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REVIEW ARTICLE

Analysis on Advantages and Disadvantages GAP 43 as Neuroregenaration Marker Examination in Rat Sciatic Nerve Injury

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Abstract

Analysis focuses on the advantages as well as the disadvantages of using Growth Associated Protein 43 (GAP-43) as a neuroregeneration marker examination tool in a rat sciatic nerve injury examination. The sources of this research were attained from past scientific publications that had been published on the NCBI website. The research is unique because no past researches have ever been performed to ascertain the advantages and disadvantages of GAP-43 as a neuroregeneration marker examination tool in a rat sciatic nerve injury examination. The analysis will focus mostly on a research that was published on September 10, 2016. It focused on the GAP-43, a growth associated protein used in the treatment of a sciatic nerve injury in a Norway rat. The keywords used to attain the access the publication included GAP-43, neuroregeneration marker and sciatic nerve injury. The results of the search yielded a total of twenty-six full journal articles from PubMed Central and one scientific and medical abstract citation from PubMed. These are all publications that contain information pertaining GAP-43 and its applications. The materials for inclusion in the research were all journals summarizing the effects of GAP-43 on a sciatic rat. The participants of this review were program professor and myself. The materials for exclusion in the research included all publications with the exception of peer-reviewed scientific journals and publications from the PubMed or NCBI website. The conclusion of the study revealed that although GAP-43 has a few disadvantages, it is an effective neurogenerational marker in a rat sciatic nerve injury examination.

Keywords: *GAP 43, Neuroregenaration marker, Sciatic nerve injury*

Introduction

GAP-43 is a plasticity protein that can be observed in high levels in the neuronal growth cones at the instance of axonal regeneration development. Persons who may lack a single allele of the GAP-43 gene may fail to attain fully developed telencephalic commissures. As such, they are considered to be mentally retarded. Over the years, model organisms such as the knockout mice have been used to study the functions of the GAP-43. From such studies, it has been ascertained that the GAP-43 can be used as an effective neuroregeneration marker during the treatment of a sciatic nerve in a knockout mouse.

Objective of the study is to find out what are the advantages as well as the disadvantages of using GAP-43 as a neuroregeneration marker examination tool in a rat sciatic nerve injury examination? The intervention available will be the available GAP-43 scientific research materials from the NCBI database. The comparison will entail contrasting the various arguments made in the different identified publications. The expected outcome is that GAP-43 is an effective neuroregeneration marker examination tool in a rat sciatic nerve injury examination exercise.

Methods

The analysis will be performed by searching for the relevant publications on the PubMed scientific database. The analysis places a special focus on a research that was published on September 10, 2016. The research focused on the GAP-43, a growth associated protein used in the treatment of a sciatic nerve injury in a Norway rat. The keywords used to attain the access the publication included GAP-43, neuroregeneration marker and sciatic nerve injury. The results of the search yielded a total of twenty-six full journal articles from PubMed Central and one scientific and medical abstract citation from PubMed.

