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Editorial

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Exosomes: Potential Target for Treatment and Diagnosis of Depression?

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Introduction

Major Depressive disorder is most prevalent psychiatric disorder that affects a person's mood, physical health and behavior. Depression is associated with prolong sadness, hopelessness, lack of energy, gloom, and anhedonia [1]. Depression has high comorbidity rate with other disorder such as anxiety. Anxiety affects one-eighth of the total population world-wide [2] Anxiety is a physiological state usually described as the emotion of fear involving feelings of tension, such as fast heart beat and rapid breathing, worry, apprehension, and dread for something considered dangerous in the future [3].

Comorbidity is the co-existence of a disease with another disorder. Depression and anxiety are highly comorbid disorders [4]. Comorbidity of psychiatric syndromes is quite common in a 12-month period; almost 50% of adults with any psychiatric disorder had 2 or more disorders. The prevalence of Major Depressive Disorder (MDD) and comorbid anxiety disorder is frequent and perhaps as high as 60 % [5].

Major Depressive Disorder (MDD) is a principal reason of morbidity worldwide. Depression has high prevalence rate [6] and also has a significant influence on functioning as well as quality of life [6] as well as on somatic health. Women are more susceptible for depression than men. Abnormalities in biotransformation of major neurotransmitters (e.g., 5-HT or serotonin, norepinephrine and dopamine) is the main reason behind MDD that is consequently dependent on the enzymes responsible for their degradation (e.g., monoamine oxidase) or production of their precursor enzyme tryptophan [7].

There has been growing interest in the discovery and development of personalized medicines for the treatment of depression over the last decade. The available treatment approaches are having one major drawback of treatment resistant depression as well as the medicines need to take over longer period [8]. Exosomes are a group of extracellular vesicles of endocytic origin. These vesicles are released by cells and are present in body fluids, such as saliva, urine, and plasma. These vesicles contain high amount of small RNA and play a role in many important body functions. Inside the brain they are involved in response to neuronal/oxidative stress, communications between the cells and generation of neurons as well synaptic plasticity [9]. The exosomes are recently well studied in the field of cancer however their role in depression is not clear till now. This editorial will try to put a highlight on the roles of exosomes in the brain, and relate newer discoveries to current insights into Major Depressive Disorders (MDD). Their role in depressive disorders needs to be explored. The basis of research will be as exosomes are able to cross the blood brain barrier they may be act as an useful tool for the treatment and diagnosis of depression and can be develop as a biomarker to find out neuronal dysfunction. These vesicles are able to take several molecules such as DNAs, proteins, mRNAs, and miRNAs to recipient cells [10].

Exosomes play major roles in communication of cells inside the brain, acting on both adjacent and distal cells. These vesicles can be used as a useful carrier of communication between similar or different types of cells. The previous studies demonstrated that release of exosomes from the cells depends on influx of calcium and glutaminergic activity (NMDA and AMPA receptors) [11]. Signalling of exosomes is linked with various functional processes in brain and change in these processes significantly relate with depression and other CNS disorders for example monocytes release exosomes and influence the permeability of Blood Brain Barrier (BBB). The change in permeability of BBB is associated with inflammation of neurons and implicated in various CNS disorders including depression. In addition, exosomes carry markers from the cell of origin and may be help them be distinguishable in bio-fluids [12].

Serotonin is one of the major neurotransmitter involved in pathogenesis of depression as well release of exosomes from non-neuronal cells in the CNS. The serotonin is involved in increase in cytosolic levels of calcium and in turn stimulates release of exosomes. As it is well documented that imbalance in serotonergic signalling pathway has been takes place in depression, so exosomes may be one of the important target for the treatment or as a biomarker for depression. Based on above statement one can understand that exosomes may have important role in pathogenesis of depression and associated with cell signalling and turnover of neurotransmitters [13].

Inter neuronal as well as glial to neuron signalling can occur through update and release of exosomes and involved majorly in synaptic plasticity. Additionally, neuron-microglial signalling also involve exosomes. Co-cultured with microglial cells with neuron leads to internalization of neuron derived exosomes into microglial cells and result in enhancement of the cells involved in removal of degenerative neuritis. After release into extracellular space exosomes can be internalized by recipient cells vial endocytosis mechanisms which include phago and pinocytosis [14]. After internalization into cell exosomes may elicit their effect on cell. Since miRNAs have previously been implicated mental disorders It would be of interest to investigate whether miRNA associated with psychiatric phenotypes are packed into exosomes, and whether these exosomal miRNA profiles are altered in mental disorders.

There are evidences are present that exosomes are involved in neurogenesis [15] and neuronal inflammation. These exosomes contained proteins involved in TNF and NF-κB signalling pathways [16]. Protein analysis of exosomes in the CNS reveals cargo involved in modulating adult neurogenesis [15]. Based on above findings we can say that exosomes may be used as a potential target for the treatment and diagnostic purpose in the field of depression.

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