Silent Inflammation in the Jaw and Neurological Dysregulation –

Case studies linking RANTES overexpression in jawbone with chemokine receptors in the central nervous system

- Lecturer: Dr.Dr.(PhD) Johann Lechner
- Head of Clinic for Integrative Dentistry
- Gruenwalder Str. 10A, 81547 Munich, Germany
- drlechner@aol.com
- <u>www.dr-lechner.de</u>
- <u>www.icosim.de</u>





What are Jawbone cavitations

without typical signs of acute inflammation

filled with fatty-degenerated adipocytes

fatty degenerated osteolysis of jawbone - FDOJ

in cases of facial/trigeminal pain is also called "NICO" (Bouquot: Neuralgia inducing cavitational osteonecrosis) The guiding question of the presented research was:

 Does FDOJ contain inflammatory immune messengers?
Can immune messengers-Cytokines in FDOJpossibly be related to silent inflammation and to Brain Disorder?





Comparision of 7 cytokines in FDOJ samples of 128 patients with Brain Disorders/Chronic Fatigue to healthy jawbone (n=19) in bead based Multiplex-Analysis in (pg/ml) 5.218 RANTES Cavity MW **FDOK** after (n=128) Jawbone Norm (n=19) **Detox**® 777,9 731 149,9 121,5_{20,3} 195,5 5,5^{101,0} 5,2 11 27,6 7,5 TNFa RANTES FGF-2 IL-1ra IL-6 IL-8 MCP-1

What is RANTES?

Proinflammatory Chemokine RANTES: regulated on activation, normal T cell expressed and secreted



Why RANTES interesting for Brain Disorders?

Chemokines and their receptors are **located throughout the brain**. Among the chemokines and their receptors, which are arranged in glial cells and neurons, is, among others, **RANTES.** (Adler M.W., Rogers T.J. Are chemokines the third major system in the brain? J. Leukoc. Biol. 78: 1204-1209; 2005.)

RANTES targets the central nervous system and is able to cause multiple sclerosis and Parkinson's disease. (Rossi, D., A. Zlotnik. 2000. The biology of chemokines and their receptors. Annu. Rev. Immunol. 18: 217-242) RANTES stimulates inflammatory cascades and receptor modulation in murine astrocytes:

"After treatment with RANTES, astrocytes release proinflammatory mediators and reprogram their surface molecules.

The effects of RANTES may be to increase

inflammatory responses within the CNS."

Luo Y et al RANTES stimulates inflammatory cascades and receptor modulation in murine astrocytes. Glia 39(1): 19-30 (2002)

Silent Inflammation in the Jaw and Neurological Dysregulation Case #1: Linking RANTES/CCL5 overexpression in jawbone with chemokine receptors in the central nervous system.

C. (19 years old woman) first experienced a loss of consciousness in the time between two wisdom tooth extractions, on October 21, 2008 and December 18, 2008 respectively. In the following months, the number of syncopal incidents increased rapidly, leading to her admission to a clinic where she was diagnosed with postural orthostatic tachycardia syndrome (POTS) and a disturbance of the autonomic nervous system. Numerous medications (see below) brought no improvement. After multiple further tests, the patient was discharged as a "psychological case".

Approximately one year later, it was "normal" for C. to lose consciousness several times a day, and she was no longer able to leave the house unaccompanied. Her losses of consciousness resulted in daily falls with painful injuries, including a concussion which required several days of bed rest.

C., aged 19, required a companion whenever she went anywhere public: she needed someone to reassure bystanders and avoid unnecessary calls to the emergency services.



Regio 49

Regio 38 39

Existence of FDOJ is neglected in dentistry because of diagnostic problems in x-rays



Inconspicuous retromolar area

Extent of softened bone marrow in retromolar area Sample of FDOJ in retromolar area



- A total of ten internal, neurological, and psychiatric evaluations were carried out in the period from June 2009 to January 2010, including two hospital admissions in university teaching hospitals.
- The patient received several months of treatment with Efectin[®], a serotonin–noradrenalin reuptake inhibitor (SNRI); Astonin H[®], a fludrocortisone approved for hormone replacement in various forms of adrenal insuffciency as well as for the short-term treatment of low blood pressure; and Mestinon[®], a cholinesterase inhibitor with application in paroxysmal tachycardia; and also Gutron[®], beta blockers, and Euthyrox[®].
- C. was last examined by a specialist in psychiatry and psychotherapeutic medicine who made a diagnosis of "recurrent falls due to dissociation." He recommended the "rigorous thematisation of psychosomatic connections with continuation of accompanying psychotherapy consultations."

