Theranostics of
Brain, Spine & Neural Disorders
ISSN: 2641-8096

Juniper Publishers
key to the Researchers

Mini Review
Volume 3 Issue 1 - January 2018
DOI: 10.19080/JOJS.2019.03.555601

Theranostics Brain,Spine & Neural Disord

The Effects of Neurodegenerative Disease on Synaptic Density and Synaptic Vesicles Protein

Saeed Vafaei-Nezhad[1,2]*, Javad Hami[1,2], Mehri shadi[2] and Samira Ezi[2]

[1]*Cellular and Molecular Research Center, Birjand University of Medical Sciences, Iran*

[2]*Department of Anatomical Sciences, Birjand University of Medical Sciences, Iran*

Submission: December 15, 2017; **Published:** January 09, 2018

***Corresponding author:** Saeed Vafaei-Nezhad, Department of Anatomical Sciences, School of Medicine, Birjand University of Medical Sciences, Ghaffari Street, Birjand, Iran, Tel: 98-56-32395361; Email: vafayisaeed@gmail.com

Abstract

Synaptophysin (SYP), a hexameric protein consisting of 38-kDa monomers, is a calcium binding glycoprotein found as an integral transmembrane protein in the small synaptic vesicles membrane. It was one of the first proteins to be identified in the synaptic vesicles. Its role in synaptic vesicle fusion and neurotransmitter release has been documented. In addition, it participates in the biogenesis and recycling of synaptic vesicles. In the previous investigations, SYP has also been considered as a reliable marker for synaptic density and synaptogenesis. Regarding several studies, increases in SYP expression have been found to correlate with long-term potentiation, suggesting that the regulation of SYP expression may contribute to the mechanisms underlying learning and memory. Earlier studies on aging and neurodegenerative disorders, such as schizophrenia, parkinson and Alzheimer disease, have correlated change in SYP immune reactivity with loss or increase in synaptic densities.

Keywords: Synaptophysin; Neurocognitive; Neurotransmitter

Introduction

Synaptophysin is an integral membrane glycoprotein of synaptic vesicles, with a molecular weight of 38,000 Da and containing four membrane-spanning domains that it has been proposed both its NH2 and COOH-termini located on the cytoplasmic surface [1-3]. It is a major component of small synaptic vesicles in central and peripheral nervous system and of a population of small vesicles in neuroendocrine cells and it was one of the first proteins to be identified in the synaptic vesicles and accounts for about 7-10 % of total synaptic vesicle proteins [1]. Based on the predicated structure, it was suggested that synaptophysin forms a channel in the synaptic vesicle membrane and acts as the major Ca2+ binding protein in synaptic vesicles, for this reason it is believed to play a critical role in regulating neurotransmitter release. Previous study has been demonstrated that transmitter secretion can be inhibited by anti-synaptophysin antibodies [2,4,5].

Several laboratories have used the marker synaptophysin to quantify the synaptic density and synaptogenesis in neural development and neurodegenerative disease. Earlier studies on aging and neurodegenerative disorders have correlated change in SYP immune reactivity with loss or increase in synaptic densities [6]. In a study by Thome et al. [7], the researchers revealed that stress exposure leads to the reduction in hippocampal expression of SYP.

Alzaimer and Synaptophysin

Alzheimer disease (AD) as well as other dementing disorders are characterized by a continuous loss of neurons in cortical and subcortical areas and probably by an extensive synaptic loss [8]. In a study by Masliah et al. [8], the researchers has been found that in the AD cases an average 50% decrease in the density of the granular neuropil immuno reaction in parietal, temporal and mid frontal cortex [9]. In addition, other study also reported that average synaptophys in level were significantly reduced in hippocampus of patients with AD [10].

The significant decrease in synaptophysin immunoreactivity found in the AD, might be explained in several ways: (a) as the result of a decrease of its synthesis, (b) secondary to increased degradation in relation to a primary increase in protease activity, (c) secondary to a decreased number of SSV pet synapse, (d) or as a direct consequence of synaptic loss preceding or following neuronal death [9].

