Reflection on the therapeutic treatment of Electrosensitive patients

Dr. Frédéric GRECO
f-greco@chu-montpellier.fr

The pathophysiology of the neurological signs of the Electrosensitive patient can probably be summarized without going into the details by:

Pulsed and polarized electromagnetic radiation activates the dependent voltage calcium channels located on nociceptive neurons and in particular in the trigeminal nerve (innervation of the face) (1), this causes an influx of calcium into the neuron and leads to the creation of free radicals (ROS) that activate the TRPA1 (2) receptor that causes secretion by the neuron of CGRP (Calcitonin Gene Related Peptide) (3) and inflammatory molecules such as Substance P, neurokinin and histamine release (4). The CGRP will cause arterial cerebral vasodilation of the dura mater without any action on the venous system, leading to migraine (4). In fact, depending on the individual, it is described as “brain fog” and can lead to migraine with vomiting and typical clinical signs. The same mechanism can be found on digestive, bladder, and pulmonary neurons (5).

TRPA1 is part of the family of TRP (transient receptor potential) receptors (9) designed to detect changes in the surrounding environment. TRPA1 is directly sensitive to chemicals, particularly chlorine and woodsmoke, as well as wasabi and menthol. It is also sensitive to cold and is activated by free radicals (among others). This explains why it can be directly activated at the digestive track, bladder, ENT and pulmonary level, accounting for the multiple chemical sensitivity of patients who breathe smoke and have chest pain by releasing CGRP(10) and inflammatory and painful substances. At the otorhinolaryngology level, the trigeminal nerve leads the information directly to the brain and triggers the "migraine". In addition, when pulmonary TRPA1 receptors are activated they can cause heart rhythm disorders (6,7,8).

The activation of TRPA1 and other receptors leads to a central sensitization phenomenon that will result in an increasingly explosive reaction for a given stimulus, and in particular to facilitate the initiation of the reaction by different stimuli: light, noise, odor, touch, electromagnetic radiation, vibrations, creating what is called a central sensitization syndrome. (11,12,13,14).

Histamine also plays a role in the phenomenon by sensitizing TRPV1 receptors, which in turn facilitate the activation of TRPA1 in the digestive tract. This has been well studied and explains the improvement in patients taking antihistamines in irritable bowel syndrome. Histamine is part of the inflammatory substances released but also acts on the phenomenon of central sensitization (15).

Chamomile, which has long been known to soothe migraine headaches, contains parthenolide, which is a partial agonist of TRPA1 receptors, it partially stimulates the receptors and causes desensitization. Menthol seems to do the same in theory but is not very practical in therapy (16).

But what makes some people EHS and others not? Probably genetics, epigenetics and exposures that will result in different and more or less sensitive calcium channels and receptors depending on the individual as described by Martin Pall (voltage-gated calcium channel (VGCC) activation). (17)

Once all this is understood, it finally gives us a practical basis to work from and offers us effective therapeutic possibilities. We have to understand that it is a neurological problem, in particular neuronal hyperexcitability.

The treatment could therefore be to avoid triggers as much as possible, eat well (organic, antioxidant intake), gluten-free diet without milk and low in sugar (moderate ketogenic diet: "anti epileptic" role), sleep well, exercise, meditate and then consider treatment with medication.

Medical disclaimer: the following suggestions should not be construed as medical advice. Always consult with your physician, preferably a neurologist.

Triptans and in particular: Frovatriptan 2.5 mg allows clinical symptoms to disappear for 24 hours (18).

Tramadol 50 mg also causes clinical symptoms (all symptoms) to disappear for 8 hours (but may cause side effects) (19).

Ketoprofen 50 to 100 mg (or other non-steroidal anti-inflammatory drug) prevents migraine for 6 hours (20).

The pseudoephedrine (Sudafed, which is a vasoconstrictor) is effective for 4 hours or more but it is not recommended.

The Anti-histamine Bilastine 1 to 2 tablets once or twice a day may bring relief for 24 hours, and makes any digestive signs disappear in digestive intolerants (21).

