and the aberrant buildup of α-syn in the remaining dopaminergic neurons, and the development of Lewy bodies (Mor et al., 2016). The tegmental aqueduct periventricular region (Aq-PVRs), which lies adjacent to the SNpc and contains clonogenic NSCs with DAergic potential, is thought to contain dormant neural progenitors (Marchetti et al., 2020). Adult Aq-PVR NSCs can be stimulated and induced to transform into DAergic neurons after PD injury both *in vitro* and *in vivo* (Marchetti et al., 2020); this represents an important sign for adult hippocampal neurogenesis in PD. A-synuclein, a well-known protein that controls adult neurogenesis, is essential for the development of PD and Lewy body dementia (Hall et al., 2014). When discharged into the extracellular area, α-synuclein can be taken up by neurons, NPCs, and astrocytes (Lee et al., 2010). Studies in transgenic rat models of PD have revealed that the accumulation of α-synuclein and the impairment of 5-HT neurotransmission have a deleterious impact on hippocampal neurogenesis in PD. This may occur before the development of protein aggregation and motor impairments in this disease (Kohl et al., 2016). After the typical period of dopaminergic neurogenesis, Lmx1a and other progenitor markers are still present in the midbrain aqueduct region, and dopamine receptor antagonists have been shown to promote their proliferation and improve neurogenesis (Hedlund et al., 2016).

Studies have also indicated that abnormal α-syn accumulation, oxidative stress, calcium homeostasis, and impaired axonal transport are the main causes of impaired neurogenesis in PD (Kline et al., 2021). Since exosome transmission between glial cells and neurons is actively involved in these processes, it follows that this mechanism is crucial for controlling neurogenesis in PD. There is evidence that α-syn aggregates can induce microglia to secrete exosomes containing α-syn oligomers. Exosome-associated a-syn oligomers are more likely to be received by nearby cells and trigger greater levels of toxicity when compared to the free oligomers (Danzer et al., 2012). Further studies demonstrated that pro-inflammatory cytokines can also trigger microglia to release more exosome-associated α-syn and enhance the inflammatory response in the brain (Guo et al., 2021). In such cases, exosomes could play a detrimental role in the transcellular spread of α-syn oligomers, thus impairing endogenous neurogenesis via toxic exosomal α-syn oligomers. More in-depth and detailed studies should aim to identify the function of exosome-associated α-syn in the regulation of adult neurogenesis in PD. Researchers have also tried to utilize exosomes generated from various stem cells *in vitro* to inhibit the aggregation of α-syn and stop the degeneration process in dopaminergic neurons. For example, some studies have indicated that exosomes also exhibit significant therapeutic potential to improve the function of neurogenesis in the niche. Exosomes derived from bone marrow mesenchymal stem cells have been shown to reverse the pathogenic features of PD by remodeling the inflammatory microenvironment in the SNpc region and by repairing DA nerve injury (Li et al., 2022b). Studies have also indicated that astrocyte atrophy in the early stages of PD may be pathologically relevant to the disturbance of exosome biogenesis in the niche, although their significance in disease progression remains unknown (Gómez-Gonzalo et al., 2017). Exosomes and microvesicles were previously generated from dental pulp stem cells and investigated for their ability to protect human dopaminergic neurons from oxidative stress under 6-hydroxydopamine treatment (Jarmalavičiūtė et al., 2015). Exosomes generated from dental pulp stem cells are thought to represent new therapeutic tools for the treatment of PD since the treatment of human DA neurons with these exosomes was shown to significantly reduce apoptosis induced by 6-hydroxydopamine.

The regulatory role of exosomes in the neurogenic niche in AD

AD is a neurodegenerative disease characterized by memory loss, cognitive impairment, and eventually, the loss of ability to carry out the simplest tasks. In 2013, a report on the epidemiology of AD was published by the World Health Organization; this report predicted that the global number of subjects with dementia could double by 2050 (Khan et al., 2020). Along with granulovacuolar degeneration and cerebrovascular alterations, there are two other key pathogenic abnormalities in AD: neuronal fibrillary tangles in brain cells created by tau hyperphosphorylation and senile plaques caused by the deposition of amyloid beta (Blennow et al., 2006). Neurodegeneration, with neuronal shrinkage triggered by the loss of synapses and cell bodies, is one of the progressive signs of AD (Schneider et al., 2009), especially in the hippocampus of AD patients (Benitez et al., 2015). Only a small number of studies have reported neurogenesis in AD even though research has shown that AD exacerbates the process of neurogenesis to a greater extent than physiological aging. A previous study used Mushashi as a marker and identified fewer progenitor cells in the SVZ of AD patients, despite an increase in nestin-positive stem cells (Babcock et al., 2021). Based on the expression of doublecortin (DCX), polysialic acid-neural cell adhesion molecule, and TUC4, a neurogenic differentiation factor, another study found that AD patients experienced enhanced neurogenesis in the hippocampus (Jin et al., 2004). Numerous studies employing transgenic mouse models of familial Alzheimer's disease have identified changes and dysfunctions in the SGZ of the DG (Wilke et al., 2014). Early findings also revealed changes in the neurogenic niche of AD patients, thus indicating impaired neurogenesis. The proliferation and survival of NPCs, as well as the quantity of new neurons in the DG of the hippocampus, were reported to be affected at 3, 6, and 9 months of age when compared to non-transgenic littermates when using a Tg2576 transgenic mouse model overexpressing APP (Pan et al., 2016).

Reactive astrogliosis is a process that protects the CNS by isolating damaged areas and reconstructing the blood brain barrier to support neural circuit remodeling; this is also a typical morphological feature of the brain in the late stages of AD (Vardjan et al., 2015). A previous study also found that amyloid-beta (Aβ) can be internalized into astrocytes and may alter the dynamics of vesicles, thus promoting the development of AD (Nagele et al., 2004). The neurotoxicity of Aβ and cell-to-cell dissemination have been associated with exosomes. A recent study reported the exosome-mediated transmission of neurotoxic proteins in AD; this study found that exosomes can be loaded with oligomer Aβ, thus leading to the transmission of exosomal Aβ from astrocytes to nearby neurons (Sardar Sinha et al., 2018). By investigating the proteomic profiles of exosomes isolated from different human-induced pluripotent stem cell-derived neural cell types, researchers have also found that cell-type-specific exosomes are involved in the progression of AD. A protein module enriched in astrocyte-specific exosomal markers was shown to be significantly associated with the pathology of AD and cognitive impairment. Further research should aim to investigate the role of astrocyte-specific exosome cargoes in the neurogenic niche since astrocytes contribute to neurogenesis in two distinct pathways: as NSCs and as niche cells. The microglia serve as primary phagocytes in the brain and are capable of ingesting neuronal exosomes that carry intact and hyperphosphorylated tau or Aβ proteins, thus enabling them to exert clearance functionality (Wang et al., 2017). However, microglia-derived exosomes have also been shown to significantly increase Aβ neurotoxicity (Guo et al., 2021). Microglia were shown to spread tau via the secretion of exosomes and by inhibiting exosome synthesis, thus significantly reducing the propagation of tau *in vitro* and *in vivo* (Asai et al., 2015). A previous study reported that exosomes secreted from sick cells may have detrimental effects on neurogenesis and promote disease progression in AD. Exosomes derived from the conditioned medium of HEK293-APP Swe/Ind cells were injected into the hippocampal DG region; subsequent analysis revealed high neurotoxicity and impaired neurogenesis in the hippocampus of AD mice (Zheng et al., 2017).