Schizophrenia and Synaptophysin

At the cellular and molecular level, microscopic histopathologic studies have demonstrated a reduced neuronal size and decreased density of dendritic spines in schizophrenia patient [11,12]. Changes in synaptic components may reflect a decrease in cortical volume,

and it is believed that such changes may underlie the aberrant functional connectivity in schizophrenia [12,13]. For these reasons, some synaptic proteins have been utilized as proxy markers of synapses to determine whether synaptic alterations are a feature of schizophrenia [13,14]. One such synaptic protein repeatedly reported in schizophrenia is synaptophysin (SYP) [13]. Several studies have been shown that the expression of synaptophysinis altered in schizophrenia [15]. As synaptophysin is present in N95% of synaptic terminals, immunostaining for this protein is considered a reliable measure of synaptic density [16]. Synaptophysin has been shown to be critical for regulating neurotransmitter release and synaptic plasticity, a process thought to be disrupted in schizophrenia [12]. Decreased levels of synaptophysin protein and mRNA were observed in several brain regions including the frontal cortex, medial temporal lobe, visual association cortex, thalamus, cerebellum, and hippocampus of patients with schizophrenia [17-22].These findings lend support to the notion that SYP disturbance in specific brain regions might be part of the pathogenesis of schizophrenia [13]. Some studies suggested that reduced levels of synaptophysin protein in the schizophrenic cases are may occur by posttranscriptional abnormalities of synaptophysin [15].

Diabetes during Pregnancy and Synaptophysin

Diabetes during pregnancy period is one of the most common metabolic disorder which can cause significantly increase the risk of congenital anomalies in the offspring. The congenital anomalies associated with maternal diabetes affect many major organs, including central nervous system (CNS) [6,23,24]. There are multiple lines of evidence suggesting that the maternal diabetes during pregnancy can causes neurostructural and neurofunctional abnormalities in the offspring by alteration of many developmental events such as neurogenesis, migration, differentiation, and cell survival [25,26]. But the precise mechanisms that diabetes in pregnancy can affect the development of nervous system are not yet understood [27]. In humans, children from diabetic mothers may exhibit abnormalities, which include learning defects, motor difficulties, attention deficit, and also the risk of developing schizophrenia [28-30].

In a recent study by Vafaei Nezhad et al. [3] indicated that the gestational diabetes in pregnancy is associated with a significant down regulation in hippocampal expression/localization of SYP in the neonatal rats at two week after birth [6]. Another recent study by Hami et al. [23], they reported that the cerebellar expression of SYP was significantly down regulated in at 1 and 2 weeks old of age rats. In addition, their results also demonstrated that the localization of SYP protein was strikingly reduced in all three distinct layers of cerebellar cortex of neonates born to diabetic animals, especially at 14 day after birth [23].

Discussion

Adequate synapse function is an essential prerequisite of all neuronal processing [31]. True connection between neurons is fundamental to the physiological function of the nervous system [32] and perception, learning, and memory are only possible when the nervous system is functioning normally [33]. Some studies have demonstrated that neurodegenerative disorder can cause, reduce neuronal size and decrease synaptic density [17,22,28,30,34]. Since SYP and other synaptic vesicle proteins have been implicated in the mechanisms of cellular plasticity underlying learning and alternation of them can induced neurostructural and neurofunctional abnormalities [6]. In addition, in the previous investigations, SYP has also been considered as a reliable marker for synaptic density. The early decrease in SYP expression/ localization may reflect a down regulation of synaptic function and may be related to the reduction in synaptic density [6,23,35].

Conclusion

Our results indicated that the reduction of synaptic vesicle protein and synaptic density in neurodegenerative disorder may can cause the clinical symptoms of this disorders. Since these proteins have important functions in vesicle trafficking, duking and fusion to the synaptic plasma membrane and in neurotransmitter exocytosis. Disruptions in this function could be a reason for the structural, behavioral, and cognitive abnormalities observed in this patients.

