

Crozats in Pain Management

The Trigeminal System



**Neurological basis necessitating
orthopedic precision**

Dwight Jennings, DDS, MICCMO
Alameda, California

Dwight Jennings, DDS educational background

- 1973 B.A. Mathematics
- 1976 DDS- University of Pacific
- 1977 Started Functional orthodontic training/Crozats
- 1978 Started Neuromuscular Dentistry
- 1986 limited practice to TMD/Orthodontics
- Extensive studies in functional orthodontics, neuromuscular dentistry, neurological research

Evolution of My Current Understanding of trigeminal/ systemic connection

- Gradual evolution of understanding
 - 1987: discovered connection between TMD and seizures
 - Approx. 1990: published paper on use of speech as a diagnostic tool in assessing jaw position
 - 1993: Identified connection between TMD and neuropeptides
 - 2001: Realization of connection between TMD and generalized hypersensitivity
 - 2006: Further ownership of neuropeptides/TMD relationship (associated pathology is recognized medically collectively as neuroinflammatory disorders)
 - 2007: Coalescence of insight on Biomechanical Principles of Occlusion
 - 2008: wrote articles on bite connection with Parkinson's, Cerebral Palsy, and Autism

Crozats in Pain Management

Lecture Overview

- Glossary
- Neurological basis necessitating orthopedic precision
 - Neurology review of the trigeminal system
 - Why do we need to know this?
 - Special characteristics of the trigeminal system and need for precision
- Precise Biomechanical dentofacial orthodpedics
 - Comparative Orthopedic concepts
 - Advanced concepts of occlusion
 - Medical integration
 - Treatment implications
 - Diagnostics
 - Treatment goals
 - Appliances that support precision 3-dimensionally

Glossary

- Jaw Orthopedics
- Neuromuscular dental Principles
- TMJ models and their implications
- Biomechanical Principles of Occlusion
- Dental Medicine
- Neuropeptides/Substance P
- Chaos and complexity

Jaw Orthopedics

- **Definition:**

1. utilization of removable dental appliances to recruit muscle forces so as to effect changes in jaw position and tooth alignment.

Jaw Orthopedics

Neuromuscular dental Principles

TMJ models and their implications

Biomechanical Principles of Occlusion

Dental Medicine

Neuropeptides/Substance P

Chaos and complexity

Shortcomings of Jaw Orthopedics:

- Same theory of occlusion-Angle classification
- Medical history is not integrated
- Primary goal is functional dental occlusion, not integrated physiologic function
- Does not understand the places where there exists critical steps in the treatment process
- Does not understand nor advocate for correction of the primary etiology causing the orofacial pathology (diet)

Neuromuscular Dental Principles

- **dentistry, neuromuscular**(ner'ōmus'ky l r),
n a subsdiscipline of dentistry concerned with correcting alignment problems at the temporomandibular joint. This branch of dentistry focuses on caring for the muscles, nerves, and other tissue well as the teeth and bones.

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Neuromuscular Dental Principles 101

- Abbreviated concepts
 - Occlusion should be established on relaxed muscles
 - Tens used to generate a relaxed closing trajectory
 - Open and close on a fair arc
 - Instrumentation helpful in assessing physiological occlusion:
 - Tens, EMG, Kinesiograph, Sonography

Neuromuscular Dental Principles vs. Biomechanical Principles

- Tens establishes correct resting position
 - Lower full coverage orthosis
 - Contracture prohibits tens from being correct
 - Using “fair arc” to initially set bite trajectory
 - Distraction appliances as needed
 - Tens used to finalize bite once contracture/posture corrected
- 

TMJ Models and their implications

- Hard vs soft tissue
- Psychological component
- Cause of TMJ dysfunction
 - Occlusal influence
 - Metabolic influence

Jaw Orthopedics

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Biomechanical Principles of Occlusion

- Hypothesis: Biomechanical principles of all joints must also be satisfied for the TMJ.
- Hypermobility of joints has negative sequella; joints do best when their range of motion is minimized
- excess range of motion increases stress on the musculature, joint tissues, and the supporting nervous system

That is:

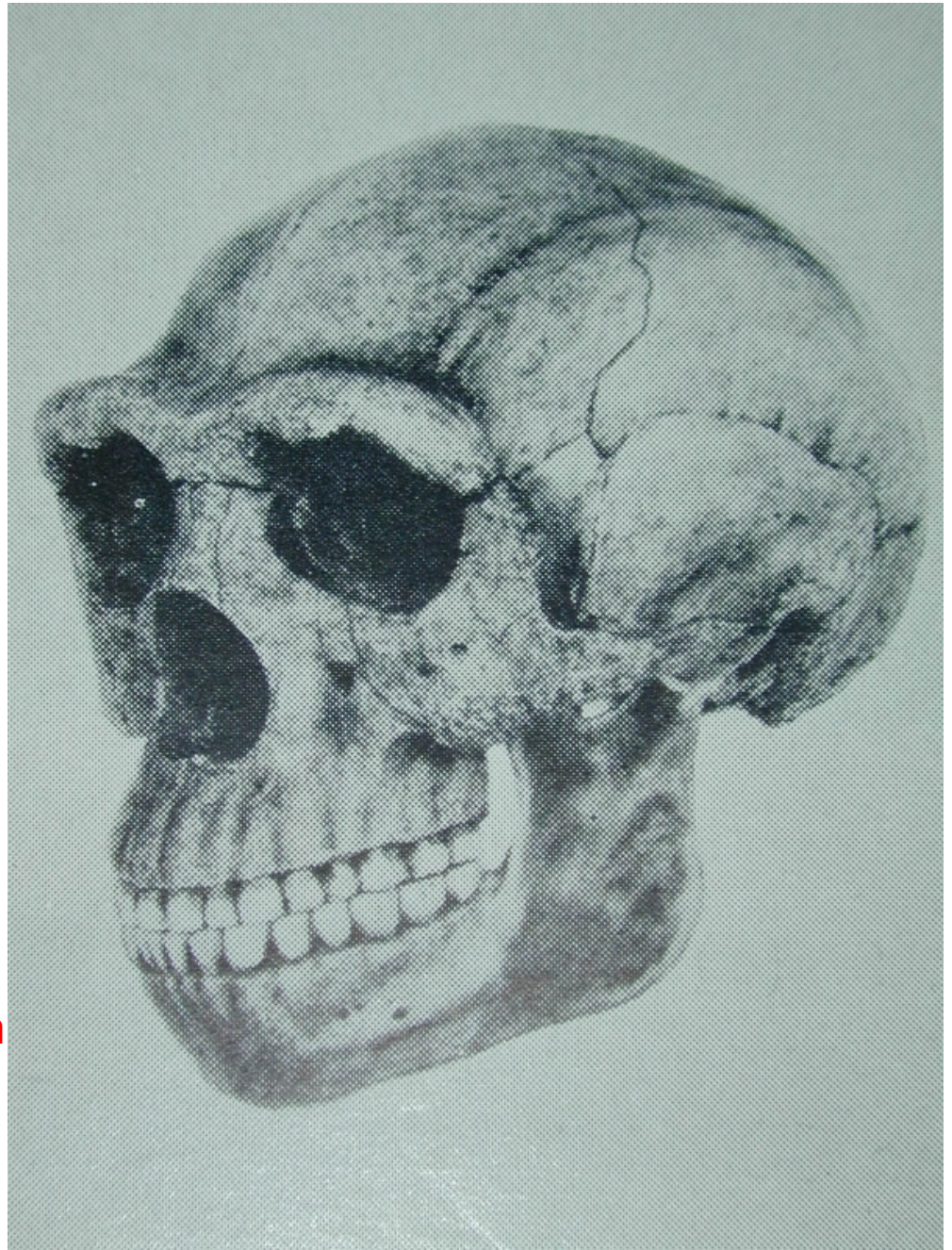
- the temporomandibular joint functions best when occlusion is such that it supports jaw functions within a minimal range of motion (i.e. speech, rest, and open/close arcs are superimposed)
- Even though the TMJ has the ability to translate, the TMJ functions best when function requires it to translate least

Biomechanic Principles of Occlusion

Satisfying these conditions infers the following corollaries:

- speech and centric occlusion should be on the same trajectory
- there should exist a fair arc in open/close without anterior/posterior shifting of the mandible
- end on end bite (class III) creates an ideal functional jaw relationship in most cases (i.e. no translation for incising)