In contrast, a greater number of NSCs in the hippocampus has been linked to reduced rates of cognitive decline in animal models of AD. According to a recent study, exosomes secreted from NSCs were enriched with a particular set of miRNAs that protected synapses from Aβ oligomer (Aβo)-binding and Aβo-induced LTP inhibition, thus protecting AD mice from subsequent memory deficits. Exosomes derived from NSCs were also found to contain a variety of proteins with functions that were positively related to neuroprotection, neurite outgrowth-promoting activity and neurogenesis. Exosomes have also been shown to reduce nerve injury in different regions of the brain and regulate inflammatory responses to promote neurogenesis in mice models of AD (Micci et al., 2019). Exosomes released from mesenchymal stem cells have also been demonstrated to ameliorate cognitive impairment and boost neuroplasticity. Exosomes produced from mesenchymal stem cells have been shown to promote neurogenesis in the SVZ and reduced $A\beta_{1-42}$-induced cognitive impairment; this finding supports the development of cell-free therapeutic strategies for AD (Reza-Zaldivar et al., 2019).

The regulation of neurogenesis by exosomes in HD

HD, a form of gene dynamic mutation illness or polyglutamine repeat disease, is a dominant hereditary neurodegenerative disease characterized by involuntary movements, mental problems, and gradual dementia. Based on current epidemiological research, the estimated prevalence of this inherited neurological disorder is approximately 1 in 20,000 to 25,000 individuals. (Pascu et al., 2015). The cause of this disease is a CAG repeat expansion on the huntingtin (*Htt*) gene on chromosome 4. In the brain, this expansion causes the translation of the mutant Htt protein (mHtt) which results in the generation of intracellular mHTT aggregates (inclusions) (Reindl et al., 2019). These inclusions have been linked to a series of harmful events that cause gradual changes in the structure and function of the brain.

Research has also shown that the expression of *mHtt* causes delayed striatal NPC development, thus resulting in changes in the striatal circuits (Lebouc et al., 2020). Alterations in striatal development caused by reduced *Htt* expression and/or mHtt overexpression may make striatal neurons more

susceptible to cell death, thus resulting in neurodegeneration and motor abnormalities (Fu et al., 2018). With increased cell proliferation and the loss of mature neurons, adult neurogenesis appears to be reduced in the striatum of HD patients, thus indicating that neurogenesis may be initiated but limited during the maturation stage (Khuu et al., 2019). Research findings related to neurogenesis in human brains raise the prospect of endogenous neural repair for the treatment of patients with HD. A previous study indicated a statistically significant increase in cell proliferation in the subependymal layer adjacent to the caudate nucleus in response to neurodegeneration in this region in HD (Curtis et al., 2003). A previous study showed that increased severity of the pathology and the quantity of CAG repeats in the *HD* gene led to an increase in the level of cellular proliferation in a group of patients with HD. The most significant finding in this previous study was the proliferation of nuclear antigen positive cells co-localized with βIII-tubulin or GFAP, thus indicating that neurons and astrocytes are produced in the subependymal layer of patients with HD (Parent et al., 2002).

Exosomes are actively involved in the transmission of mHTT proteins and RNA between cells (Jeon et al., 2016). In a previous study, exosomes isolated from fibroblasts derived from HD patients were injected into the ventricles of newborn mice; this led to the development of clinical symptoms associated with HD (Jeon et al., 2016). Another study used an *in vitro* model of HD to demonstrate that polyglutamine and toxic CAG-repeat trinucleotide were transferred via extracellular vesicles (Zhang et al., 2016a). On the other hand, a recent study showed that exosomes derived from astrocytes reduced the density of mHTT aggregates in HD (Hong et al., 2017). In another cellular HD model, exosomes derived from adipose-derived stem cells (ASC-exo) were found to reduce mHTT aggregates and reverse mitochondrial dysfunction, thus reducing the extent of apoptosis in neurons (Lee et al., 2016). These authors found that ASC-exo considerably reduced mHtt aggregates in R6/2 mice-derived neuronal cells. Mechanically, ASC-exo upregulated PGC-1, phosphorylated CREB, and reduced aberrant levels of apoptotic proteins. ASC-exo also reduced mitochondrial dysfunction and apoptosis in a cellular model of HD as demonstrated by MitoSOX Red, JC-1, and cell viability assays. The regulatory function of exosomes isolated from different resource cells also indicated that exosome cargoes in the neurogenic niche could represent an important regulator of neurogenesis in HD patients, although this hypothesis needs to be validated by further research.

In addition to their role in regulating the progression of HD, exosomes are also thought to be a promising delivery tool for treating HD by improving endogenous neurogenesis. In the SVZ region, miR-124 was shown to induce adult neurogenesis and regulate the cell cycle in striatal neurons (Cheng et al., 2009). The delivery of miR-124 was proven to be a practical method to stimulate neuronal regeneration; this was beneficial because the striatum of HD patients exhibit neurogenic damage, thus leading to brain atrophy. In animal models of HD, exosome-based miR-124 delivery has been proven to represent a feasible method for inducing nerve regeneration (Lee et al., 2017). These results indicate that exosomes play an important role in cell communication in HD. However, the direct connection between neurogenesis and various exosomes in HD has yet to be fully elucidated. Further research is needed before exosomes can be used clinically to promote neurogenesis in HD.

Regulation of neurogenesis by exosomes in ALS

ALS, a chronic neurodegenerative disorder, usually leads to the dysfunction of lower motor neurons (the cranial nerve nuclei and anterior horn cells of the spinal cord), upper motor neurons (in the brain, brainstem, and spinal cord), and their innervated trunk, limbs and craniofacial muscles. The signs and symptoms of ALS vary greatly from person to person and depend on which neurons are affected (van Es et al., 2017). Most ALS cases (80–90%) are sporadic (sALS) while 10–20% of cases are familial (fALS) (Renton et al., 2014). Excitotoxicity and intracellular protein aggregation are thought to be mostly caused by mutations in the SOD1 gene. Other genetic factors linked to sALS and fALS include mutations in *TDP43* (TAR-DNA-binding protein 43) and *FUS* (sarcoma fusion protein) which impair RNA processing and cause proteins to aggregate (Wu et al., 2019). The most frequent genetic cause of ALS has recently been identified as hexanucleotide repeat expansion in *C9orf72*, which encodes proteins that disrupt RNA and protein homeostasis (Deng et al., 2011). The ability of NPC to proliferate can be irreversibly altered by changes in the neurogenic niche of *SOD1* (G93A) transgenic mice, an *in vivo* model of ALS (Lee et al., 2012). By using transgenic mice models, the temporal response of NPCs to motor neuron degeneration in the spinal cord and brain has been gradually revealed. Researchers often use brdU incorporation is used to identify proliferation of NPCs in the ependymal zone (EZ) around the central canal. Following treatment, NPCs lost their ability to proliferate after they migrated away from the EZ. NPCs in the EZ initially moved towards the dorsal horn; during the progression of ALS, they subsequently moved toward the region of the ventral horn where motor neurons began to deteriorate (Chi et al., 2006).

After studying the autopsies of patients with ALS, Galán et al. (2017) observed a statistically significant increase of NPC proliferation in the SVZ of all patients with ALS; this was also directly correlated with the levels of pTDP-43, a pathological hallmark for most cases of ALS, in the SVZ region. In contrast, all patients showed a reduction in the proliferation of NPCs in the SGZ region (Galán et al., 2017). Based on these findings, studies focused on the distribution of endogenous adult NPCs in an ALS mice model should be carried out during the onset of disease and during progression in order to provide fundamental guidelines for regenerative therapy in ALS by increasing *de novo* neurogenesis.