References

1. Arthur CP, Stowell MH (2007) Structure of synaptophysin: a hexameric MARVEL-domain channel protein. Structure 15(6): 707-714.
2. Elferink LA, Scheller RH (1993) Synaptic vesicle proteins and regulated exocytosis. J Cell Sci 17: 75-79.
3. Jahn R, Schiebler W, Ouimet C, Greengard P (1985) A 38,000-dalton membrane protein (p38) present in synaptic vesicles. Proc Natl Acad Sci 82(12): 4137-4141.
4. Gincel D, Shoshan-Barmatz V (2002) The synaptic vesicle protein synaptophysin: purification and characterization of its channel activity. Biophys J 83(6): 3223-3229.
5. Valtorta F, Pennuto M, Bonanomi D, Benfenati F (2004) Synaptophysin: leading actor or walk-on role in synaptic vesicle exocytosis? Bioessays 26(4): 445-453.
6. Vafaei-Nezhad S, Hami J, Sadeghi A, Ghaemi K, Hosseini M, et al. (2016) The impacts of diabetes in pregnancy on hippocampal synaptogenesis in rat neonates. Neuroscience 318: 122-133.
7. Thome J, Pesold B, Baader M, Hu M, Gewirtz JC, et al. (2001) Stress differentially regulates synaptophysin and synaptotagmin expression in hippocampus. Biol Psychiatry 50(10): 809-812.
8. Masliah E, Terry RD, Alford M, DeTeresa R, Hansen LA (1991) Cortical and subcortical patterns of synaptophysinlike immunoreactivity in Alzheimer's disease. Am J Pathol 138(1): 235-246.
9. Masliah E, Terry RD, DeTeresa RM, Hansen LA (1989) Immunohistochemical quantification of the synapse-related protein synaptophysin in Alzheimer disease. Neurosci Lett 103(2): 234-239.
10. Sze CI, Troncoso JC, Kawas C, Mouton P, Price DL, et al. (1997) Loss of the presynaptic vesicle protein synaptophysin in hippocampus correlates with cognitive decline in Alzheimer disease. J Neuropathol Exp Neurol 56(8): 933-944.
11. Selemon LD, Goldman-Rakic PS (1999) The reduced neuropil hypothesis: a circuit based model of schizophrenia. Biol Psychiatry 45(1): 17-25.

How to cite this article: Saeed V N, Javad H, Mehri s, Samira E. The Effects of Neurodegenerative Disease on Synaptic Density and Synaptic Vesicles Protein. Theranostics Brain,Spine & Neural Disord. 2018; 3(1): 555601. DOI: 10.19080/JOJS.2019.03.555601

12. Shen YC, Tsai HM, Ruan JW, Liao YC, Chen SF, et al. (2012) Genetic and functional analyses of the gene encoding synaptophysin in schizophrenia. Schizophr Res 137(1): 14-19.

13. Eastwood SL (2004) The synaptic pathology of schizophrenia: is aberrant neurodevelopment and plasticity to blame. Int Rev Neurobiol 59(1): 47-72.

14. Frankle WG, Lerma J, Laruelle M (2003) The synaptic hypothesis of schizophrenia. Neuron 39(2): 205-216.

15. Glantz LA, Austin MC, Lewis DA (2000) Normal cellular levels of synaptophysin mRNA expression in the prefrontal cortex of subjects with schizophrenia. Biol Psychiatry 48(5): 389-397.

16. Südhof TC, Lottspeich F, Greengard P, Mehl E, Jahn R (1987) A synaptic vesicle protein with a novel cytoplasmic domain and four transmembrane regions. Science 238(4830): 1142-1145.

17. Eastwood SL, Burnet PW, Harrison PJ (1995) Altered synaptophysin expression as a marker of synaptic pathology in schizophrenia. Neuroscience 66(2): 309-319.

18. Chambers JS, Thomas D, Saland L, Neve RL, Perrone-Bizzozero NI (2005) Growth-associated protein 43 (GAP-43) and synaptophysin alterations in the dentate gyrus of patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 29(2): 283-290.

19. Arnold SE (2000) Cellular and molecular neuropathology of the parahippocampal region in schizophrenia. Ann N Y Acad Sci 911(1): 275-292.