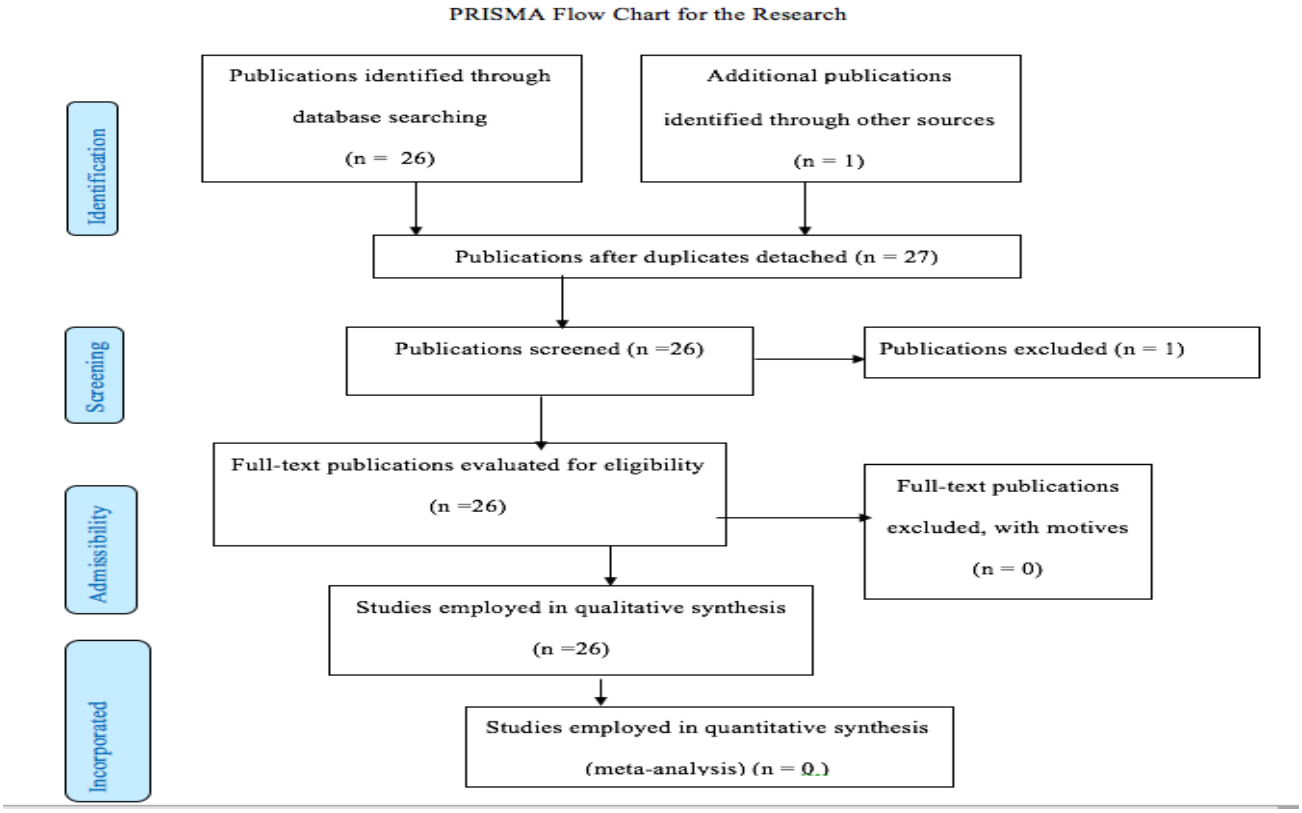

Fig 1: Analysis step on the advantages and disadvantages of GAP-43

Discussion

The term neuroregeneration characterizes the repair as well as regrowth of cells, cell products and nervous tissues [1]. In most cases, such mechanisms are inclusive of the generation of glia, new neurons, synapses, axons as well as and myelin [2]. Neuroregeneration is different from the central nervous system (CNS) and the peripheral nervous system (PNS) [3]. This is in terms of functional mechanisms and also in terms of speed and extent of development.

If an axon is destroyed, the tissue distal segment goes through a Wallerian degeneration [4]. As a result, it loses its myelin sheath. In addition, the proximal segment may ether die through the process of apoptosis or it can undergo through chromatolytic reaction [5]. The chromatolytic reaction is considered an attempt of the proximal segment to repair the destroyed axons [6]. In the CNS, synaptic stripping can take place if the glial foot overruns the dead synapse. The abbreviation GAP-43 is used to denote the growth associated protein 43, which is a protein situated in human beings and it is encoded by the GAP-43 gene [7]. GAP-43 in the past has also been termed as a "growth" or a "protein" [8]. This is because it is manifested in very elevated levels during the development of the neuro growth cones in humans. This is also, during the axonal regeneration.