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- **A cephalometric comparison of skulls from the fourteenth, sixteenth and twentieth centuries.**
 - [Rock WP](#), [Sabieha AM](#), [Evans RI](#). Br Dent J. 2006 Jan 14;200(1):33-7
- School of Dentistry, St. Chad's Queensway, Birmingham, B4 6NN, UK. w.p.rock@bham.ac.uk
- **OBJECTIVES:** To evaluate changes in the size and shape of the skull and jaws in British populations between the thirteenth and twentieth centuries.
- **RESULTS:** Horizontal measurements in the base of the anterior cranial fossa and in the maxillary complex were greater in the modern group than in the medieval skulls. Cranial vault measurements were significantly higher ($P=0.000$) in the twentieth century skulls, especially in the anterior cranial fossa.
- **CONCLUSION:** [Results suggest that our medieval ancestors had more prominent faces and smaller cranial vaults than modern man.](#)

- **Transverse dental and dental arch depth dimensions in the mixed dentition in a skeletal sample from the 14th to the 19th century and Norwegian children and Norwegian Sami children of today.**
- [Lindsten R](#), [Ogaard B](#), [Larsson E](#), [Bjerklin K](#).
- Department of Orthodontics, The Institute for Postgraduate Dental Education, Jonkoping, Sweden. rune.lindsten@ltjkpg.se
- Secular changes in transverse dental arch dimensions and dental arch depth were studied. Four cohorts with mixed dentitions were selected.
- The skull group comprised 48 skulls dating from the 14th to the 19th century. The 1980s Sami group was comprised of 39 boys and 34 girls born in 1987 and living in the northern part of Norway. The 1960s Oslo group was comprised of 31 boys and 30 girls born in 1963 and living in the southern part of Norway.
- The arch depth was smaller in the skull group compared with the modern groups; the 1960s Oslo group deviated because of a higher prevalence of caries in the second deciduous molars. The overjet was smaller among the skulls. It was concluded that smaller arch depths are found in skeletal samples at early ages and that attrition does not explain the more upright incisors found in skeletal samples. A secular trend was found in the intermaxillary relation, which indicated that children in the 1980s Oslo group were at greater risk of developing a posterior cross-bite than children born in the 14th to 19th centuries.

- **Dimensional variation of craniofacial structures in relation to changing masticatory-functional demands.**
 - [Varrela J.](#) Eur J Orthod. 1992 Feb;14(1):31-6.
- Department of Oral Development and Orthodontics, University of Turku, Finland.
- A reduction in masticatory stress has been an important factor in the evolution of the human skull. Similarly, the recent increase in the occlusal variation has been related to a change in masticatory activity. The present study investigates short-term variation in craniofacial dimensions by examining cephalometrically two Finnish samples, one exposed to a hard and the other to a soft diet. The samples comprised 32 skulls, derived from the 16th and 17th centuries, and 50 living individuals. Out of 18 dimensions measured, 12 showed only non-significant differences between the samples.
- In the present-day sample, the cranial length and the anterior cranial base were significantly longer, and the upper incisors segment significantly higher.
- In the skull sample, the posterior facial height, the height of the mandibular ramus, and the antero-posterior width of the pharynx were significantly larger. The results suggest that hard diet, which requires more chewing force and time, promotes vertical growth of the ramus and anterior translocation of the maxilla. These findings support the hypothesis that the growth of the craniofacial skeleton is regulated by masticatory stress. It is suggested that both the dimensional changes and the lack of dental attrition may have contributed to the higher occlusal variation of modern individuals.

Dental Medicine

- Definition
- Pushing the envelope of understanding (limitation of human focus)
- Symptomatology/pathology
- System analysis (beyond pathology)
- Utilizing and contributing to integrated medical therapies

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Dental Medicine

- Definition:

Treatment of medical disorders by impacting the Trigeminal System through various therapies, some dental, including but not limited to jaw orthopedics, splint therapy, cavitation treatment, elimination of galvanic interactions, metal removal, removal of oral allergic substances, removal of toxic root canals, cranio-sacral therapy, diet, etc.

Substance P

- **Substance P**
- In [neuroscience](#), **Substance P** is a neuropeptide: a short-chain [polypeptide](#) that functions as a [neurotransmitter](#). It is especially involved in the transmission of [pain](#) impulses from peripheral receptors to the [central nervous system](#) (it derives its name from the first letter of *pain*). It has been theorised that it plays a part in [fibromyalgia](#). [Capsaicin](#) has been shown to reduce the levels of Substance P.

Neuropeptides/Substance P

- The most significant characteristic of the trigeminal system is the high density of pain fibers (c fibers are 100 times greater density than any other nerve in the body)
- Consequently trigeminal disturbances have a strong and predominant effect on substance P levels in the body unbeknownst to the medical profession
- Trigeminal importance is acknowledged in neural therapy, acupuncture, cranio-sacral therapy, and trigger point therapy

- J Comp Neurol. 1997 Feb 17;378(3):425-42.
- [Related Articles](#), Links
-

Central projection of calcitonin gene-related peptide (CGRP)- and substance P (SP)-immunoreactive trigeminal primary neurons in the rat.

[Sugimoto T](#), [Fujiyoshi Y](#), [Xiao C](#), [He YF](#), [Ichikawa H](#).

Department of Oral Anatomy II, Okayama University Dental School, Japan.

Substance P (SP) is implicated in transmission of primary afferent nociceptive signals. In primary neurons, SP is colocalized with calcitonin gene-related peptide (CGRP), which is another neuropeptide marker for small to medium primary neurons. CGRP coreleased with SP augments the postsynaptic effect of SP and thereby modulates the nociceptive transmission. This study demonstrates the distribution of CGRP-like immunoreactivity (-ir) and SP-ir in the lower brainstem of normal rats. The medullary dorsal horn (MDH) and the lateral edge of Vo received convergent CGRP-ir projection from the ipsilateral trigeminal primaries and other neurons. The glossopharyngeal and vagal primaries are candidates for the source of CGRP-ir projection to the subnucleus oralis(Vo) and the MDH, while the dorsal root axons supply the MDH with CGRP-ir terminals. In addition, contralateral primary neurons crossing the midline appear to contain CGRP and to terminate in the MDH.