With regards to the mechanisms underlying neurodegeneration in ALS, numerous molecular mechanisms have been proposed, including mitochondrial failure, axonal transport, toxic protein aggregation, defective protein degradation, excitotoxicity, reduced neurotrophic support, oxidative stress, inflammation, and deficiencies of RNA metabolism. Exosomes have recently been shown to participate in the degenerative process of ALS. For example, exosomes can facilitate the transmission of mutant or misfolded SOD1 protein across cells in familial ALS (fALS) (Qualls et al., 2013). In astrocytes, mutant SOD1 causes dysfunction of the protein secretory system and exosome biogenesis. These exosomes then transmit mutant SOD1 to neurons in the spinal cord and cause motor neuron death in a selective manner (Basso et al., 2013). Studies have also indicated that misfolded SOD1 protein, produced in wild-type or mutant cells overexpressing SOD1, is associated with the secretion of exosome-like vesicles. Furthermore, this misfolded SOD1 protein can be transferred across cells in an EV-dependent manner (Grad et al., 2014).

In addition to misfolded SOD1 protein, another pathological marker, TPD-43, has also been found in exosomes derived from the CNS cells of ALS patients or animal models. Previous research showed that exosomal TDP43 oligomers were taken up preferentially by HEK-293 cells and exerted greater levels of toxicity than free TDP (Feiler et al., 2015). It has also been demonstrated that exosomal TDP-43 can activate peripheral monocytes and regulates the release of pro-inflammatory cytokines by monocytes (Zondler et al., 2017). Exosomes from hSOD1-G93A-transfected NSC-34 cells were previously loaded with miR-124 and shown to modulate the phenotype of microglia in a model of ALS (Pinto et al., 2017). Other studies have indicated that the inhibition of endogenous exosome biogenesis by GW4849, a pharmacological inhibitor, exacerbated the progression of disease in human TDP-43A315T transgenic mice. This study also indicated that exosomal signaling be beneficial for cell-to-cell communication at disease onset. Exosomal signaling may alter neuroinflammation in the neurogenic niche and significantly impact the regenerative properties of neurons in neurodegenerative diseases such as ALS. Additional regional specific or cell-type specific inhibition of exosome signaling will be needed to fully elucidate the relative contributions of exosomes in the regulation of neurogenesis in ALS.

Limitations

This paper has some limitations that need to be considered. First, we only reviewed the most common neurodegenerative diseases; we did not include acute CNS injuries such as stroke and brain disorders related to viral infection such as HIV associated neurological disorder. Second, we do not provide a comprehensive overview of the biogenesis of exosomes. Third, exosome cargoes are strictly dependent on the status of the parental cells, making these biological entities critical for the transmission of both physiological and pathological signals. We primarily focused on the pathological functions of exosomes in various diseases instead of health conditions. Exosomes derived from the cells in the neurogenic niches has also been demonstrated to play essential role in regulating adult neurogenesis. Exosomal contents such as miRNAs, proteins as well as lipids could be further caterorized to disccuss their involvement in the process of neurogenesis. Exosomes derived from the cells in the neurogenic niche has also been proved to play essential role in regulating regular adult neurogenesis. Exosomal contents such as miRNAs, proteins as well as lipids could be discussed in categories to summarize their involvement in each stage of adult neurogenesis in future.

Conclusions and Prospects

In this study, we reviewed dysfunctional patterns of neurogenesis in several neurodegenerative diseases, including PD, AD, HD and ALS. We also outlined the role of exosomes in neurogenesis and brain impairment in disease stated, as summarized in **Figure 3**. Exosomes can easily move across the blood-brain barrier and therefore represent an important tool for cellular communication within a neurogenic niche to modulate the process of neurogenesis. Emerging studies have also indicated that exosomes can serve as potent therapeutic carriers since they offer low immunogenicity, high stability, and both innate and acquired targetability. The transmission of exosomes between various cells has been shown to modulate the fate of NSCs within a neurogenic niche, although this form of regulation can be either beneficial or harmful; the functional effects are dependent on the cargo loaded inside the exosomes and the stage of disease (**Table 1**).

The protein oligomers in exosomal cargoes usually develop greater levels of aggregation than free oligomers; this leads to the preferential internalization of exosome-loaded oligomers and greater levels of toxicity than exosome-free oligomers. The uptake of intact exosomes by target cells involves multiple mechanisms, including caveolin-mediated endocytosis and cell membrane fusion. In neurodegenerative diseases, the phagocytosis of glial cells leads to the activation of microglia; in addition, astrocytes become actively involved in the regulation of exosomal cargo in the brain. Oligomers in a diseased brain can frequently be internalized; this can exert impact on genetic and non-genetic material in the cargo of glial cells, at least to some extent, thus leading to changes in the regulatory ability of glial exosomes within the niche (**Tables 1** and **2**). The role of exosomes in the pathogenesis of neurodegenerative diseases and the influence of glial exosomes on neurogenesis have yet to be fully elucidated. Further studies are needed to carefully investigate exosomal cargoes both *in vitro* and *in vivo* and determine the specific role of exosomes within the neurogenic niche, especially with regards to disease onset and progression.

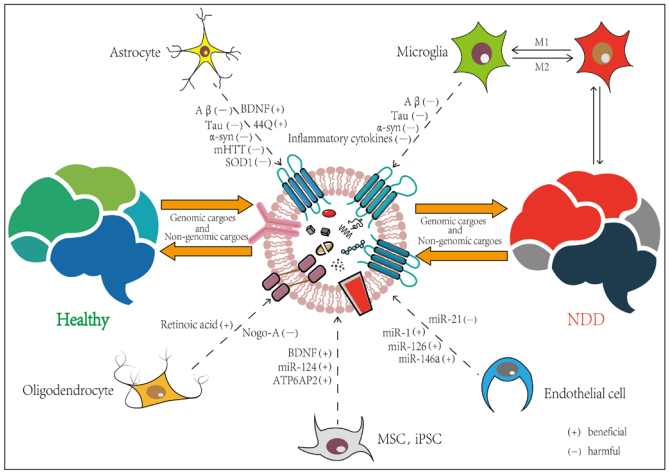

Figure 3 | Exosomes are secreted by glial cells and have a significant impact on the central nervous system.
Exosomes can stimulate the growth and development of synapses, neurons, and other cell types by transmitting various neurotropic factors, miRNAs, and bioactive proteins that protect neurons. Exosomes produced by glial cells also play roles in the development of neurodegenerative illnesses, including Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. For instance, exosomes are secreted to transfer inflammatory substances to stimulate immunological responses and transmit pathogenic proteins. Created using Adobe Illustrator. Aβ: Amyloid-beta; BDNF: brain-derived neurotrophic factor; iPSC: induced pluripotent stem cell; mHTT: mutant huntingtin protein; miRNAs: microRNAs; MSC: mesenchymal stem cell; SOD1: superoxide dismutase 1; α-syn: α-synuclein.

Table 1 | Exosomal protein as biomarkers for neurodegenerative disorders

Diseases	Exosome sources	Biomarkers	References
AD	Plasma, CSF	$A\beta_{42}$, pT181-tau, pS396-tau, total-tau	Tapiola et al., 2009; Goetzl et al., 2016; Xiao et al., 2017; Muraoka et al., 2020
PD	Blood, CSF	α-syn, DJ-1	Shi et al., 2014; Zhao et al., 2018
HD	CSF	mHTT, Nf1, NSE	Ciancarelli et al., 2014; Wild et al., 2015; Byrne et al., 2017
ALS	Plasma, CSF, serum	TDP-43, Nfl, p-Nfh, SOD1	Kasai et al., 2009; Noto et al., 2011; Boylan et al., 2013

AD: Alzheimer's disease; ALS: amyotrophic lateral sclerosis; $A\beta_{42}$: amyloid-beta 42; CSF: cerebrospinal fluid; HD: Huntington's disease; mHTT: mutant huntingtin protein; NfL: neurofilament light chain; PD: Parkinson's disease; p-NfH: phosphorylated neurofilament heavy chain; pS396-Tau: Tau phosphorylated at S396; pT181-Tau: Tau phosphorylated at T181; SOD1: superoxide dismutase 1; TDP-43: transactive response DNA-bindingprotein 43 kDa; α-syn: α-synuclein.