Caffeine (zero coca, red bull without sugar...), peppermint and menthol can also help.

A medication for migraine prophylaxis can help you sleep (Nocertone, Epitomax, Sibelium, Laroxyl, Keppra...) and sometimes suffice (20,22).

Finally, what treatment regimen can be considered? The ideal for tolerance would be to find a migraine prophylactic treatment for each patient that could prevent any sign of exposure to electromagnetic radiation and that is risk-free, in which case Triptans, Tramadol or NSAIDs would be used as rescue therapy. However, for those who do not respond to this therapy, would it be possible for Bilastine (1 to 2 tablets twice daily) combined with one tablet of Frovatriptan per day, if necessary, to be considered as a long term therapy?

References

1) Electromagnetic fields act via activation of voltage-gated calcium channels to produce beneficial or adverse effects. Pall ML. J Cell Mol Med. 2013 Aug;17(8):958-65. doi: 10.1111/jcmm.12088. Epub 2013 Jun 26. Review.

2) Activation of transient receptor potential ankyrin 1 by hydrogen peroxide.Sawada Y[1], Hosokawa H, Matsumura K, Kobayashi S. Eur J Neurosci. 2008 Mar;27(5):1131-42. doi: 10.1111/j.1460-9568.2008.06093.x.

3) CGRP and NO in the trigeminal system: mechanisms and role in headache generation.Messlinger K, Lennerz JK, Eberhardt M, Fischer MJ. Headache. 2012 Oct;52(9):1411-27. doi: 10.1111/j.1526-4610.2012.02212.x.Epub 2012 Jul 12. Review.

4) ROS/TRPA1/CGRP signaling mediates cortical spreading depression.
Jiang L, Ma D, Grubb BD, Wang M. J Headache Pain. 2019 Mar 6;20(1):25. doi: 10.1186/s10194-019-0978-z.

5) TRPA1 and other TRP channels in migraine.
Benemei S, De Cesaris F, Fusi C, Rossi E, Lupi C, Geppetti P. J Headache Pain. 2013 Aug 13;14:71. doi: 10.1186/1129-2377-14-71. Review.

6) Transient Receptor Potential Ankyrin 1 (TRPA1) Channel and Neurogenic Inflammation in Pathogenesis of Asthma. Yang H[1], Li S[1]. Med SciMonit. 2016 Aug 19;22:2917-23.

7) TRPA1 mediates changes in heart rate variability and cardiac mechanical function in mice exposed to acrolein. Kurhanewicz N[1], McIntosh-Kastrinsky R[2], Tong H[3], Ledbetter A[3], Walsh L[3], Farraj A[3], Hazari M[4]. ToxicolApplPharmacol. 2017 Jun 1;324:51-60. doi: 10.1016/j.taap.2016.10.008. Epub 2016 Oct 13.

8) TRPA1 mediates the cardiac effects of acrolein through parasympathetic dominance but also sympathetic modulation in mice. Kurhanewicz N[1], Ledbetter A[2], Farraj A[2], Hazari M[3]. ToxicolApplPharmacol. 2018 May 15;347:104-114. doi: 10.1016/j.taap.2018.03.027. Epub 2018 Apr 5.

9) Transient Receptor Potential (TRP) Channels. Samanta A[1,2], Hughes TET[1], Moiseenkova-Bell VY[3,4]. SubcellBiochem. 2018;87:141-165. doi: 10.1007/978-981-10-7757-9_6.

10) Calcitonin gene-related peptide (CGRP) and migraine.
Durham PL. Headache. 2006 Jun;46 Suppl1:S3-8. Review.

11) Diverse Physiological Roles of Calcitonin Gene-Related Peptide in Migraine Pathology: Modulation of Neuronal-Glial-Immune Cells to Promote Peripheral and Central Sensitization. Durham PL[1]. Curr Pain Headache Rep. 2016 Aug;20(8):48. doi: 10.1007/s11916-016-0578-4.