20. Harrison PJ, Eastwood SL (2001) Neuropathological studies of synaptic connectivity in the hippocampal formation in schizophrenia. Hippocampus 11(5): 508-519.

21. Benes FM, Berretta S (2000) Amygdalo-Entorhinal Inputs to the Hippocampal Formation in Relation to Schizophrenia. Ann N Y Acad Sci 911(1): 293-304.

22. Davidsson P, Gottfries J, Bogdanovic N, Ekman R, Karlsson I, et al. (1999) The synaptic-vesicle-specific proteins rab3a and synaptophysin are reduced in thalamus and related cortical brain regions in schizophrenic brains. Schizophr Res 40(1): 23-29.

23. Hami J, Saeed Vafaei N, Ghasem I, Akram S, Kazem G, et al. (2016) Altered expression and localization of synaptophysin in developing cerebellar cortex of neonatal rats due to maternal diabetes mellitus. Metab Brain Dis 31(6): 1369-1380.

24. Hami J, Shojae F, Vafaee-Nezhad S, Lotfi N, Kheradmand H, et al. (2015) Some of the experimental and clinical aspects of the effects of the maternal diabetes on developing hippocampus. World J Diabetes 6(3): 412-422.

25. Haghir H, Rezaee AA, Sankian M, Kheradmand H, Hami J (2013) The effects of induced type-I diabetes on developmental regulation of insulin & insulin like growth factor-1 (IGF-1) receptors in the cerebellum of rat neonates. Metab Brain Dis 28(3): 397-410.

26. Suzuki N, Svensson K, Eriksson UJ (1996) High glucose concentration inhibits migration of rat cranial neural crest cells in vitro. Diabetologia 39(4): 401-411.

27. Eidelman AI, Samueloff A (2002) The pathophysiology of the fetus of the diabetic mother, Semin Perinatol 26(3): 232-236.

28. Cannon M, Caspi A, Moffitt TE, Harrington H, Taylor A, et al. (2002) Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder: results from a longitudinal birth cohort. Arch Gen Psychiatry 59(5): 449-456.

29. Isohanni M, Jones PB, Moilanen K, Rantakallio P, Veijola J, et al. (2001) Early developmental milestones in adult schizophrenia and other psychoses. A 31-year follow-up of the Northern Finland 1966 Birth Cohort. Schizophr Res 52(1): 1-19.

30. Delascio Lopes C, Sinigaglia-Coimbra R, Mazzola J, Camano L, Mattar R (2011) Neurofunctional evaluation of young male offspring of rat dams with diabetes induced by streptozotocin. ISRN Endocrinol. DOI: 10.5402/2011/480656.

31. Petzoldt AG, Sigrist SJ (2014) Synaptogenesis. Current Biology 24(22): R1076-R1080.

32. Yamaguchi Y (2002) Glycobiology of the synapse: the role of glycans in the formation, maturation, and modulation of synapses. Biochimica et Biophysica Acta (BBA)-General Subjects 1573(3): 369-376.

33. Poon VY, Choi S, Park M (2013) Growth factors in synaptic function. Front Synaptic Neurosci 5: 6.

34. Hami J, Vafaei-Nezhad S, Ghaemi K, Sadeghi A, Ivar G, et al. (2016) Stereological study of the effects of maternal diabetes on cerebellar cortex development in rat. Metabolic brain disease 31(3): 643-652.

35. Hami J, Vafaei-Nezhad S, Sadeghi A, Ghaemi K, Taheri MH, et al. (2017) Synaptogenesis in the cerebellum of offspring born to diabetic mothers. J Pediatr Neurosci 12(3): 215-221.

DOI: 10.19080/JOJS.2019.03.555601

How to cite this article: Saeed V N, Javad H, Mehri s, Samira E. The Effects of Neurodegenerative Disease on Synaptic Density and Synaptic Vesicles Protein. Theranostics Brain,Spine & Neural Disord. 2018; 3(1): 555601. DOI: 10.19080/JOJS.2019.03.555601