An increasing number of studies have also demonstrated the beneficial properties of exogenous cell-derived exosomes in regenerative medicine (**Tables 2** and **3**). MSC-derived exosomes have already been directly injected into the neurogenic niche to promote neurogenesis in several models of neurodegenerative disease models. Using cargo in endogenous or exogenous cell-derived exosomes to control adult neurogenesis has significant potential for the treatment and prognosis of neurodegenerative diseases. However, we still need to investigate the specific contents of exosomal cargo, along with associated regulatory mechanisms, if we are to fully understand the functional role of exosomes within the neurogenic niche. Furthermore, investigating the exosomal cargoes released by numerous niche cells that can impair neurogenesis could also identify useful targets to rescue the impaired environment provided by the niche and promote neurogenesis in neurodegenerative diseases. Before exosomes can be translated from the laboratory to the clinic, it is important to consider targeted delivery in more detail. This is because the delivery of exosomes to specific types of cells in the neurogenic niche could increase the local concentration of therapeutics and minimize side effects. Finally, we believe that future collaboration between researchers from various disciplines, such as clinicians, neurobiologists, technology authorities, and computer experts, could result in significant advancements in the future development of exosome-based therapy to promote neurogenesis in neurodegenerative diseases.

Author contributions: *ZY and LY searched literature and wrote the first draft of this manuscript, LY revised the manuscript and developed the main content of this manuscript. JY and TY provided great help for polishing the manuscript. All authors approved the final version of the manuscript.*
Conflicts of interest: *The authors declare that there are no conflicts of interest.*
Data availability statement: *Not applicable.*

Table 2 | Distinct non-genomic cargoes and effects identified in exosomes from different cells in the brain

Non-genomic cargo	Cell types	Effects	References
α-syn	Microglia	Pathological protein aggregation promotes Parkinson's disease development	Zhao and Yang, 2021
Aβ	Microglia, astrocyte	Pathological protein aggregation promotes Alzheimer's disease development	Kim et al., 2020; Kaur et al., 2021; Zhao et al., 2022
mHTT	Astrocyte	Pathological protein aggregation promotes Huntington's disease development	Hong et al., 2017
SOD1	Astrocyte	Transfer to spinal cord neurons and induce selective motor neuron death	Silverman et al., 2019
TDP-43	Astrocyte	Transfer to spinal cord neurons and induce selective motor neuron death	Iguchi et al., 2016; Maguire et al., 2019
IL-1β	Microglia	Induce and propagate inflammatory reactions throughout the brain	Jiang et al., 2021; Liu et al., 2022; Xian et al., 2022
BDNF	MSCs	Reduce amyloid-beta induced cognitive impairment	Xu et al., 2020; Ahn et al., 2021
Lipids	Oligodendrocyte	Neuroprotection and long-term axonal maintenance	Reiter and Bongarzone, 2020
44Q	Fibrocyte	Neuroprotection	Ren et al., 2009
Hsp70	Astrocyte	Promote neuronal survival	Attili et al., 2020
Wnt5a	BMSC	Inhibit the release of inflammatory factors and reduce M1 polarization in microglia	Xu et al., 2022
caspase-1	Microglia	IL-1β processing enzyme	Zhou et al., 2022
synapsin-1	Astrocyte	Neuroprotection	Upadhya et al., 2020
Myelin proteins	Oligodendrocyte	Neuroprotection and long-term axonal maintenance	Aneesh et al., 2021

Aβ: Amyloid-beta; BDNF: brain-derived neurotrophic factor; BMSC: bone marrow mesenchymal stem cell; Hsp70: heat shock protein 70; IL-1β: Interleukin-1 beta; mHTT: mutant huntingtin protein; SOD1: superoxide dismutase 1; TDP-43: transactive response DNA-bindingprotein 43 kDa; Wnt5a: Wingless-related MMTV integration site 5A; α-syn: α-synuclein.

Table 3 | Distinct genomic cargoes and effects identified in exosomes from central nervous system cells in neurodegenerative disorders

Genomic cargo	Cell types	Effects	References
miR-1	NSC	Increases hippocampal neurogenesis	Micci et al., 2019
miR-17-92	MSC	Reducing binding of Aβ to synapses increases synaptic resistance protectingtheprotecting the hippocampus from Aβ-induced LTP inhibition	Micci et al., 2019
miR-124	NSC	Induced adult neurogenesis in the subventricular zone and regulated cell cyclein striatal neurons	Cheng et al., 2009
miR-124	NSC-34	Drives changes in microglial phenotype and suppresses inflammatory responses	Pinto et al., 2017
miR-322	NSC	Reducing binding of Aβ to synapses increases synaptic resistance protectingtheprotecting the hippocampus from Aβ-induced LTP inhibition	Micci et al., 2019

Aβ: Amyloid-beta; LTP: long-term potentiation; MSC: mesenchymal stem cell; NSC: neural stem cell.

References

Ahn SY, Sung DK, Kim YE, Sung S, Chang YS, Park WS (2021) Brain-derived neurotropic factor mediates neuroprotection of mesenchymal stem cell-derived extracellular vesicles against severe intraventricular hemorrhage in newborn rats. Stem Cells Transl Med 10:374-384.