12) Elevated levels of calcitonin gene-related peptide in upper spinal cord promotes sensitization of primary trigeminal nociceptive neurons. Cornelison LE[1], Hawkins JL[1], Durham PL[2]. Neuroscience. 2016 Dec 17;339:491-501. doi:10.1016/j.neuroscience.2016.10.013. Epub 2016 Oct 13.

13) Applying modern pain neuroscience in clinical practice: criteria for the classification of central sensitization pain. Nijs J[1], Torres-Cueco R, van Wilgen CP, Girbes EL, Struyf F, Roussel N, van Oosterwijck J, Daenen L, Kuppens K, Vanwerweeen L, Hermans L, Beckwee D, Voogt L, Clark J, Moloney N, Meeus M. Pain Physician. 2014 Sep-Oct;17(5):447-57.

14) The development and psychometric validation of the central sensitization inventory. Mayer TG, Neblett R, Cohen H, Howard KJ, Choi YH, Williams MJ, Perez Y, Gatchel RJ. Pain Pract. 2012 Apr;12(4):276-85. doi: 10.1111/j.1533-2500.2011.00493.x.Epub 2011 Sep 27.

15) Histamine-mediated potentiation of transient receptor potential (TRP) ankyrin 1 and TRP vanilloid 4 signaling in submucosal neurons in patients with irritable bowel syndrome. Balemans D[1], Aguilera-Lizarraga J[1], Florens MV[1], Jain P[1], Denadai-Souza A[1], Viola MF[1], Alpizar YA[2,3], Van Der Merwe S[4], VandenBerghe P[1], Talavera K[2,3], Vanner S[5], Wouters MM[1], Boeckxstaens GE[1]. Am J PhysiolGastrointest Liver Physiol. 2019 Mar 1;316(3):G338-G349. doi: 10.1152/ajpgi.00116.2018. Epub 2019 Jan 10.

16) Parthenolide inhibits nociception and neurogenic vasodilatation in the trigeminovascular system by targeting the TRPA1 channel. Materazzi S[1], Benemei S, Fusi C, Gualdani R, De Siena G, Vastani N, Andersson DA, Trevisan G, Moncelli MR, Wei X, Dussor G, Pollastro F, Patacchini R, Appendino G, Geppetti P, Nassini R. Pain. 2013 Dec;154(12):2750-8. doi: 10.1016/j.pain.2013.08.002. Epub 2013 Aug 8.

17)Microwave frequency electromagnetic fields (EMFs) produce widespread neuropsychiatric effects including depression. Pall ML[1]. J ChemNeuroanat. 2016 Sep;75(Pt B):43-51. doi: 10.1016/j.jchemneu.2015.08.001. Epub 2015 Aug 21.

18) Spotlight on frovatriptan: a review of its efficacy in the treatment of migraine. Allais G, Benedetto C. Drug Des DevelTher. 2016 Oct 3;10:3225-3236. eCollection 2016. Review.

19) Tramadol and its metabolite m1 selectively suppress transient receptor potential ankyrin 1 activity, but not transient receptor potential vanilloid 1 activity. Miyano K[1], Minami K, Yokoyama T, Ohbuchi K, Yamaguchi T, Murakami S, Shiraishi S, Yamamoto M, Matoba M, Uezono Y. AnesthAnalg. 2015 Apr;120(4):790-8. doi: 10.1213/ANE.0000000000000625.

20) Migraine.Dodick DW.Lancet. 2018 Mar 31;391(10127):1315-1330. doi: 10.1016/S0140-6736(18)30478-1. Epub 2018 Mar 6. Review.

21) Histamine and migraine revisited: mechanisms and possible drug targets. Worm J[1], Falkenberg K[1], Olesen J[2]. J Headache Pain. 2019 Mar 25;20(1):30. doi: 10.1186/s10194-019-0984-1.

22) Levetiracetam improves symptoms of multiple chemical sensitivity: Case report. Kakisaka Y[1], Jin K[1], Fujikawa M[1], Kitazawa Y[1], Kato K[2], Nakasato N[1]. J Med Invest. 2017;64(3.4):296-298. doi: 10.2152/jmi.64.296.