Syncopes/ per month



Conclusion Case #1

- We draw attention to the question of whether certain dental procedures may be responsible for the development of otherwise inexplicable systemic inflammatory reactions by RANTES overexpression
- Our case study suggests the need to integrate aseptic, jawbone cavitations/FDOJ [7, 8] into an immunopathogenetic trigger model in Brain Disorders
- The problem of cross-linking RANTES in FDOJ begins when local inflammation of the healing wound becomes chronic and FDOJ triggers RANTES overexpression.
- The appropriate **Jawbone Detox**® of FDOJ is recommended as therapy where applicable.



"Silent inflammation" of the jaw and chronic fatigue

syndrome – case study on supplementing diagnostic dental X-rays with ultrasound The patient, 28 years of age, had been suffering from CFS for approximately four years. His symptoms included dizziness, the inability to work, impaired concentration, and depression. Previous treatment approaches, which were primarily psychologically oriented, showed no significant improvement.



In contrast to the 2D-**OPG and CBCT** images, the Ultrasonography measurements in theedentulous retromolar area 38/39 clearly indicated the suspicion of cavitations

in the jawbone

Jawbone Detox® procedure by Dr. Dr. (PhD) J. Lechner





Within the cancellous medullary cavity in the edentulous jaw area 38/39, an aspergilloma ("fungal ball") formed a large, spherical colony of mold together with a fungal network that also contained a mixture of inflammatory cells (see the "Histological findings" section).



Conclusion Case #2

- The X-ray diagnostics alone would not have identified this **jawbone** cavitation contributing to the patient's Brain Disorder.
- Neither 2D-OPG nor 3D-CBCT detected the jawbone cavitation for surgical Jawbone Detox[®].
- Without complementary Ultrasonography neither the chronic inflammatory signaling pathways (as identified as RANTES over expression) nor the extensive fungal colonization would have been recognized or eliminated.
- The case presented herein in particular demonstrates inflammatory cytokine RANTES found in jawbone and visualizes diminished bone density by Ultrasonography.

Why are jawbone FDOJ Cavitations neclected and unknown in dentistry?

Validation of dental X-ray by cytokine RANTES – comparison of X-ray findings with cytokine overexpression in jawbone Link in PubMed: <u>http://www.ncbi.nlm.nih.gov/pubmed/25170282</u>



FDOJ sample: Bone marrow of jawbone changed to fatty-degenerative osteonecrosis



How to detect and locate

cavitations in jawbones?



Or: How to find the source of chronic overexpression of RANTES in jawbone in **Brain Disorder cases**?





Transmitter and receiver in fixed coplanar position





Conclusion: " Smoldering fire in the brain"



"It is becoming increasingly clear that **immune mechanisms** a second essential for the normal, healthy functions of the brain," (Frauke Zipp, Director of the Department of Neurology; University Medical Center Mainz).

"Immune system and brain constantly communicate with each other.... In the tiny lymphatic vessels of the meningy, body immune cells also flow around the brain. ..If necessary, they **cross the blood-brain barrier** from the blood vessels and also influence the activity of nerve cells by means of **immune messengers**. (= such as **RANTES**)

List of reference

Lechner, J. Validation of dental X-ray by cytokine RANTES – comparison of X-ray findings with cytokine overexpression in jawbone. Clinical, Cosmetic and Investigational Dentistry 2014:6 71–79.

Lechner J, von Baehr V. Peripheral Neuropathic Facial/Trigeminal Pain and RANTES/CCL5 in Jawbone Cavitation, Evidence-Based Complementary and Alternative Medicine, vol. 2015, Article ID 582520, 9 pages, 2015. doi:10.1155/2015/582520).

Lechner J, von Baehr V. RANTES and fibroblast growth factor 2 in jawbone cavitations: triggers for systemic disease? Int. Jour. of General Medicine; 2013:6 Pages 277 – 290.

Appay V & Rowland-Jones SL. RANTES: a versatile and controversial chemokine. Trends in Immunology 2001 22 83–87.

Ek M, Engblom D, Saha S, Blomqvist A, Jakobsson P. & Ericsson-Dahlstrand A. Inflammatory response: Pathway across the blood–brain barrier. Nature 410, 430-431 (22 March 2001)

Tran, P. B., Miller, R. J. (2003) Chemokine receptors in the brain: a developing story. J. Comp. Neurol. 457, 1-6.

Ransohoff R.M. The Chemokine System in Neuroinflammation: An Update. The Journal of Infectious Diseases 2002;186(Suppl 2):S152–6.

٠