Nevertheless, it can also be used as a neuro regeneration marker when investigating the inflammation of the sciatic nerve in rats [9]. The GAP-43 protein is classified to be a very imperative component of both presynaptic terminal and axon, and its non-mutation can lead to the death of rat in a few days after its birth [10]. This is essentially due to pathfinding defects of the axon. GAP-43 is considered to be a cytoplasmic protein of the nervous tissue, which becomes stuck to the membrane through the process of dual

palmitoylation sequence [11]. This occurs during the cysteines sequences number 3 and 4. The sequence of neuroregeneration marker targets the lipid rafts [12]. It is a primary protein kinase C substrate (PKC), and it is believed to play a leading role in the formation of neurite, plasticity as well as regeneration [13].

The function of GAP-43 in the development of the CNS is not limited to just the effects of axons. It is also considered to be a component of centrosome and the differentiating neurons, which do not show the GAP-43. In addition, it shows mislocalization of both the mitotic spindles as well as centrosome, and this is specifically in the divisions of neurogenic cells [14]. Consequently, in the cellular cerebrum, there is a failure in the neuronal precursor pool to expand optimally. As a result, the cerebrum becomes essentially small.

Steps for Using GAP-43 in Rats Examination

When using the GAP-43 protein for a rat examination, the rat must first be intracardially perfused with approximately four percent paraformaldehyde [15]. Then, a DRG tissue must be post-fixed overnight using the same fixative. It should then be cryoprotected in approximately twenty percent of sucrose and later frozen inside an OCT. Later, the IHC free floating is carried out on the 20μm sections of the rat tissue, which have been fixed, iced and then cut.

The primary antibody to be used is then incubated at a room temperature for 1/300 over a night while the secondary antibody is incubated for two hours at room temperature at 1/1000 [16]. In this case, the GAP-43 protein is used as the antibody. The results of this examination can be well observed within two weeks following the sciatic nerve injury in a rat. The staining of GAP-43 proteins in the rat body tissues around the injured region of the rat's body can be observed. In most cases, the staining is usually localized in the cytoplasm sections of several of lesioned neurons and also in most axons.

Advantages of GAP-43 When Employed as a Neuroregenaration Marker

There are various merits that can be associated with using GAP-43 protein compound as a neuroregenerational marker. This is during the process of correcting a rat sciatic nerve injury. This is because the GAP-43 plays a fundamental role in the growth as well as the development of the mammalian Central Nervous System (CNS) [17]. First, GAP-43 is essential for the maintenance of both the structure as well as the dynamics of the axonal fibers [18].

It is also essential for the correction of the rat's synaptic terminals at optimal conditions as well as in the cases of lesion-triggered axonal sprouting. In addition, the GAP-43 proteins are attributed to ideal nerve growth, since they belong to the neuromodulin families that also possess a 1 IQ domain [19]. It is also associate to be a primary constituent of the motile, which is also referred to as the growth cones. The motile is responsible for the formation of the tips of the cells elongating axons [20]. All these characteristics of the GAP-43 make it an ideal choice if used as a marker during a rat sciatic injury investigation.

In addition, GAP-43 is also essential for this examination because of its phosphorylation properties through a compound formed by the protein kinase C. In this case, phosphorylation is precisely matched with particular types of synaptic plasticity. In addition, GAP-43 facilitates cellular localization in the rat's cell membranes. It also supports cellular projection that helps in the growth of the cone membranes. In addition, the GAP-43 creates a cell junction through the synapse process.

Ultimately the protein creates a cytoplasmic surface made of growth cones as well as synaptic plasma membranes. The GAP-43 protein also facilitates clear visibility of the healing progress during a sciatic nerve examination in rats. This is because it offers colored results of the dorsal root ganglion tissues, in a rat that is either subjected to a spinal nerve ligation or a spinal cord tissue lysate. In addition, the GAP-43 protein is an efficient indicator as it has been validated as a marker by other tests with excellent results. Some of the tests where the GAP-43 has been used include the Immunocytochemistry/ Immunofluorescence (ICC/IF), western blot (WB) Immunohistochemistry-Frozen (IHC-Fr) as well as the IHC (paraformaldehyde (PFA) fixed).