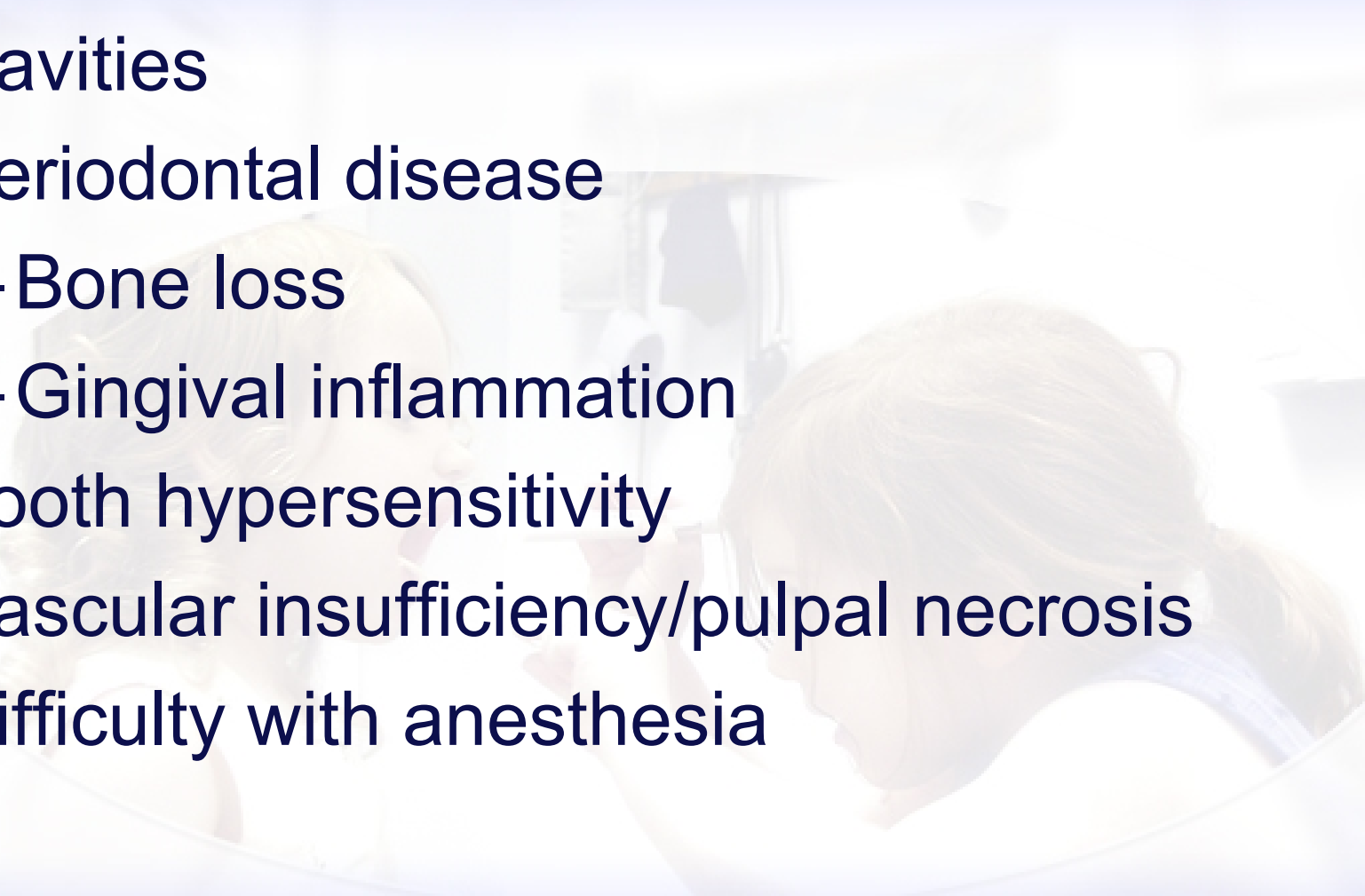
PMID: 9034901

- **Inflammation of craniofacial muscle induces widespread mechanical allodynia.**
- [Ambalavanar R](#), [Moutanni A](#), [Dessem D](#).
- Department of Biomedical Sciences, University of Maryland, Rm 4E-02, 666 West Baltimore Street, Baltimore, MD 21201, USA.
- The modulation of behavioral responses evoked by local and distant nociceptive stimuli following a discrete somatic injection of complete Freund's adjuvant (CFA) was examined in rats. **Inflammation of one craniofacial muscle evoked mechanical allodynia not only in the region of inflammation but also secondary mechanical allodynia in the contralateral head, ipsilateral hindpaw, and contralateral hindpaw.** In contrast to this, CFA-induced inflammation of either the hindpaw or gastrocnemius muscle evoked mechanical allodynia restricted to the hindlimb region. The **widespread modulation of nocifensive behavior** evoked by inflammation of deep craniofacial tissue found in this study resembles the widespread deep tissue pain reported in fibromyalgia, whiplash injury and some temporomandibular disorders and thus may provide insight into the mechanisms of these musculoskeletal pathologies.
- PMID: 16510243

Effects of Substance P

- Hypersensitizes all sensory neurons
- Mediates the inflammatory response
- In the brain substance P has been associated in the regulation of mood disorders, anxiety, stress, reinforcement, neurogenesis, respiratory rhythm, neurotoxicity, nausea / emesis, hormone regulation, and pain.
- Calcium utilization dysfunction (i.e. cell membrane disturbance)

Dental effects of elevated Substance P

- Cavities
 - Periodontal disease
 - Bone loss
 - Gingival inflammation
 - Tooth hypersensitivity
 - Vascular insufficiency/pulpal necrosis
 - Difficulty with anesthesia
- 

- Eur J Neurosci. 2004 Feb;19(3):650-8.
- Sensory neuropeptide mRNA up-regulation is bilateral in periodontitis in the rat: a possible neurogenic component to symmetrical periodontal disease.
- Abd El-Aleem SA, Morales-Aza BM, Donaldson LF.
- Department of Physiology, School of Medical Sciences, University Walk, University of Bristol, Bristol BS8 1TD, UK.
- Periodontal disease is a common multifactorial chronic inflammatory disease in humans. In inflammatory conditions that are known to be associated with changes in nociception, such as arthritis, the neuronal expression of the proinflammatory neuropeptides, substance P and calcitonin gene-related peptide is altered. In this study the expression of these neuropeptides' mRNAs has been studied in an inflammatory model that shows no behavioural evidence of altered nociception. Periodontitis was induced in male rats by intragingival injection of lipopolysaccharide adjacent to the second right mandibular molar. Expression of both neuropeptide mRNAs was significantly increased only in small neurons in the mandibular division of the trigeminal ganglion ipsilateral to the LPS injection from 3 to 10 days postinjection. Neuropeptide mRNA expression was also significantly increased in the contralateral trigeminal ganglion at day 10.
- **The up-regulation of substance P and CGRP mRNAs in periodontal disease suggests that this is associated with the inflammatory process rather than nociception, as this disease does not appear to result in altered nociception in either rats or humans. The contralateral alteration in neuropeptide mRNA expression suggests a role for neurogenic mechanisms in the development of periodontal disease.**
- PMID: 14984415

Dental effects of elevated Substance P

- Hypersensitive patients/elevated stress response
- Implant failure
- Allergic reaction
- Post surgical infection



- J Musculoskelet Neuronal Interact. 2008 Apr-Jun;8(2):154-65. [Links](#)
 - **Osteotropic effects by the neuropeptides calcitonin gene-related peptide, substance P and vasoactive intestinal peptide.**
 - [Lerner UH](#), [Persson E](#).
 - Department of Oral Cell Biology, Umea University, Umea, Sweden.
 - Immunohistochemical phenotypic characterization of skeletal nerve fibers has demonstrated the expression of a restricted number of neuropeptides, including calcitonin gene-related peptide (CGRP), **substance P (SP)** and vasoactive intestinal peptide (VIP). According to the neuro-osteological hypothesis, **such neuropeptides can be released and exert paracrine biological effects on bone cells** present close to the nerve endings expressing these signaling molecules. The existence of such interplay is most convincingly shown by the hypothalamic control of bone formation, in the case of leptin stimulation of hypothalamic nuclei mediated by the sympathetic nervous system and inhibitory beta-adrenergic receptors on osteoblasts. **In addition to these receptors, osteoblasts and osteoclasts express functional receptors for CGRP, SP and VIP, which can regulate both bone formation and bone resorption.** The evidence for these observations is summarized in the present paper.
 - PMID: 18622084

- Acta Orthop. 2008 Jun;79(3):342-5.Links
 - **High levels of substance P and CGRP in pseudosynovial fluid from patients with aseptic loosening of their hip prosthesis.**
 - [Qian Y](#), [Zeng BF](#), [Zhang XL](#), [Jiang Y](#).
 - Department of Orthopedic Surgery, the Sixth People's Hospital, College of Medicine, Shanghai Jiaotong University, Shanghai, China.
 - BACKGROUND: Aseptic loosening is the most important complication after total hip arthroplasty (THA). The nervous system has been implicated in the etiology and pathogenesis of joint diseases. METHODS: We compared levels of substance P (SP) and calcitonin gene-related peptide (CGRP) in pseudosynovial fluid from patients with aseptic loosening after THA with those in synovial fluid from patients undergoing primary THA for osteoarthritis, who served as controls. Levels of SP and CGRP were measured using an enzyme immunoassay. RESULTS: **We found that SP and CGRP levels were significantly higher in the pseudosynovial fluid of loose artificial joints than in the synovial fluid of controls.** INTERPRETATION: SP and CGRP may have a role in aseptic loosening.

Substance P

- Elevated substance P levels are associated with certain types of cancer: pancreatic and colon
- Substance P is known to modulate differentiation of stem cells in bone marrow for blood production, hence implicated in numerous blood disorders

Substance P

- Substance P is known to increase permeability of cell membrane to viral infiltration:
- Implicating its involvement in all viral diseases e.g. HIV, Herpes, Flu, West Nile, etc.