Alenquer M, Amorim MJ (2015) Exosome biogenesis, regulation, and function in viral infection. Viruses 7:5066-5083.
Aneesh A, Liu A, Moss HE, Feinstein D, Ravindran S, Mathew B, Roth S (2021) Emerging concepts in the treatment of optic neuritis: mesenchymal stem cell-derived extracellular vesicles. Stem Cell Res Ther 12:594.
Asai H, Ikezu S, Tsunoda S, Medalla M, Luebke J, Haydar T, Wolozin B, Butovsky O, Kugler S, Ikezu T (2015) Depletion of microglia and inhibition of exosome synthesis halt tau propagation. Nat Neurosci 18:1584-1593.
Attili D, Schill DJ, DeLong CJ, Lim KC, Jiang G, Campbell KF, Walker K, Laszczyk A, McInnis MG, O'Shea KS (2020) Astrocyte-derived exosomes in an iPSC model of bipolar disorder. Adv Neurobiol 25:219-235.
Babcock KR, Page JS, Fallon JR, Webb AE (2021) Adult hippocampal neurogenesis in aging and Alzheimer's disease. Stem Cell Reports 16:681-693.
Basso M, Pozzi S, Tortarolo M, Fiordaliso F, Bisighini C, Pasetto L, Spaltro G, Lidonnici D, Gensano F, Battaglia E, Bendotti C, Bonetto V (2013) Mutant copper-zinc superoxide dismutase (SOD1) induces protein secretion pathway alterations and exosome release in astrocytes: implications for disease spreading and motor neuron pathology in amyotrophic lateral sclerosis. J Biol Chem 288:15699-15711.
Bátiz LF, Castro MA, Burgos PV, Velásquez ZD, Muñoz RI, Lafourcade CA, Troncoso-Escudero P, Wyneken U (2015) Exosomes as novel regulators of adult neurogenic niches. Front Cell Neurosci 9:501.
Benitez BA, Cairns NJ, Schmidt RE, Morris JC, Norton JB, Cruchaga C, Sands MS (2015) Clinically early-stage CSPα mutation carrier exhibits remarkable terminal stage neuronal pathology with minimal evidence of synaptic loss. Acta Neuropathol Commun 3:73.
Blennow K, de Leon MJ, Zetterberg H (2006) Alzheimer's disease. Lancet 368:387-403.
Bonaguidi MA, Wheeler MA, Shapiro JS, Stadel RP, Sun GJ, Ming GL, Song H (2011) In vivo clonal analysis reveals self-renewing and multipotent adult neural stem cell characteristics. Cell 145:1142-1155.
Boylan KB, Glass JD, Crook JE, Yang C, Thomas CS, Desaro P, Johnston A, Overstreet K, Kelly C, Polak M, Shaw G (2013) Phosphorylated neurofilament heavy subunit (pNF-H) in peripheral blood and CSF as a potential prognostic biomarker in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 84:467-472.
Byrne LM, Rodrigues FB, Blennow K, Durr A, Leavitt BR, Roos RAC, Scahill RI, Tabrizi SJ, Zetterberg H, Langbehn D, Wild EJ (2017) Neurofilament light protein in blood as a potential biomarker of neurodegeneration in Huntington's disease: a retrospective cohort analysis. Lancet Neurol 16:601-609.
Cameron HA, McKay RD (2001) Adult neurogenesis produces a large pool of new granule cells in the dentate gyrus. J Comp Neurol 435:406-417.
Cameron HA, Glover LR (2015) Adult neurogenesis: beyond learning and memory. Annu Rev Psychol 66:53-81.
Cano A, Ettcheto M, Bernuz M, Puerta R, Esteban de Antonio E, Sánchez-López E, Souto EB, Camins A, Martí M, Pividori MI, Boada M, Ruiz A (2023) Extracellular vesicles, the emerging mirrors of brain physiopathology. Int J Biol Sci 19:721-743.
Cheng LC, Pastrana E, Tavazoie M, Doetsch F (2009) miR-124 regulates adult neurogenesis in the subventricular zone stem cell niche. Nat Neurosci 12:399-408.
Chi L, Ke Y, Luo C, Li B, Gozal D, Kalyanaraman B, Liu R (2006) Motor neuron degeneration promotes neural progenitor cell proliferation, migration, and neurogenesis in the spinal cords of amyotrophic lateral sclerosis mice. Stem Cells 24:34-43.
Ciancarelli I, De Amicis D, Di Massimo C, Di Scanno C, Pistarini C, D'Orazio N, Tozzi Ciancarelli MG (2014) Peripheral biomarkers of oxidative stress and their limited potential in evaluation of clinical features of Huntington's patients. Biomarkers 19:452-456.
Cope EC, Gould E (2019) Adult neurogenesis, glia, and the extracellular matrix. Cell Stem Cell 24:690-705.
Curtis MA, Penney EB, Pearson AG, van Roon-Mom WM, Butterworth NJ, Dragunow M, Connor B, Faull RL (2003) Increased cell proliferation and neurogenesis in the adult human Huntington's disease brain. Proc Natl Acad Sci U S A 100:9023-9027.
D'Anca M, Fenoglio C, Serpente M, Arosio B, Cesari M, Scarpini EA, Galimberti D (2019) Exosome determinants of physiological aging and age-related neurodegenerative diseases. Front Aging Neurosci 11:232.
Danzer KM, Kranich LR, Ruf WP, Cagsal-Getkin O, Winslow AR, Zhu L, Vanderburg CR, McLean PJ (2012) Exosomal cell-to-cell transmission of alpha synuclein oligomers. Mol Neurodegener 7:42.
de Fisenne MA, Yilmaz Z, De Decker R, Suain V, Buée L, Ando K, Brion JP, Leroy K (2022) Alzheimer PHF-tau aggregates do not spread tau pathology to the brain via the Retino-tectal projection after intraocular injection in male mouse models. Neurobiol Dis 174:105875.
Deng HX, Chen W, Hong ST, Boycott KM, Gorrie GH, Siddique N, Yang Y, Fecto F, Shi Y, Zhai H, Jiang H, Hirano M, Rampersaud E, Jansen GH, Donkervoort S, Bigio EH, Brooks BR, Ajroud K, Sufit RL, Haines JL, et al. (2011) Mutations in UBQLN2 cause dominant X-linked juvenile and adult-onset ALS and ALS/dementia. Nature 477:211-215.
Egeland M, Zunszain PA, Pariante CM (2015) Molecular mechanisms in the regulation of adult neurogenesis during stress. Nat Rev Neurosci 16:189-200.
Eriksson PS, Perfilieva E, Björk-Eriksson T, Alborn AM, Nordborg C, Peterson DA, Gage FH (1998) Neurogenesis in the adult human hippocampus. Nat Med 4:1313-1317.
Feiler MS, Strobel B, Freischmidt A, Helferich AM, Kappel J, Brewer BM, Li D, Thal DR, Walther P, Ludolph AC, Danzer KM, Weishaupt JH (2015) TDP-43 is intercellularly transmitted across axon terminals. J Cell Biol 211:897-911.
Fu H, Hardy J, Duff KE (2018) Selective vulnerability in neurodegenerative diseases. Nat Neurosci 21:1350-1358.
Galán L, Gómez-Pinedo U, Guerrero A, García-Verdugo JM, Matías-Guiu J (2017) Amyotrophic lateral sclerosis modifies progenitor neural proliferation in adult classic neurogenic brain niches. BMC Neurol 17:173.
Goetzl EJ, Mustapic M, Kapogiannis D, Eitan E, Lobach IV, Goetzl L, Schwartz JB, Miller BL (2016) Cargo proteins of plasma astrocyte-derived exosomes in Alzheimer's disease. FASEB J 30:3853-3859.
Gómez-Gonzalo M, Martin-Fernandez M, Martínez-Murillo R, Mederos S, Hernández-Vivanco A, Jamison S, Fernandez AP, Serrano J, Calero P, Futch HS, Corpas R, Sanfeliu C, Perea G, Araque A (2017) Neuron-astrocyte signaling is preserved in the aging brain. Glia 65:569-580.
Gonçalves JT, Schafer ST, Gage FH (2016) Adult neurogenesis in the hippocampus: from stem cells to behavior. Cell 167:897-914.