Table 1: Tabulation Summary of the Advantages of Using Gap-43 as a Neuroregenerational Marker

	Advantage	Description	Sources of Information
1.	Gap-43 protein also aids in grown and development.	It plays a fundamental role in the growth as well as the development of the mammalian Central Nervous System (CNS). It is also essential for the maintenance of both the structure as well as the dynamics of the axonal fibers. It is also essential for the correction of the rat's synaptic terminals at optimal conditions as well as in the cases of lesion-triggered axonal sprouting.	Huebner, E. A., & Strittmatter, S. M. (2009)
2.	Supports the ideal growth of nerves.	This is because it belongs to the neuromodulin family that also possess a 1 IQ domain. It is also associate to be a primary constituent of the motile, which is also referred to as the growth cones. The motile is responsible for the formation of the tips of the cells elongating axons.	Liu, Y., Fisher, D., & Storm, D. (1994)
3.	It has phosphorylation properties.	This is through a compound formed by the protein kinase C. In this case, phosphorylation is precisely matched with particular types of synaptic plasticity.	Caroni, P., Aigner, L., & Schneider, C. (1997)
4.	Facilitates cellular localization.	This is achieved through the rat's cell membranes.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
5.	Supports cellular projection	This helps in the growth of the cone membranes.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
6.	Creates a cell junction.	This is achieved through the synapse process.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
7.	Gap-43 protein creates a cytoplasmic surface.	The surface is made of growth cones as well as synaptic plasma membranes.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
8.	Facilitates clear visibility of the healing progress during a sciatic nerve examination in rats.	This is because it offers colored results of the dorsal root ganglion tissues, in a rat that is either subjected to a spinal nerve ligation or a spinal cord tissue lysate.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
9.	It has been validated as a marker by other tests with excellent results.	It has been validated by tests such as the ICC/IF, WB IHC-Fr as well as the IHC (PFA fixed).	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)

Disadvantages of GAP-43 When Employed as a Neuroregenaration Marker

The GAP-43 compound has haploinsufficiency characteristics, which is manifested for the cortical phenotypes. Haploinsufficiency is a condition where diploid organisms possess one copy of a functional gene only. The copy is not capable of producing enough gene products for creating a wild type condition in the rat. In such a case, it could make the rat remain in a diseased state. This means that if the correct procedures are not employed when using GAP-43 as a marker for neuroregenaration, it may render the rat used as the specimen to remain in an anomalous condition.

In addition, studies have portrayed that the GAP-43 gene can be extremely lethal if administered on a knockout mouse line. A knockout mouse is a term used to refer to a genetically modified mouse, whose existing gene has been disrupted or entirely replaced with an artificial strand of DNA. The lethality of GAP-43 is manifested just a few days after the mouse line is born. This is because GAP-43 takes an imperative role in the creation of the mammalian CNS. In such a case, the telencephalic commissures may

fail to develop, and as a result, the thalamocortical afferents could become mistargeted. This is more so in the rat's somatosensory predominant barrel of the cortex. In addition, GAP-43 is not suitable for use in the IHC-P. The IHC-P the abbreviation for Immunohistochemistry, which is a procedure, employed to demonstrate the presence as well as the location of proteins in a body tissue [21]. The method has less sensitivity quantitatively when compared to other immunoassays like the ELISA or the Western Blotting. Nevertheless, it enables a researcher the processes being undergone by a treatment in intact body tissues. However, GAP-43 inhibits the clear observation of these results if an IHC-P test is administered.