- J Neuroimmunol. 2004 Dec;157(1-2):48-55. Click here to read Links
- Substance P and neurokinin-1 receptor modulation of HIV.
- * Ho WZ,
- * Douglas SD.
- Division of Allergy and Immunology, Joseph Stokes Jr. Research Institute at Children's Hospital of Philadelphia, Department of Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA 19104, USA.
- There is a high incidence of life event stress, depression, and associated symptoms in individuals with HIV infection/AIDS. Psychological and psychiatric symptomatology in individuals with HIV and AIDS may be related to the progression of AIDS disease. The association between depression, anxiety, and stress with HIV disease progression suggests that neurobiologic and neurophysiologic factors have an important role in modulating HIV. The immune effects caused by changes in behavioral state or brain activity are affected, at least in part, through the neuroendocrine-immune pathways. Life stress and depression may be associated with altered blood levels of CNS-released neuropeptides, including substance P (SP). SP is a powerful immunomodulator which is a critical link between the nervous and immune system. We have investigated the role of the neuropeptide SP and its preferred receptor, neurokinin-1, in HIV infection and AIDS. There are compelling data from our laboratories, as well as the findings in the literature, which demonstrate that **SP may play an important role in the pathophysiology of neuropsychiatric disorders, including stress and depression in HIV-infected individuals and in the immunopathogenesis of HIV disease. Modulation of SP activity and SP receptor may offer a novel approach to the treatment of psychiatric disorders and to the design of new anti-HIV therapy.**
- PMID: 15579279

Substance P

- It also has effects as a potent vasodilator. This is caused by the release of nitric oxide from the endothelium
- substance P appears to be within the final common pathway to regulate vomiting
- Substance P modulates sneezing, coughing, and asthmatic symptoms

Substance P

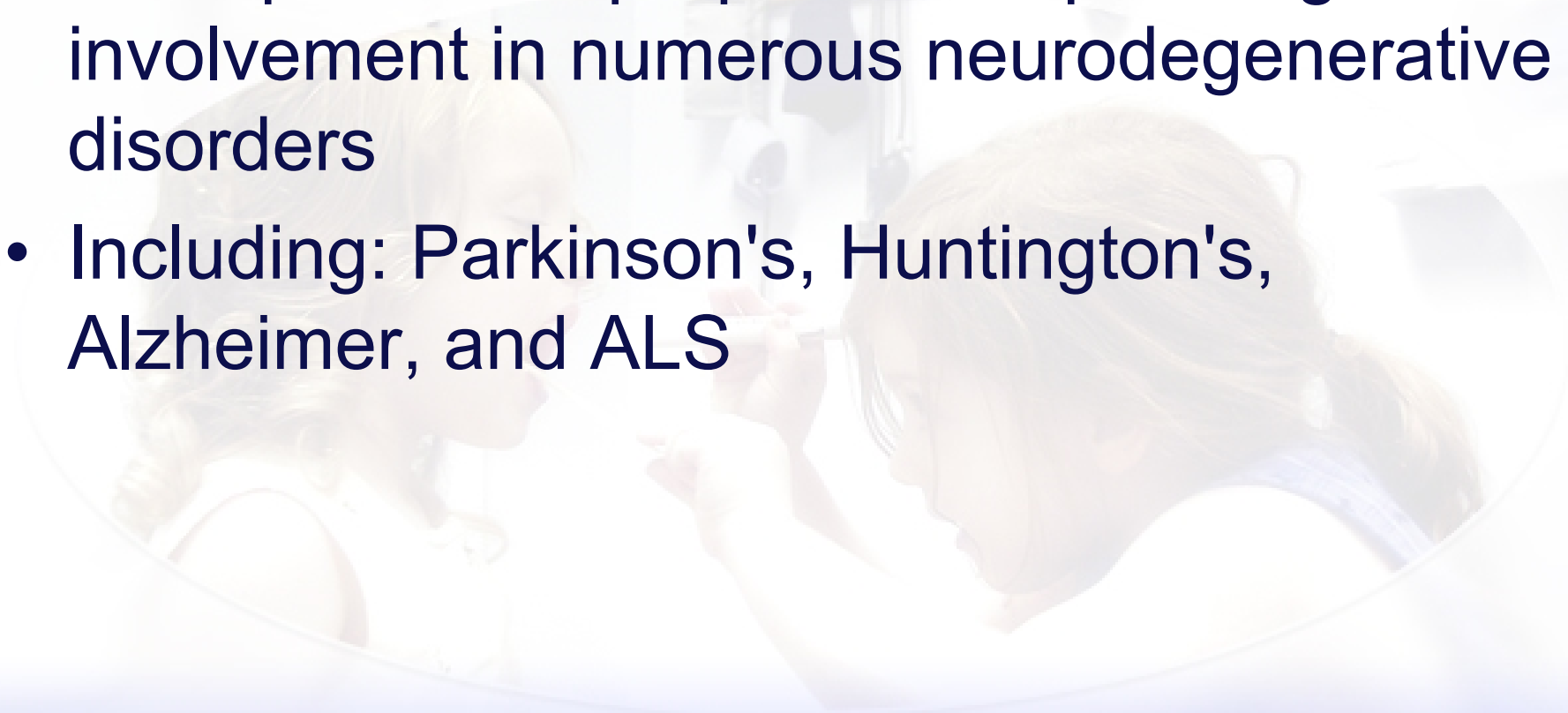
- Substance P is known to be elevated in a broad classification of medical disorders known as “neurogenic inflammatory disorders”
- That includes: migraine, seizures, all autoimmune disorders, IBS, all skin disorders, cystitis, fibromyalgia, sympathetic reflex dystrophy, allergies, asthma, diabetes

- BJU Int. 2008 Mar;101 Suppl 3:2-6. _ Links

- **The concept of neurogenic inflammation.**
- [Geppetti P](#), [Nassini R](#), [Materazzi S](#), [Benemei S](#).
- Department of Critical Care Medicine and Surgery, Clinical Pharmacology Unit, University of Florence, Florence, Italy. pierangelo.geppetti@unifi.it
- **Neurogenic inflammatory responses** have recently been linked to both acute and chronic pathological conditions in the urinary tract. Neurogenic inflammation encompasses a series of vascular and non-vascular inflammatory responses, **triggered by the activation of primary sensory neurons and the subsequent release of inflammatory neuropeptides, including substance P and calcitonin gene-related peptide.** The reduction of neurogenic inflammatory responses may be key in the mode of action of the adrenergic alpha(1)-adrenoceptor antagonists used to treat lower urinary tract symptoms (LUTS). Indeed, the alpha(1)-adrenoceptor antagonist alfuzosin inhibits expression of the oncogene c-fos- a marker of nociceptive pathway activation - evoked by cyclophosphamide in rats. **Capsaicin ameliorates urinary bladder symptoms** through its stimulatory action on the transient receptor potential vanilloid 1 (TRPV1) calcium channel, resulting in desensitization of bladder sensory nerve terminals. Involvement of the TRP cation channel, subfamily A, member 1 (TRPA1) has also been reported in models of neurogenic inflammation and nociception promoted by the cyclophosphamide metabolite, acrolein. Blockade by alfuzosin demonstrates the beneficial effects of alpha(1)-adrenoceptor antagonists on neurogenic inflammation via the transient receptor potential family of ionic channels. Consequently, these drugs may have an important role in reducing LUTS.
- PMID: 18307678

Substance P

- Substance P is known to have neuroprotective properties, implicating its involvement in numerous neurodegenerative disorders
- Including: Parkinson's, Huntington's, Alzheimer, and ALS



Substance P

- Modulates calcium utilization: ie bone generation
- Modulates hair growth



Substance P

- Reflectively I believe substance P is the most primordial sensory system in the body
- It is the basis upon which all sensory, endocrine, and modulatory systems are founded
- Consequently, disturbances in substance P levels leads to homeostatic instability

Chaos

- The origin of the word is a Greek verb which means ***to gape open*** and was often used to refer to the primeval emptiness of the universe before things came into being (Encyclopedia Britannica, Vol. 5, p. 276)

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Chaos

- Chaos is normally considered to be about disorder or confusion.
- However, in science it describes an important conceptual paradox which has a precise mathematical meaning:
 - A chaotic system is a deterministic system which is difficult to predict.
- Pathology generated as a result of cranio-mandibular dysfunction is chaotic

Chaos theory

- Chaos-theory, touted as the third revolution in 20th-century science after relativity and quantum mechanics, uses traditional mathematics to understand complex natural systems with too many variables to study.



Chaos

- The paradox of chaos strikes at the roots of traditional concepts of science
- It is a recognition of nonlinear systems and a rethinking of the linear mathematics education that misleads students and scientists about the true nature of our world
- It suggests that increasing knowledge will lead to predictability.
- Chaos and complexity go together

Chaos

- The game of Roulette is an interesting example that might illustrate the distinction between random and chaotic systems: If we study the statistics of the outcome of repeated games, then we can see that the sequence of numbers is completely random. But over time, the numbers repeat in a statistically predictable manner.

Chaos

- Chaos is not the only source of unpredictability of a system's behavior.
- there are three sources for the lack of predictability:
 - The first is the influence of random noise (sensory input)
 - the second is the effect of the environment on the system
 - the third is lack of knowledge of the initial conditions (bite, underlying nutrition, stress, etc.)