Grad LI, Yerbury JJ, Turner BJ, Guest WC, Pokrishevsky E, O'Neill MA, Yanai A, Silverman JM, Zeineddine R, Corcoran L, Kumita JR, Luheshi LM, Yousefi M, Coleman BM, Hill AF, Plotkin SS, Mackenzie IR, Cashman NR (2014) Intercellular propagated misfolding of wild-type Cu/Zn superoxide dismutase occurs via exosome-dependent and -independent mechanisms. Proc Natl Acad Sci U S A 111:3620-3625.
Guo M, Hao Y, Feng Y, Li H, Mao Y, Dong Q, Cui M (2021) Microglial exosomes in neurodegenerative disease. Front Mol Neurosci 14:630808.
Hall H, Reyes S, Landeck N, Bye C, Leanza G, Double K, Thompson L, Halliday G, Kirik D (2014) Hippocampal Lewy pathology and cholinergic dysfunction are associated with dementia in Parkinson's disease. Brain 137:2493-2508.
Hedlund E, Belnoue L, Theofilopoulos S, Salto C, Bye C, Parish C, Deng Q, Kadkhodaei B, Ericson J, Arenas E, Perlmann T, Simon A (2016) Dopamine receptor antagonists enhance proliferation and neurogenesis of midbrain Lmx1a-expressing progenitors. Sci Rep 6:26448.
Hessvik NP, Llorente A (2018) Current knowledge on exosome biogenesis and release. Cell Mol Life Sci 75:193-208.
Hong Y, Zhao T, Li XJ, Li S (2017) Mutant huntingtin inhibits αB-crystallin expression and impairs exosome secretion from astrocytes. J Neurosci 37:9550-9563.
Iguchi Y, Eid L, Parent M, Soucy G, Bareil C, Riku Y, Kawai K, Takagi S, Yoshida M, Katsuno M, Sobue G, Julien JP (2016) Exosome secretion is a key pathway for clearance of pathological TDP-43. Brain 139:3187-3201.
Izco M, Carlos E, Alvarez-Erviti L (2022) Impact of endolysosomal dysfunction upon exosomes in neurodegenerative diseases. Neurobiol Dis 166:105651.
Jarmalavičiūtė A, Tunaitis V, Pivoraitė U, Venalis A, Pivoriūnas A (2015) Exosomes from dental pulp stem cells rescue human dopaminergic neurons from 6-hydroxy-dopamine-induced apoptosis. Cytotherapy 17:932-939.
Jeon I, Cicchetti F, Cisbani G, Lee S, Li E, Bae J, Lee N, Li L, Im W, Kim M, Kim HS, Oh SH, Kim TA, Ko JJ, Aubé B, Oueslati A, Kim YJ, Song J (2016) Human-to-mouse prion-like propagation of mutant huntingtin protein. Acta Neuropathol 132:577-592.
Jiang S, Maphis NM, Binder J, Chisholm D, Weston L, Duran W, Peterson C, Zimmerman A, Mandell MA, Jett SD, Bigio E, Geula C, Mellios N, Weick JP, Rosenberg GA, Latz E, Heneka MT, Bhaskar K (2021) Proteopathic tau primes and activates interleukin-1β via myeloid-cell-specific MyD88- and NLRP3-ASC-inflammasome pathway. Cell Rep 36:109720.
Jiang Y, Wang F, Wang K, Zhong Y, Wei X, Wang Q, Zhang H (2022) Engineered exosomes: a promising drug delivery strategy for brain diseases. Curr Med Chem 29:3111-3124.
Jin K, Peel AL, Mao XO, Xie L, Cottrell BA, Henshall DC, Greenberg DA (2004) Increased hippocampal neurogenesis in Alzheimer's disease. Proc Natl Acad Sci U S A 101:343-347.
Jones LB, Bell CR, Bibb KE, Gu L, Coats MT, Matthews QL (2018) Pathogens and their effect on exosome biogenesis and composition. Biomedicines 6:79.
Kasai T, Tokuda T, Ishigami N, Sasayama H, Foulds P, Mitchell DJ, Mann DM, Allsop D, Nakagawa M (2009) Increased TDP-43 protein in cerebrospinal fluid of patients with amyotrophic lateral sclerosis. Acta Neuropathol 117:55-62.
Kaur S, Verma H, Dhiman M, Tell G, Gigli GL, Janes F, Mantha AK (2021) Brain exosomes: friend or foe in Alzheimer's disease? Mol Neurobiol 58:6610-6624.
Khan S, Barve KH, Kumar MS (2020) Recent advancements in pathogenesis, diagnostics and treatment of Alzheimer's disease. Curr Neuropharmacol 18:1106-1125.
Khuu MA, Pagan CM, Nallamothu T, Hevner RF, Hodge RD, Ramirez JM, Garcia AJ, 3rd (2019) Intermittent hypoxia disrupts adult neurogenesis and synaptic plasticity in the dentate gyrus. J Neurosci 39:1320-1331.
Kim E, Otgontenger U, Jamsranjav A, Kim SS (2020) Deleterious alteration of glia in the brain of Alzheimer's disease. Int J Mol Sci 21.
Kline EM, Houser MC, Herrick MK, Seibler P, Klein C, West A, Tansey MG (2021) Genetic and environmental factors in Parkinson's disease converge on immune function and inflammation. Mov Disord 36:25-36.
Kohl Z, Ben Abdallah N, Vogelgsang J, Tischer L, Deusser J, Amato D, Anderson S, Müller CP, Riess O, Masliah E, Nuber S, Winkler J (2016) Severely impaired hippocampal neurogenesis associates with an early serotonergic deficit in a BAC α-synuclein transgenic rat model of Parkinson's disease. Neurobiol Dis 85:206-217.
Kruh-Garcia NA, Wolfe LM, Dobos KM (2015) Deciphering the role of exosomes in tuberculosis. Tuberculosis (Edinb) 95:26-30.
Lässer C (2015) Exosomes in diagnostic and therapeutic applications: biomarker, vaccine and RNA interference delivery vehicle. Expert Opin Biol Ther 15:103-117.
Lebouc M, Richard Q, Garret M, Baufreton J (2020) Striatal circuit development and its alterations in Huntington's disease. Neurobiol Dis 145:105076.
Lee HJ, Suk JE, Patrick C, Bae EJ, Cho JH, Rho S, Hwang D, Masliah E, Lee SJ (2010) Direct transfer of alpha-synuclein from neuron to astroglia causes inflammatory responses in synucleinopathies. J Biol Chem 285:9262-9272.
Lee JC, Shin JH, Park BW, Kim GS, Kim JC, Kang KS, Cha CI (2012) Region-specific changes in the immunoreactivity of SIRT1 expression in the central nervous system of SOD1(G93A) transgenic mice as an in vivo model of amyotrophic lateral sclerosis. Brain Res 1433:20-28.
Lee M, Liu T, Im W, Kim M (2016) Exosomes from adipose-derived stem cells ameliorate phenotype of Huntington's disease in vitro model. Eur J Neurosci 44:2114-2119.
Lee ST, Im W, Ban JJ, Lee M, Jung KH, Lee SK, Chu K, Kim M (2017) Exosome-based delivery of miR-124 in a Huntington's disease model. J Mov Disord 10:45-52.
Lepousez G, Valley MT, Lledo PM (2013) The impact of adult neurogenesis on olfactory bulb circuits and computations. Annu Rev Physiol 75:339-363.
Li C, Ni YQ, Xu H, Xiang QY, Zhao Y, Zhan JK, He JY, Li S, Liu YS (2021) Roles and mechanisms of exosomal non-coding RNAs in human health and diseases. Signal Transduct Target Ther 6:383.
Li Y, Guo W (2021) Neural stem cell niche and adult neurogenesis. Neuroscientist 27:235-245.
Li Y, Meng L, Li B, Li Y, Shen T, Zhao B (2022a) The exosome journey: from biogenesis to regulation and function in cancers. J Oncol 2022:9356807.
Li Y, Li Z, Gu J, Xu X, Chen H, Gui Y (2022b) Exosomes isolated during dopaminergic neuron differentiation suppressed neuronal inflammation in a rodent model of Parkinson's disease. Neurosci Lett 771:136414.
Liu C, Sun R, Huang J, Zhang D, Huang D, Qi W, Wang S, Xie F, Shen Y, Shen C (2017) The BAF45D protein is preferentially expressed in adult neurogenic zones and in neurons and may be required for retinoid acid induced PAX6 expression. Front Neuroanat 11:94.