As such, it would be hard to check the progress of healing when treating a sciatic nerve injury in a rat. In addition, in a transgenic rat, the overexpression of the GAP-43 protein results in an instantaneous creation of new synapses [22]. This also results to an enhanced sprouting of the injured sciatic nerves. In addition, the null mutation of the protein gene GAP-43 in most cases distorts the process of axonal pathfinding, and it is often lethal a few minutes after birth [23].

Likewise, the manipulation of the GAP-43 during a rat nerve injury manipulation may have substantial negative effects on the neurite development of cells subjected to a culture [24]. In addition, GAP-43 is also involved in the process of transducing the intra as well as the extracellular signals through the regulation of the cytoskeletal organization of the nerve endings. Also, the phosphorylation of the Kinase C protein is essentially significant in this process because is associated with the long-term potentiation as well as the nerve-terminal sprouting [25].

Table 2: Tabulation Summary of the Advantages of Using Gap-43 as a Neuroregenerational Marker

	Disadvantage of GAP-43	Description	Sources of Information
1.	The GAP-43 compound has haploinsufficiency characteristics.	Haploinsufficiency is a condition where diploid organisms possess one copy of a functional gene only. The copy is not capable of producing enough gene product for creating a wild type condition in the rat. In such a case, it could make the rat remain in a diseased state.	Dent, E. W., Gupton, S. L., & Gertler, F. B. (2011)
2.	GAP-43 gene can be extremely lethal if administered on a knockout mouse line.	This is because GAP-43 takes an imperative role in the creation of the mammalian CNS[26]. In such a case, the telencephalic commissures may fail to develop, and as a result, the thalamocortical afferents could become mistargeted.	Williams, R. R., Venkatesh, I., Pearse, D. D., Udvadia, A. J., & Bunge, M. B. (2015)
3.	GAP-43 is not suitable for use in the IHC-P or Immunohistochemistry	The method is less sensitivity quantitatively when compared to other immunoassays like the ELISA or the Western Blotting. Nevertheless, it enables a researcher the processes being undergone by a treatment in intact body tissues. However, GAP-43 inhibits the clear observation of these results if an IHC-P test is administered. As such, it would be hard to check the progress of healing when treating a sciatic nerve injury in a rat.	Ivell, R., Teerds, K., & Hoffman, G. E. (2014)
4.	Overexpression of the GAP-43 protein results in an instantaneous creation of new synapses.	This causes an enhanced sprouting of the injured sciatic nerves[27].	L. Aigner, S Arber, J.P Kaphammer, T Laus, C Schneider, F Botteri, H.-R Brenner, P Caroni. (1995)
5.	The null mutation of the protein gene GAP-43 in most cases distorts the process of axonal pathfinding.	It causes death in rats a few minutes after birth. It addition, the manipulation of the GAP-43 during a rat nerve injury treatment may have substantial negative effects on the neurite development of cells subjected to a culture	Godenschwege, A. T., Simpson, J. H., Xiaoliang, S., Bashaw, G. J., Goodman, C. S., & Murphey, R. K. (2002).

Conclusion

In summary, the aim of this study was to investigate the advantages as well as the disadvantages of using GAP-43 as a neuroregenaration marker. This is during the examination of a sciatic nerve injury in a rat. The finding of this manuscript ascertained that GAP-43 is an essential tool that can be used as a neuroregenaration marker when examining a sciatic nerve injury in a rat.

This study was developed on a research that was published on the NCBI website. A total of 26 manuscripts from the NCBI website were used to support the findings attained in this manuscript. The keywords used to attain access of the publication included GAP-43, neuroregeneration marker and sciatic nerve

injury. The results of the search yielded twenty-six manuscripts from PubMed Central and one manuscript from the medical abstract citation from PubMed. The materials for inclusion in the research were all journals summarizing the effects of GAP-43 on a sciatic rat. The materials for exclusion in the research included all publications with the exception of peer-reviewed scientific journals and publications from the PubMed or NCBI website.

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