Chaos and Complexity

- A hallmark of physiologic systems is their extraordinary complexity. The nonstationarity and nonlinearity of illnesses generated by living organisms defy traditional mechanistic approaches based on homeostasis and conventional biostatistical methodologies. Recognition that physiologic time series contain “hidden information” has fueled growing interest in applying concepts and techniques from statistical physics, including chaos theory, to a wide range of biomedical problems from molecular to organismic level
(**Chaotic and Fractal Dynamics: An Introduction for Applied Scientists and Engineers** by Francis C. Moon)

Chaos and health history

- Chaos theory allows us to recognize that a physiologic time series can contain “hidden information”
- A thorough medical history is the key to understanding the current and future stability of the patient

Is it Bite or Chaos?

- So when do we know if an illness is caused by faulty trigeminal input?
- The truth is not found in creating an illness from bite instability (as outcome is chaotic), or correlating bite dysfunction with the illness, but reveals itself when the illness is reversed subsequent to correction of faulty trigeminal input

Why ?



- Cranio. 1998 Jul;16(3):185-93. Links
- Health care utilization by patients with temporomandibular joint disorders.
- * Shimshak DG,
- * DeFuria MC.
- Management Science & Information Department, University of Massachusetts, Boston 02125, USA.
- The claims data base of a large New England managed care organization was used to compare the health care utilization patterns of patients with TMJ disorders to non-TMJ subjects. Inpatient, outpatient and psychiatric claims data were examined over a wide range of diagnostic categories. Age and sex adjusted results showed that, overall, patients with TMJ disorders were greater utilizers of health care services and had higher associated costs than non-TMJ subjects. For some of the major diagnostic categories, such as nervous, respiratory, circulatory, and digestive, the inpatient and outpatient claims differences in utilization and costs were as large as 3 to 1. For only one diagnostic category, pregnancy and childbirth, were utilization and costs greater for non-TMJ subjects than TMJ patients. The psychiatric claims for TMJ patients exhibited differences that were at least twice as large as those for the non-TMJ subjects.
- PMID: 9852811

- Int Dent J. 1998 Dec;48(6):540-8.Links
 - **Masticatory function and its effects on general health.**
 - [Nakata M.](#)
 - Department of Pediatric Dentistry, Kyushu University, Faculty of Dentistry, Fukuoka, Japan.
 - One of the main goals of dentistry is to preserve a lifelong healthy masticatory function. Recent studies have shown that mastication is of great importance, not only for the intake of food but also for the systemic, mental and physical functions of the body. The purpose of this review is to compile the latest scientific information concerning the relationship between mastication and general health.
 - PMID: 9881286

- In Vivo. 1999 Nov-Dec;13(6):519-24.Links
 - **Systemic effects of the occlusal destruction in guinea pigs.**
 - [Azuma Y](#), [Maehara K](#), [Tokunaga T](#), [Hashimoto M](#), [leoka K](#), [Sakagami H](#).
 - Department of Dental Pharmacology, Asahi University School of Dentistry, Gifu, Japan.
 - Although there is an increasing amount of information pertaining to the systemic effects of malocclusion, its mechanisms still remain unclear in many ways. This study was conducted to find out the systemic effects of the occlusal destruction in guinea pigs. The animals showed an abnormality in posture and a reversal of the T wave in electrocardiogram (ECG) about 6 days after the grinding of all molar teeth. All the animals died about 7 days after the occlusal destruction. We established the optimal condition of occlusal destruction for the induction of the above symptoms in guinea pigs: at least 6 molars, both side premolar, 1st and 2nd molar of upper jaw, because of the ease for repair. The following results were obtained: 1. The experimental group died about 5 days earlier than the fasting group. 2. The animals could not hold their head positions and dropped the head to the earth. 3. The animals died about 12 hours after the onset of postural abnormality. 4. Ninety percent of the animals with postural abnormalities showed T wave inversion on ECG. 5. None of the above symptoms occurred with bite rising. These results indicate that occlusal destruction affects head position, preventing the animals to hold their head positions and causing the head to drop to the ground. Occlusal destruction may also cause abnormality of the masticatory muscles, which control posture and modulate cardiac function via the trigeminal system. This experimental model is suitable for the analysis of the systemic effects of occlusal destruction.

- Cranio. 2005 Apr;23(2):119-29. Links
 - **The influence of an experimentally-induced malocclusion on vertebral alignment in rats: a controlled pilot study.**
 - [D'Attilio M](#), [Filippi MR](#), [Femminella B](#), [Festa F](#), [Tecco S](#).
 - Department of Orthodontics, University of Chieti, Italy. simtecc@tin.it
 - There is a growing interest in the relationship between occlusion and posture because of a greater incidence of neck and trunk pain in patients with occlusal dysfunction. The study was designed to verify whether an alteration of the spinal column alignment may be experimentally induced in rats as a consequence of altering dental occlusion and also to investigate whether the spinal column underwent any further changes when normal occlusion was then restored. Thirty rats were divided into two groups. Fifteen (15) rats (test group) wore an occlusal bite pad made of composite resin on the maxillary right first molar for a week (T1). The same rats wore a second composite bite pad for another week on the left first molar in order to rebalance dental occlusion (T2). Fifteen rats were included in an untreated control group. All the rats underwent total body radiographs at T0 (before the occlusal pad was placed), at T1 (one week after application of a resin occlusal bite pad on the maxillary left first molar) and at T2 (one week after application of a second resin occlusal bite pad on the maxillary right first molar). A scoliotic curve developed in all the test rats at T1. There were no alterations of spinal position observed in any of the control rats. Additionally, **the spinal column returned to normal condition in 83%** of the test rats when the balance in occlusal function was restored. The alignment of the spinal column seemed to be influenced by the dental occlusion.
 - PMID: 15898568

- J. Kyoto Pref. Univ. Med. 98(10) p.1077-1085. 1989
- **Systemic effects of the peripheral disturbance of the trigeminal system: Influences of the occlusal destruction in dogs.** Abstract: Although there is an increasing amount of information pertaining to intracranial pathways of the trigeminal nerve, its clinical significance still remains unclear in many ways. I assumed that dental disorders including malocclusion would lead to the disturbance of the central nervous system via the trigeminal nerve. Based on this belief, this study was conducted to find out systemic effects of the occlusal destruction by grinding teeth unilaterally in dogs. As the result, abnormal involuntary movement and symptoms of autonomic failure were observed. These experimental results indicate that the trigeminal nuclear complex contains not only the functions of the sensory relay in the face and the control of chewing movement, but it is likely that it **modulates motor, especially postural control and autonomic system**. It is believed that the dental aspects especially occlusion, play an important role for the proper functioning of the trigeminal system.