Liu S, Fan M, Xu JX, Yang LJ, Qi CC, Xia QR, Ge JF (2022) Exosomes derived from bone-marrow mesenchymal stem cells alleviate cognitive decline in AD-like mice by improving BDNF-related neuropathology. J Neuroinflammation 19:35.
Lojewski X, Hermann A, Wegner F, Araúzo-Bravo MJ, Hallmeyer-Elgner S, Kirsch M, Schwarz J, Schöler HR, Storch A (2014) Human adult white matter progenitor cells are multipotent neuroprogenitors similar to adult hippocampal progenitors. Stem Cells Transl Med 3:458-469.
Losurdo M, Grilli M (2020) Extracellular vesicles, influential players of intercellular communication within adult neurogenic niches. Int J Mol Sci 21:8819.
Luarte A, Bátiz LF, Wyneken U, Lafourcade C (2016) Potential therapies by stem cell-derived exosomes in CNS diseases: focusing on the neurogenic niche. Stem Cells Int 2016:5736059.
Ma Y, Li C, Huang Y, Wang Y, Xia X, Zheng JC (2019) Exosomes released from neural progenitor cells and induced neural progenitor cells regulate neurogenesis through miR-21a. Cell Commun Signal 17:96.
Maguire G, Paler L, Green L, Mella R, Valcarcel M, Villace P (2019) Rescue of degenerating neurons and cells by stem cell released molecules: using a physiological renormalization strategy. Physiol Rep 7:e14072.
Marchetti B, Tirolo C, L'Episcopo F, Caniglia S, Testa N, Smith JA, Pluchino S, Serapide MF (2020) Parkinson's disease, aging and adult neurogenesis: Wnt/β-catenin signalling as the key to unlock the mystery of endogenous brain repair. Aging Cell 19:e13101.
Matsubara S, Matsuda T, Nakashima K (2021) Regulation of adult mammalian neural stem cells and neurogenesis by cell extrinsic and intrinsic factors. Cells 10:1145.
Men Y, Yelick J, Jin S, Tian Y, Chiang MSR, Higashimori H, Brown E, Jarvis R, Yang Y (2019) Exosome reporter mice reveal the involvement of exosomes in mediating neuron to astroglia communication in the CNS. Nat Commun 10:4136.
Micci MA, Krishnan B, Bishop E, Zhang WR, Guptarak J, Grant A, Zolochevska O, Tumurbaatar B, Franklin W, Marino C, Widen SG, Luthra A, Kernie SG, Taglialatela G (2019) Hippocampal stem cells promotes synaptic resistance to the dysfunctional impact of amyloid beta oligomers via secreted exosomes. Mol Neurodegener 14:25.
Mor DE, Ugras SE, Daniels MJ, Ischiropoulos H (2016) Dynamic structural flexibility of α-synuclein. Neurobiol Dis 88:66-74.
Muraoka S, DeLeo AM, Sethi MK, Yukawa-Takamatsu K, Yang Z, Ko J, Hogan JD, Ruan Z, You Y, Wang Y, Medalla M, Ikezu S, Chen M, Xia W, Gorantla S, Gendelman HE, Issadore D, Zaia J, Ikezu T (2020) Proteomic and biological profiling of extracellular vesicles from Alzheimer's disease human brain tissues. Alzheimers Dement 16:896-907.
Nagele RG, Wegiel J, Venkataraman V, Imaki H, Wang KC, Wegiel J (2004) Contribution of glial cells to the development of amyloid plaques in Alzheimer's disease. Neurobiol Aging 25:663-674.
Nasirishargh A, Kumar P, Ramasubramanian L, Clark K, Hao D, Lazar SV, Wang A (2021) Exosomal microRNAs from mesenchymal stem/stromal cells: Biology and applications in neuroprotection. World J Stem Cells 13:776-794.
Noto Y, Shibuya K, Sato Y, Kanai K, Misawa S, Sawai S, Mori M, Uchiyama T, Isose S, Nasu S, Sekiguchi Y, Fujimaki Y, Kasai T, Tokuda T, Nakagawa M, Kuwabara S (2011) Elevated CSF TDP-43 levels in amyotrophic lateral sclerosis: specificity, sensitivity, and a possible prognostic value. Amyotroph Lateral Scler 12:140-143.
Pan BT, Johnstone RM (1983) Fate of the transferrin receptor during maturation of sheep reticulocytes in vitro: selective externalization of the receptor. Cell 33:967-978.
Pan H, Wang D, Zhang X, Zhou D, Zhang H, Qian Q, He X, Liu Z, Liu Y, Zheng T, Zhang L, Wang M, Sun B (2016) Amyloid β is not the major factor accounting for impaired adult hippocampal neurogenesis in mice overexpressing amyloid precursor protein. Stem Cell Reports 7:707-718.
Pardal R, Lopez Barneo J (2016) Mature neurons modulate neurogenesis through chemical signals acting on neural stem cells. Dev Growth Differ 58:456-462.
Parent JM, Valentin VV, Lowenstein DH (2002) Prolonged seizures increase proliferating neuroblasts in the adult rat subventricular zone-olfactory bulb pathway. J Neurosci 22:3174-3188.
Pascu AM, Ifteni P, Teodorescu A, Burtea V, Correll CU (2015) Delayed identification and diagnosis of Huntington's disease due to psychiatric symptoms. Int J Ment Health Syst 9:33.
Pegtel DM, Gould SJ (2019) Exosomes. Annu Rev Biochem 88:487-514.
Pinto S, Cunha C, Barbosa M, Vaz AR, Brites D (2017) Exosomes from NSC-34 cells transfected with hSOD1-G93A are enriched in miR-124 and drive alterations in microglia phenotype. Front Neurosci 11:273.
Qin J, Xu Q (2014) Functions and application of exosomes. Acta Pol Pharm 71:537-543.
Qualls DA, Prudencio M, Roberts BL, Crosby K, Brown H, Borchelt DR (2013) Features of wild-type human SOD1 limit interactions with misfolded aggregates of mouse G86R Sod1. Mol Neurodegener 8:46.
Reindl W, Baldo B, Schulz J, Janack I, Lindner I, Kleinschmidt M, Sedaghat Y, Thiede C, Tillack K, Schmidt C, Cardaun I, Schwagarus T, Herrmann F, Hotze M, Osborne GF, Herrmann S, Weiss A, Zerbinatti C, Bates GP, Bard J, et al. (2019) Meso scale discovery-based assays for the detection of aggregated huntingtin. PLoS One 14:e0213521.
Reiter CR, Bongarzone ER (2020) The role of vesicle trafficking and release in oligodendrocyte biology. Neurochem Res 45:620-629.
Ren PH, Lauckner JE, Kachirskaia I, Heuser JE, Melki R, Kopito RR (2009) Cytoplasmic penetration and persistent infection of mammalian cells by polyglutamine aggregates. Nat Cell Biol 11:219-225.
Renton AE, Chiò A, Traynor BJ (2014) State of play in amyotrophic lateral sclerosis genetics. Nat Neurosci 17:17-23.
Reza-Zaldivar EE, Hernández-Sapiéns MA, Gutiérrez-Mercado YK, Sandoval-Ávila S, Gomez-Pinedo U, Márquez-Aguirre AL, Vázquez-Méndez E, Padilla-Camberos E, Canales-Aguirre AA (2019) Mesenchymal stem cell-derived exosomes promote neurogenesis and cognitive function recovery in a mouse model of Alzheimer's disease. Neural Regen Res 14:1626-1634.
Rong Y, Liu W, Wang J, Fan J, Luo Y, Li L, Kong F, Chen J, Tang P, Cai W (2019) Neural stem cell-derived small extracellular vesicles attenuate apoptosis and neuroinflammation after traumatic spinal cord injury by activating autophagy. Cell Death Dis 10:340.
Salimi L, Akbari A, Jabbari N, Mojarad B, Vahhabi A, Szafert S, Kalashani SA, Soraya H, Nawaz M, Rezaie J (2020) Synergies in exosomes and autophagy pathways for cellular homeostasis and metastasis of tumor cells. Cell Biosci 10:64.
Sardar Sinha M, Ansell-Schultz A, Civitelli L, Hildesjö C, Larsson M, Lannfelt L, Ingelsson M, Hallbeck M (2018) Alzheimer's disease pathology propagation by exosomes containing toxic amyloid-beta oligomers. Acta Neuropathol 136:41-56.
