AQP-4 is also expressed in the sensory organs. Thus, it is present in the Muller retinal cells (its absence leading to subtle alterations in the electroretinogram) or in the internal ear (its lack leading to impaired hearing, which can be explained by the osmotic caliber alterations in the Corti organ, caused by its absence) (10).

Moreover, AQP-4 is also involved in the regulation of the nervous impulse transmission, such as the regulation of the excitability. Thus, the absence of AQP-4 decreases, in the brain, the level of theta waves, which are dependent on the brain-derived neurotrophic factor (BDNF) and the receptor for its tyrosin-kinase (TrkB). The cause for which the theta wave potential is dependent on AQP-4 hasn't been understood yet, but it is thought that the lack of AQP-4 decreases the level of neurotrophins. Thus, in mice which do not express AQP-4 there have been recorded long periods of depression, which has been neutralized after the removal of the brain-derived neurotrophic factor (BDNF) (10).

Furthermore, although the mechanisms responsible for these processes have not been elucidated yet, it was found that the lack of this water channel led to impaired locative memory (10).

Although the most abundant, AQP-4 is not the only channel protein in the brain, at this level being present, albeit in a smaller quantity, other aquaporins such as AQP-1, AQP-9 or AQP-11, factors which must be taken into account in the analysis and modulation of the process of maintaining the hydric balance in the brain (10).

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REFERENCES

1. **Cui J., Bastien D.A.** Molecular Dynamics Simulation and Bioinformatics Study on Yeast Aquaporin Aqy1 from Pichia Pastoris. *Int J Biol Sci.* 2012; 8(7): 1026-1035
2. **Benga G.** Water Channel Proteins (Later Called Aquaporins) and Relatives: Past, Present and Future. *Life.* 2009; 61(2): 112-133
3. **Ching-Hei Jeung**. Aquaporins in spermatozoa and testicular germ cells: identification and potential role. *Asian J Androl.* 2010; 12: 490-499
4. **Palmgren M.** Regulation and Transport Mechanisms of Eukariotic Aquaporins. Doctoral Thesis. Department of Chemistry and Molecular Biology, Microbiology, University of Gothenburg, Sweden. 2013
5. **Papadopoulos M.C., Verkman A.S.** Aquaporin water channels in the nervous system. *Nat Rev Neurosci.* 2013; 14(4):265-277.
6. **Sorani M.** The Role of Genetic Variation in Aquaporin-4 on Therapeutic and Physiological Response After Traumatic Brain Injury. 2007. ProQuest. ISBN: 0549333150, 9780549333159
7. **Gohar O.** Aquaporins: The Waterways of Nature. *Modulator.* 2010; 24: 4-9.
8. **Verkman A.S.** Aquaporins at a glance. *J Cell Sci.* 2011; 124: 2107-2112
9. **Fukuda A.M., Badaut J.** Aquaporin 4: A Player in Cerebral Edema and Neuroinflammation. *J Neuroinflammation.* 2012; 9 (279)
10. **Nagelhus E.A., Ottersen O.P.** Physiological Roles of Aquaporin-4 in Brain. *Physiol Rev.* 2013; 93(4):1543-1562
11. **Benga G.** Water transport in red blood cell membranes. *Prog. Byophis. Molec. Biol.,* 51, 193-245, 1988.
12. **Verkman A.S., Ratelade J., Rossi A., Zhang H. et al.** Aquaporin-4: Orthogonal Array Assembly, CNS Functions, and Role in Neuromyelitis Optica. *Acta Pharmacol Sin.* 2011; 32: 702-710
13. **Yool A.J., Brown E.A., Flynn G.A.** Roles for novel pharmacological blockers of aquaporins in the treatment of brain oedema and cancer. *Clin Exp Pharmacol Physiol.* 2010; 37(4): 403-9.
14. **Benarroch E.E.** Aquaporin-4, homeostasis, and neurologic disease. *Neurology*. 2007; 69(24): 2266-8
15. **Nicchia G.P., Rossi A., Mola M.G., Pisani F. et al.** Higher order structure of aquaporin-4. *Neuroscience*. 2010; 168(4): 903 - 14.
16. **Nagelhus E.A., Veruki M.L., Torp R., Haug F.M. et al.** Aquaporin-4 Water Channel Protein in the Rat Retina and Optic Nerve: Polarized Expression in Muller Cells and Fibrous Astrocytes. *J Neurosci.* 1998; 18(7): 2506-19
17. **Gundersen G.A.** (2013). *Roles of aquaporin-4 in brain fluid dynamics.* PhD. Thesis. University of Oslo: Norway.
18. **Noell S., Wolburg-Buchholz K., Mack A.F., Beedle A.M. et al.** Evidence for a Role of Dystroglycan Regulating the Membrane Architecture of Astroglial Endfeet. *EJN.* 2011; 33: 2179-2186
19. **Verbavatz J.M., Ma T., Gobin R., Verkman A.S.** Absence of Orthogonal Arrays in Kidney, Brain and Muscle from Transgenic Knockout Mice Lacking Water Channel Aquaporin-4. *J Cell Sci.* 1997; 110: 2855-2860
20. **Jang B., Brown D., Verkman A.S.** The Mercurial Insensitive Water Channel (AQP-4) Forms Orthogonal Arrays in Stably Transfected Chinese Hamster Ovary Cells. *J Biol Chem.* 1996; 271(9): 4577-80
21. **Manley G.T., Fujimura M., Ma T., Noshita T., et al.** Aquaporin-4 Deletion in Mice Reduces Brain Edema after Acute Water Intoxication and Ischemic Stroke. *Nat Med.* 2000; 6(2): 159-63
22. **Verkman A.S., Binder D.K., Bloch O., Auguste K., et al.** Three distinct roles of aquaporin-4 in brain function revealed by knockout mice. *Biochim Biophys Acta.* 2006; 1758: 1085-1903.
23. **Liang D., Bhatta S., Gerzanich, Simard J.M.** Cytotoxic Edema. Mechanisms of Pathological Cell Swelling. *Neurosurg Focus.* 2007; 22(5): E2.
24. **Mogoanta L., Ciurea M. Pirici I., Margaritescu C., Simionescu C., Ion D.A., Pirici D.** Different Dynamics of Aquaporin 4 and Glutamate Transporter-1 Distribution in the Perineuronal and Perivascular Compartmentsduring Ischemic Stroke. *Brain Pathol.* 2014; 24(5): 475-93