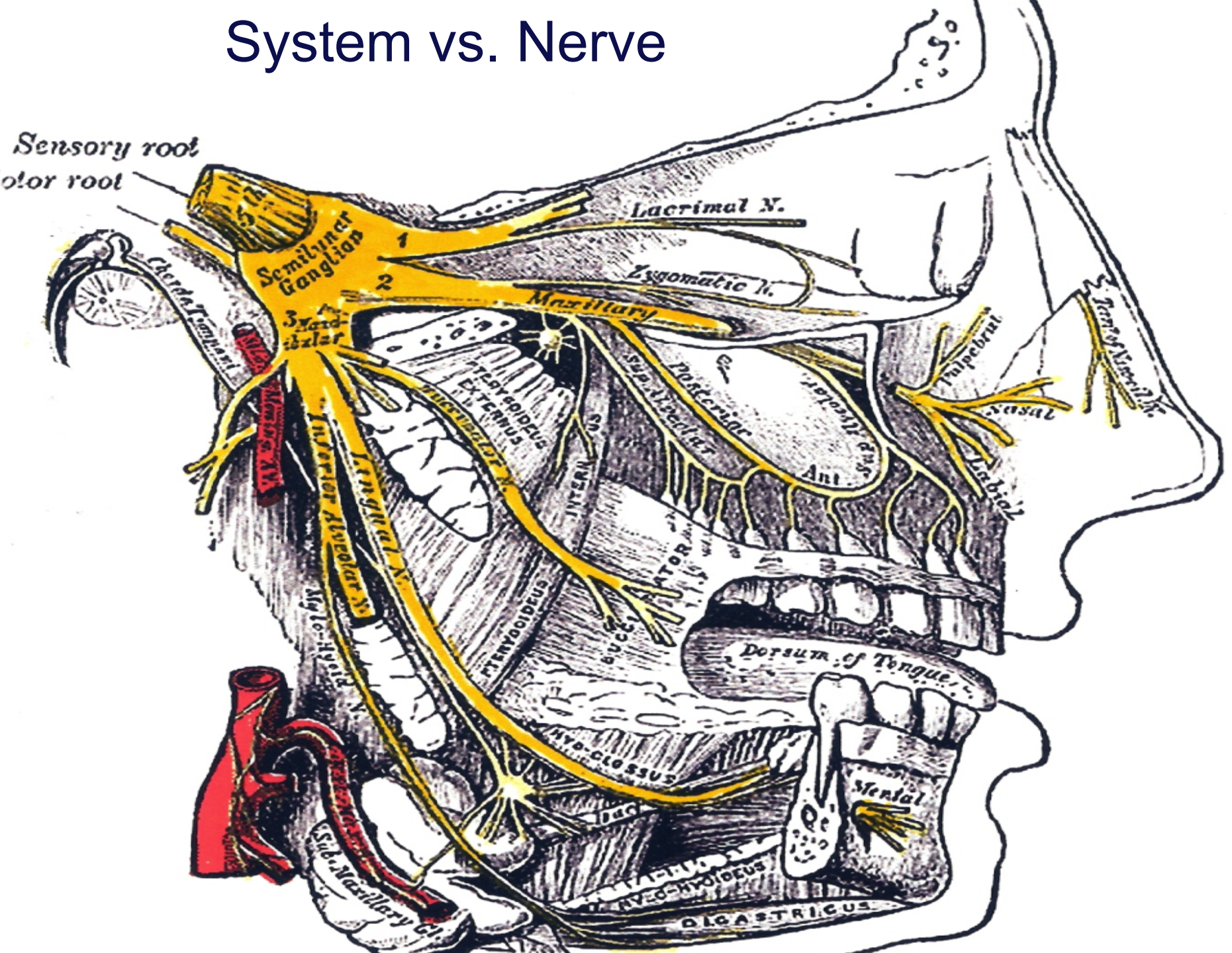
- J Orofac Pain. 2001 Spring;15(2):158-69.Links
 - **Health care utilization and cost among health maintenance organization members with temporomandibular disorders.**
 - [White BA](#), [Williams LA](#), [Leben JR](#).
 - Kaiser Permanente Center for Health Research, 3800 N. Interstate Avenue, Portland, Oregon 97227-1110, USA. alex.white@kp.org
 - AIMS: Little has been reported on the use of health care services and consequent costs among persons with temporomandibular disorders (TMD). This project compared the use and cost of medical and dental care services for TMD patients and matched comparison subjects. METHODS: Patients were continuously enrolled members of Kaiser Permanente Northwest Division who had at least 1 TMD Clinic visit or TMD-related procedure between January 1990 and December 1995 (n = 8,801). An equal number of comparison subjects were identified electronically and matched on 14 variables, including age and gender. Utilization and cost estimates were determined and compared for selected medical and dental services. RESULTS: For both groups, the mean age was about 40.5 years, and approximately 80% were female. **The TMD subjects used significantly more services than did comparison subjects and had mean costs that were 1.6 times higher for all services.** Outpatient visits accounted for about 40% of the difference in mean costs. About 10% of TMD subjects and comparison subjects accounted for about 40% and 47% of the costs in each group, respectively. Female TMD subjects and comparison subjects had higher costs than their male counterparts, and male TMD subjects had higher costs than female comparison subjects. CONCLUSION: Patients with TMD used more of all types of services and had higher costs. A small proportion of the subjects accounted for a large proportion of the costs. Gender was an important factor in utilization and cost. Utilization and cost differences

- University of London, New Road, Whitechapel, London, E1 1BB.
- **The impact of two different malocclusion traits on quality of life.**
 - [Jahal A](#), [Cheung MY](#), [Marcenes W](#). , British Dent J 2007 Jan 19
- Objectives The purpose of this prospective study was to assess the impact of two occlusal traits on the quality of life of children and their families. Methods A total of 180 subjects, which included 90 consecutive patients (aged 13-15 years) and their parents, were recruited on the basis of predetermined criteria to the following groups: increased overjet, spaced dentition and control. Each subject and their parent underwent separate supervised completion of a Child or Parental-Caregiver Perception questionnaire, respectively, which are components of the Child Oral Health Quality of Life questionnaire. Results The three groups were shown not to demonstrate any differences in socio-demographic characteristics. Statistically significant differences were observed between children in the control group and their counterparts in the increased overjet ($p = 0.002$) and spaced dentition ($p < 0.001$) groups. However, no such difference was detected between children in the increased overjet and spaced dentition groups ($p = 0.5$). Parents of these children demonstrated similar statistical findings: $p = 0.007$, $p = 0.003$ and $p = 0.9$, respectively.
- **Conclusions Occlusal traits such as an increased overjet and a spaced dentition have a significant negative impact on both the children's and their families' quality of life.**

Influence of cranio-mandibular relationship on human system

- Orthopedic relationship is the predominant influence on trigeminal nerve tone in the absence of gross pathology
- In hyper sensitized individuals, orthopedic as well as occlusal precision is essential
- Individuals can be seriously affected neurologically and health wise with jaw malalignment or occlusal imbalances

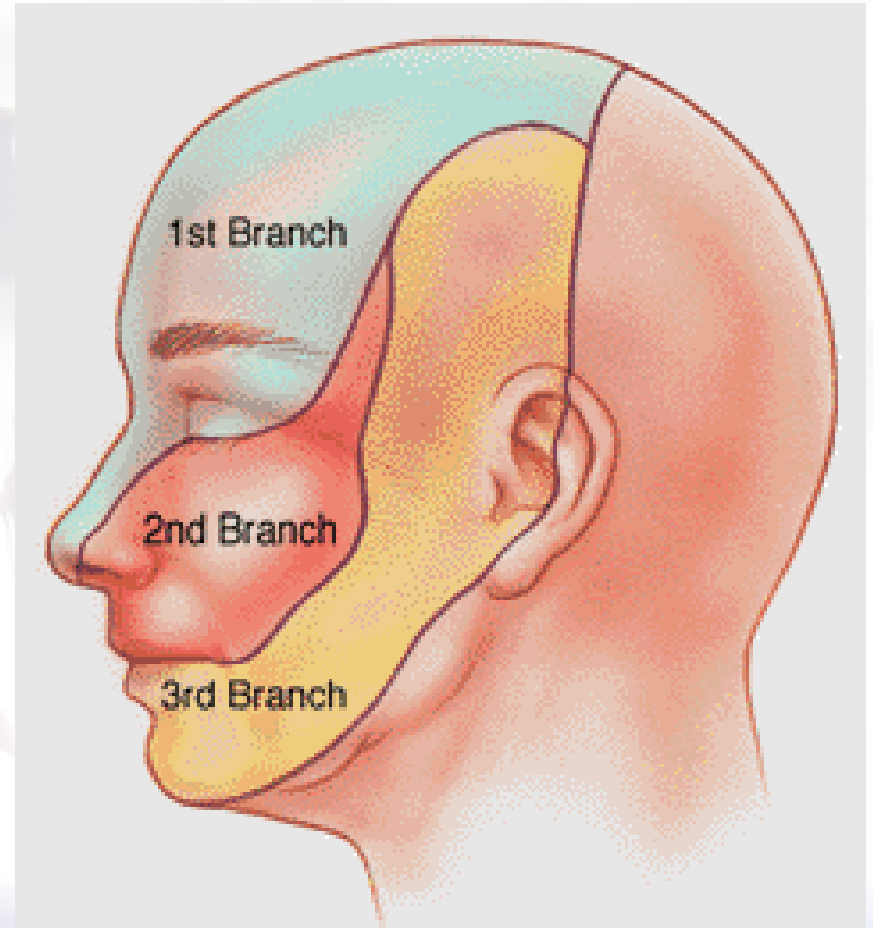
System vs. Nerve



The Trigeminal System

(possible associated pathologies)

Sensory (V1, V2, and V3)



Sensory to head

- Sensory Zones
- Skin
- Teeth and gums
- Eyes
- Ears
- Nose, sinus
- Anterior 2/3 of dura

Pathological
Consequences:

Skin disorders

Periodontal
disease

Eye diseases

Hearing loss

Chronic sinus
infections

Headaches

Hair loss

- Am J Pathol. 2007 Dec;171(6):1872-86. Epub 2007 Nov 30. [Links](#)