Schneider JA, Arvanitakis Z, Leurgans SE, Bennett DA (2009) The neuropathology of probable Alzheimer disease and mild cognitive impairment. Ann Neurol 66:200-208.
Seri B, García-Verdugo JM, McEwen BS, Alvarez-Buylla A (2001) Astrocytes give rise to new neurons in the adult mammalian hippocampus. J Neurosci 21:7153-7160.
Shi M, Liu C, Cook TJ, Bullock KM, Zhao Y, Ginghina C, Li Y, Aro P, Dator R, He C, Hipp MJ, Zabetian CP, Peskind ER, Hu SC, Quinn JF, Galasko DR, Banks WA, Zhang J (2014) Plasma exosomal α-synuclein is likely CNS-derived and increased in Parkinson's disease. Acta Neuropathol 128:639-650.
Shin Y, Yang K, Han S, Park HJ, Seok Heo Y, Cho SW, Chung S (2014) Reconstituting vascular microenvironment of neural stem cell niche in three-dimensional extracellular matrix. Adv Healthc Mater 3:1457-1464.
Silverman JM, Christy D, Shyu CC, Moon KM, Fernando S, Gidden Z, Cowan CM, Ban Y, Stacey RG, Grad LI, McAlary L, Mackenzie IR, Foster LJ, Cashman NR (2019) CNS-derived extracellular vesicles from superoxide dismutase 1 (SOD1)(G93A) ALS mice originate from astrocytes and neurons and carry misfolded SOD1. J Biol Chem 294:3744-3759.
Sun B, Peng J, Wang S, Liu X, Zhang K, Zhang Z, Wang C, Jing X, Zhou C, Wang Y (2018) Applications of stem cell-derived exosomes in tissue engineering and neurological diseases. Rev Neurosci 29:531-546.
Tapiola T, Alafuzoff I, Herukka SK, Parkkinen L, Hartikainen P, Soininen H, Pirttilä T (2009) Cerebrospinal fluid {beta}-amyloid 42 and tau proteins as biomarkers of Alzheimer-type pathologic changes in the brain. Arch Neurol 66:382-389.
Terreros-Roncal J, Moreno-Jiménez EP, Flor-García M, Rodríguez-Moreno CB, Trinchero MF, Cafini F, Rábano A, Llorens-Martín M (2021) Impact of neurodegenerative diseases on human adult hippocampal neurogenesis. Science 374:1106-1113.
Toda T, Parylak SL, Linker SB, Gage FH (2019) The role of adult hippocampal neurogenesis in brain health and disease. Mol Psychiatry 24:67-87.
Upadhya R, Zingg W, Shetty S, Shetty AK (2020) Astrocyte-derived extracellular vesicles: Neuroreparative properties and role in the pathogenesis of neurodegenerative disorders. J Control Release 323:225-239.
van Dongen HM, Masoumi N, Witwer KW, Pegtel DM (2016) Extracellular vesicles exploit viral entry routes for Cargo delivery. Microbiol Mol Biol Rev 80:369-386.
van Es MA, Hardiman O, Chio A, Al-Chalabi A, Pasterkamp RJ, Veldink JH, van den Berg LH (2017) Amyotrophic lateral sclerosis. Lancet 390:2084-2098.
Vardjan N, Verkhratsky A, Zorec R (2015) Pathologic potential of astrocytic vesicle traffic: new targets to treat neurologic diseases? Cell Transplant 24:599-612.
Wang Y, Balaji V, Kaniyappan S, Krüger L, Irsen S, Tepper K, Chandupatla R, Maetzler W, Schneider A, Mandelkow E, Mandelkow EM (2017) The release and trans-synaptic transmission of Tau via exosomes. Mol Neurodegener 12:5.
Wild EJ, Boggio R, Langbehn D, Robertson N, Haider S, Miller JR, Zetterberg H, Leavitt BR, Kuhn R, Tabrizi SJ, Macdonald D, Weiss A (2015) Quantification of mutant huntingtin protein in cerebrospinal fluid from Huntington's disease patients. J Clin Invest 125:1979-1986.
Wilke SA, Raam T, Antonios JK, Bushong EA, Koo EH, Ellisman MH, Ghosh A (2014) Specific disruption of hippocampal mossy fiber synapses in a mouse model of familial Alzheimer's disease. PLoS One 9:e84349.
Wu C, Watts ME, Rubin LL (2019) MAP4K4 activation mediates motor neuron degeneration in amyotrophic lateral sclerosis. Cell Rep 26:1143-1156.e1145.
Xian X, Cai LL, Li Y, Wang RC, Xu YH, Chen YJ, Xie YH, Zhu XL, Li YF (2022) Neuron secrete exosomes containing miR-9-5p to promote polarization of M1 microglia in depression. J Nanobiotechnology 20:122.
Xiao T, Zhang W, Jiao B, Pan CZ, Liu X, Shen L (2017) The role of exosomes in the pathogenesis of Alzheimer' disease. Transl Neurodegener 6:3.
Xu H, Jia Z, Ma K, Zhang J, Dai C, Yao Z, Deng W, Su J, Wang R, Chen X (2020) Protective effect of BMSCs-derived exosomes mediated by BDNF on TBI via miR-216a-5p. Med Sci Monit 26:e920855.
Xu X, Li Z, Zuo H, Chen H, Gui Y (2022) Mesenchymal stem cell-derived exosomes altered neuron cholesterol metabolism via Wnt5a-LRP1 axis and alleviated cognitive impairment in a progressive Parkinson's disease model. Neurosci Lett 787:136810.
Yang Y, Ye Y, Su X, He J, Bai W, He X (2017) MSCs-derived exosomes and neuroinflammation, neurogenesis and therapy of traumatic brain injury. Front Cell Neurosci 11:55.
Yanguas-Casás N, Crespo-Castrillo A, Arevalo MA, Garcia-Segura LM (2020) Aging and sex: Impact on microglia phagocytosis. Aging Cell 19:e13182.
Yoshioka Y, Konishi Y, Kosaka N, Katsuda T, Kato T, Ochiya T (2013) Comparative marker analysis of extracellular vesicles in different human cancer types. J Extracell Vesicles doi: 10.3402/jev.v2i0.20424.
Yue B, Yang H, Wang J, Ru W, Wu J, Huang Y, Lan X, Lei C, Chen H (2020) Exosome biogenesis, secretion and function of exosomal miRNAs in skeletal muscle myogenesis. Cell Prolif 53:e12857.
Zhang M, Zhang CG, Ding W (2014) Exosome in cancer diagnosis and treatment. Sheng Li Ke Xue Jin Zhan 45:372-378.
Zhang X, Abels ER, Redzic JS, Margulis J, Finkbeiner S, Breakefield XO (2016a) Potential transfer of polyglutamine and CAG-repeat RNA in extracellular vesicles in Huntington's disease: background and evaluation in cell culture. Cell Mol Neurobiol 36:459-470.
Zhang Y, Yu M, Tian W (2016b) Physiological and pathological impact of exosomes of adipose tissue. Cell Prolif 49:3-13.
Zhao Y, Yang G (2021) Potential of extracellular vesicles in the Parkinson's disease-Pathological mediators and biomarkers. Neurochem Int 144:104974.
Zhao Y, Liu B, Wang J, Xu L, Yu S, Fu J, Yan X, Su J (2022) Aβ and tau regulate microglia metabolism via exosomes in Alzheimer's disease. Biomedicines 10:1800.
Zhao ZH, Chen ZT, Zhou RL, Zhang X, Ye QY, Wang YZ (2018) Increased DJ-1 and α-synuclein in plasma neural-derived exosomes as potential markers for Parkinson's disease. Front Aging Neurosci 10:438.
Zheng T, Pu J, Chen Y, Guo Z, Pan H, Zhang L, Zhang H, Sun B, Zhang B (2017) Exosomes secreted from HEK293-APP Swe/Ind cells impair the hippocampal neurogenesis. Neurotox Res 32:82-93.
Zhou Z, Li C, Bao T, Zhao X, Xiong W, Luo C, Yin G, Fan J (2022) Exosome-shuttled miR-672-5p from anti-inflammatory microglia repair traumatic spinal cord injury by inhibiting AIM2/ASC/Caspase-1 signaling pathway mediated neuronal pyroptosis. J Neurotrauma 39:1057-1074.
Zondler L, Feiler MS, Freischmidt A, Ruf WP, Ludolph AC, Danzer KM, Weishaupt JH (2017) Impaired activation of ALS monocytes by exosomes. Immunol Cell Biol 95:207-214.

C-Editor: Zhao M; S-Editor: Li CH; L-Editors: Li CH, Song LP; T-Editor: Jia Y