25. **Tourdias T., Mori N., Dragonu I., Cassagno N. et al.** Differential aquaporin 4 expression during edema build-up and resolution phases of brain inflammation. *JNeuroinflammation.* 2011; 8:143.
26. **Rite I., Mackado A., Cano J., Venero J.L.** Intracerebral VEGF Injection Highly Upregulates AQP4 mRNA and Protein in the Perivascular Space and Glia Limitans Externa. *Neurochem Int*. 2008; 52(4-5): 897-903
27. **Chu H., Tang Y., Dong Q.** Protection of Vascular Endothelial Growth Factor to Brain Edema Following Intracerebral Hemorrhage and Its Involved Mechanisms: Effect of Aquaporin-4. *Plos One.* 2013.
28. **Zador Z., Stiver S., Wang V., Manley G.T.** Role of aquaporin-4 in cerebral edema and stroke. *Handb.Exp.Pharmacol.* 2009; (190): 159-70.
29. **Maeda A., Sobel R.A.** Matrix Metalloproteinases in the Normal Human Central Nervous System, Microglial Nodules, and Multiple Sclerosis Lesions. *J Neuropathol Exp Neurol.* 1996; 55(3): 300-9
30. **Ehmsen J., Poon E., Davies K.** The dystrophin-associated protein complex. *J Cell Sci.* 2002; 115:2801-2803
31. **Darras B.T., Miller D.T., Urion D.K.** Dystrophinopathies. *Gene Reviews*. 2000.
32. **Connors N.C., Adams M.E., Froehen S.C., Kofuji P.** The Potassium Channel Kir4.1 Associates with the Dyystrophin-Glycoprotein Complex via a-Syntrophin in Glia. *JBC*. 2004; 279: 28387-28392.
33. **De Bellis M., Pisani M., Mola M.G., Basco D. et al.** A novel human aquaporin-4 splice variant exhibits a dominant-negative activity: a new mechanism to regulate water permeability. *MBOC*. 2014; 25(4): 470-480.