- **Probing the effects of stress mediators on the human hair follicle: substance P holds central position.**
- [Peters EM](#), [Liotiri S](#), [Bodó E](#), [Hagen E](#), [Bíró T](#), [Arck PC](#), [Paus R](#).
- Department of Dermatology, University Hospital Schleswig-Holstein, University of Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany.
- **Stress alters murine hair growth, depending on substance P-mediated neurogenic inflammation and nerve growth factor (NGF)**, a key modulator of hair growth termination (catagen induction). Whether this is of any relevance in human hair follicles (HFs) is completely unclear. Therefore, we have investigated the effects of substance P, the central cutaneous prototypic stress-associated neuropeptide, on normal, growing human scalp HFs in organ culture. We show that these prominently expressed substance P receptor (NK1) at the gene and protein level. Organ-cultured HFs responded to substance P by premature catagen development, down-regulation of NK1, and up-regulation of neutral endopeptidase (degrades substance P). This was accompanied by mast cell degranulation in the HF connective tissue sheath, indicating neurogenic inflammation. Substance P down-regulated immunoreactivity for the growth-promoting NGF receptor (TrkA), whereas it up-regulated NGF and its apoptosis- and catagen-promoting receptor (p75NTR). In addition, MHC class I and beta2-microglobulin immunoreactivity were up-regulated and detected ectopically, indicating collapse of the HF immune privilege. In conclusion, we present a simplistic, but instructive, organ culture assay to **demonstrate sensitivity of the human HF to key skin stress mediators**. The data obtained therewith allow one to sketch the first evidence-based biological explanation for how stress may trigger or aggravate telogen effluvium and alopecia areata.
- PMID: 18055548

V1 proprioception- ophthalmic branch

- Sensory system
 - Trigeminal carries proprioception for eye muscles
- Pathologies
 - Visual disturbances
 - Nystagmus



- J Comp Neurol. 1986 May 8;247(2):133-43. Links
 - **Brainstem terminations of extraocular muscle primary afferent neurons in the monkey.(proprioceptors)**
 - [Porter JD.](#)
 - The central terminations of afferent nerve fibers from the extraocular muscles of the monkey were investigated by means of transganglionic transport of wheat germ agglutinin-conjugated horseradish peroxidase (WGA/HRP). Following injections of selected extraocular muscles with WGA/HRP, **terminal labeling was apparent in the ipsilateral trigeminal sensory and cuneate nuclei. The density of trigeminal projections varied markedly from one rostrocaudal level to the next, being heaviest within the ventrolateral portion of pars interpolaris of the spinal trigeminal nucleus.** A second extraocular muscle afferent representation was noted in ventrolateral portions of the cuneate nucleus. This projection was restricted to rostral portions of pars triangularis of the cuneate nucleus, partially overlapping the afferent termination from dorsal neck muscles. It is likely that some of the problems encountered in formulating conclusions regarding the functional role of extraocular muscle proprioception are due to a lack of detailed information of the central termination pattern of muscle afferents. Taken together, the present findings should provide a basis for further anatomical and physiological studies designed to elucidate the **role played by extraocular muscle proprioceptors in vision and oculomotor control.**

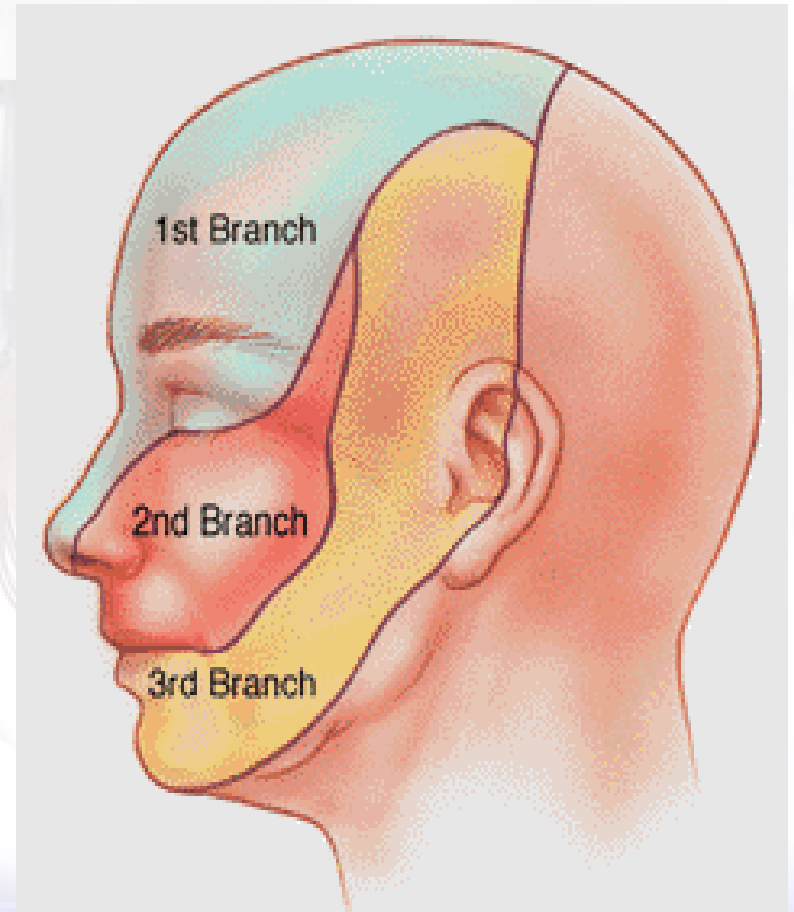
V3- Motor and Proprioception

Pathologies

speech disorders

lisping

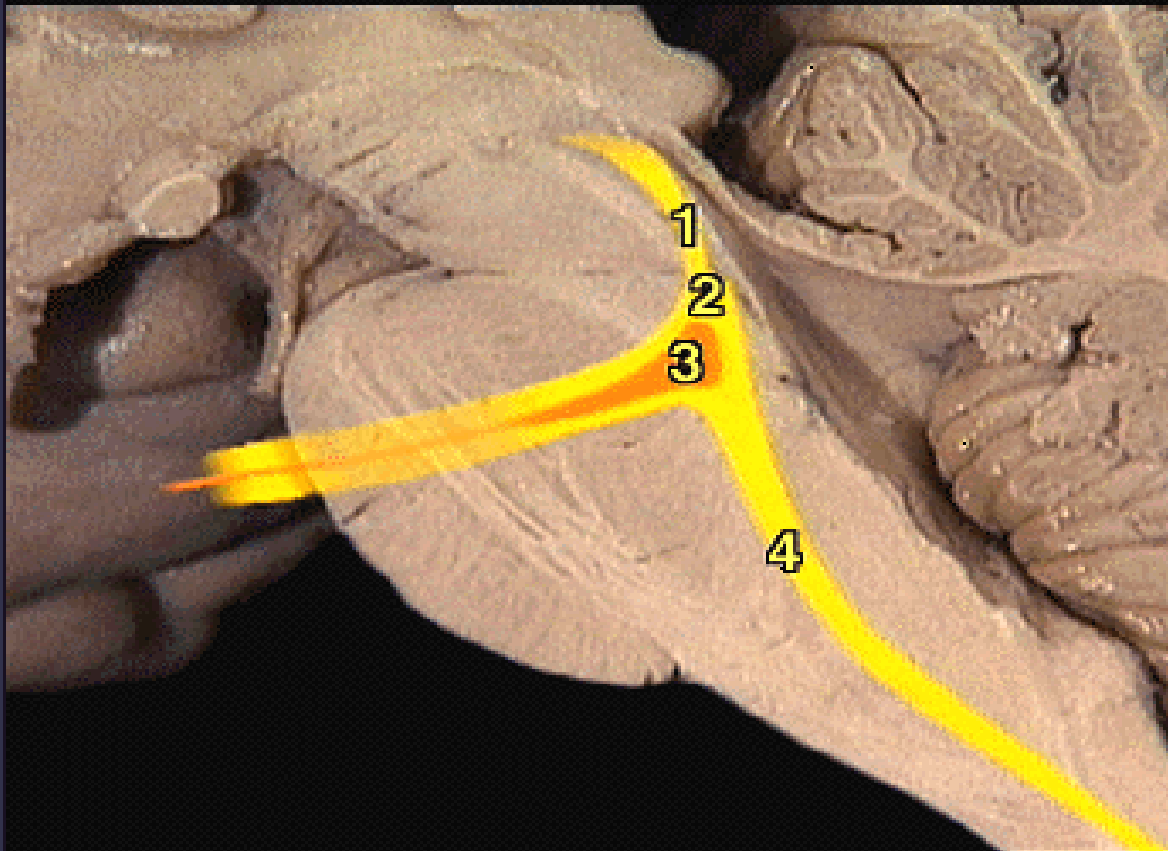
limited opening



Proprioception / Trigeminal mesencephalic

- Definition: The ability to sense the position and location and orientation and movement of the body and its parts.
 - Has its own nucleus in the brain (trigeminal mesencephalic) which is composed of the only sensory cell bodies in the brain
 - Seems to be the most critical aspect of trigeminal system with regard to systemic influence

Trigeminal mesencephalic



- 1. Mesencephalic nucleus
- 2. Sensory nucleus
- 3. Motor nucleus
- 4. Spinal nucleus

- The sensory **trigeminal nerve nucleus** is the largest of the [cranial nerve](#) nuclei, and extends through the whole of the [brainstem](#), [midbrain](#) to [medulla](#).
- The nucleus is divided into three parts, from rostral to caudal (top to bottom in humans):
- The [mesencephalic nucleus](#)
- The [chief sensory nucleus](#) (or "pontine nucleus" or "main sensory nucleus" or "primary nucleus")
- The [spinal trigeminal nucleus](#)
- The spinal trigeminal nucleus is further subdivided into three parts, from rostral to caudal:
 - Pars Oralis
 - Pars Interpolaris
 - Pars Caudalis
- There is also a distinct [trigeminal motor nucleus](#) that is medial to the chief sensory nucleus.

Mesencephalic Modulation

- Modulates pineal function
- Modulates golgi tendon apparatus systemically
- Appears to be major influence on systemic neuropeptide levels (Substance P) through unknown mechanisms
- Pathologies
 - Sleep disorders
 - Scoliosis, sport injuries, strength
 - Generalized Hypersensitivity syndrome
 - Major contributor to vestibular sensory input

Motor (V₃)

Sensory Zones

Muscles of mastication

Tensor veli palatini

Tensor tympani

mylohyoid

**anterior belly of the
digastic**

• Pathological Consequences

- Facial pain
- Eustachian tube dysfunction/ear infections
- Hearing Loss
- Tinnitus
- Swallow disorders
- Speech disorders

- Hear Res. 2006 Jun-Jul;216-217:90-9. Epub 2006 Mar 2. [Links](#)
 - **Somatosensory influence on the cochlear nucleus and beyond.**
 - [Shore SE](#), [Zhou J](#).
 - University of Michigan, Otolaryngology, 1301 E Ann St, Ann Arbor, MI 48109, USA. sushore@umich.edu
 - Interactions between somatosensory and auditory systems occur at peripheral levels in the central nervous system. **The cochlear nucleus (CN) receives innervation from trigeminal sensory structures: the ophthalmic division of the trigeminal ganglion and the caudal and interpolar regions of the spinal trigeminal nucleus (Sp5l and Sp5C).** These projections terminate primarily in the granule cell domain, but also in magnocellular regions of the ventral and dorsal CN. Additionally, new evidence is presented demonstrating that cells in the lateral paragiganticular regions of the reticular formation (RF) also project to the CN. Not unlike the responses obtained from electrically stimulating the trigeminal system, stimulating RF regions can also result in excitation/inhibition of dorsal CN neurons. The origins and central connections of these projection neurons are associated with systems controlling vocalization and respiration. Electrical stimulation of trigeminal and RF projection neurons can suppress acoustically driven activity of not only CN neurons, but also neurons in the inferior colliculus. Together with the anatomical observations, these physiological observations suggest that one function of somatosensory input to the auditory system is to suppress responses to "expected" body-generated sounds such as vocalization or respiration. This would serve to enhance responses to "unexpected" externally-generated sounds, such as the vocalizations of other animals.
 - PMID: 16513306

Second order trigeminal influences

- Systemic muscle tonicity
- Vestibular modulation
- Chemoreceptors in the nose
- Mesencephalic nucleus
- Reticular formation influence
- Speech, eating
- Predominant influence on substance P levels

Brain modulation

Sensory Zones

Strong influence on the reticular activation system

Trigeminal controls blood supply to the brain

Alters neurotransmitter levels (substance P, serotonin, dopamine)

Pathological Consequences:

Sleep disorders, ADD, Tremor/dystonia

Fainting Spells, CFS, ADD/ADHD

Cognitive dysfunction
ADD/ ADHD
Fibromyalgia
Mood disorders

Brain modulation

Sensory Effect

Sensory modulation of spinal input

Metabolic Homeostasis modulation

Limbic modulation

Pathology

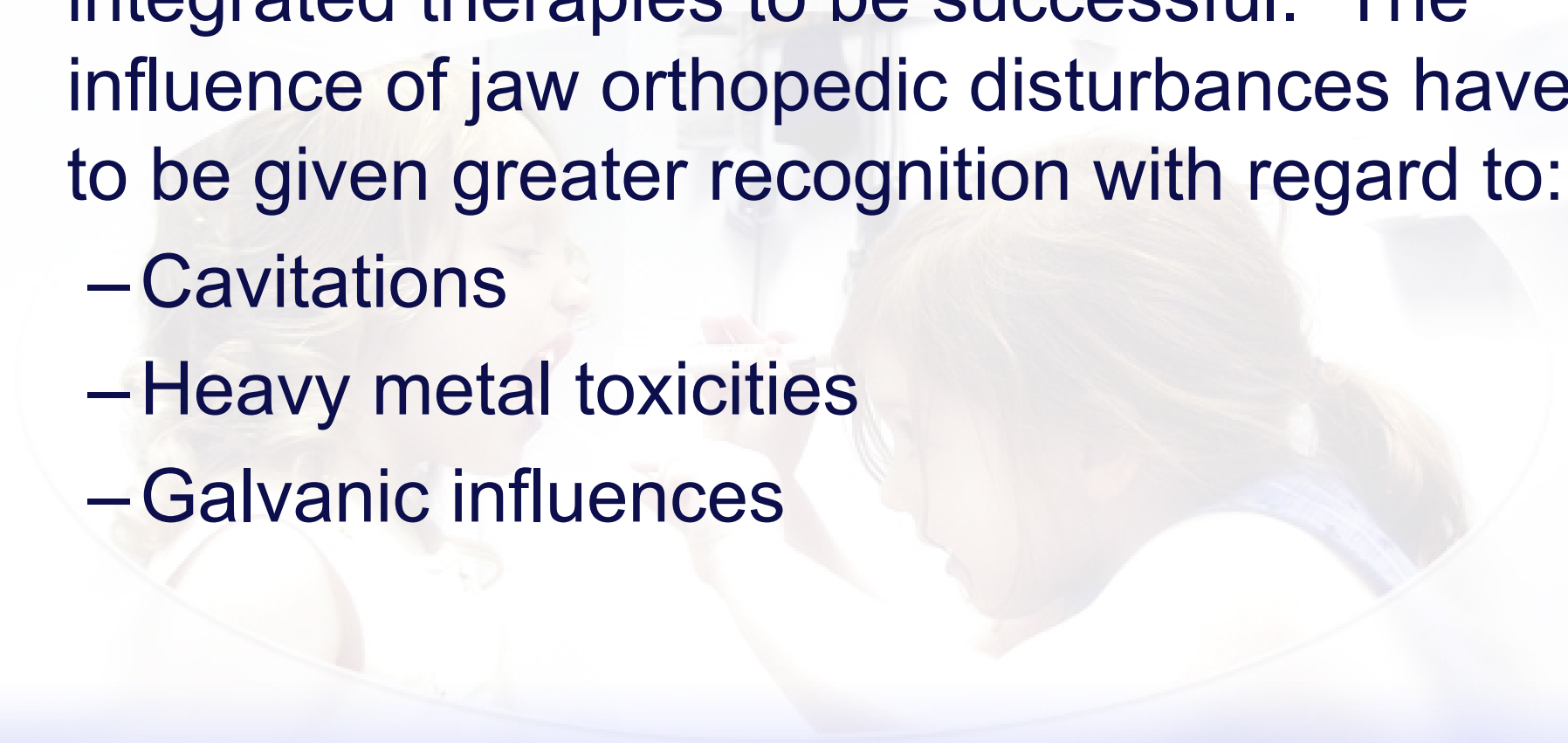
Fibromyalgia, chronic pain

Calcium and other mineral dysregulation
Modulation of nutrient levels in the blood

Mood disorders, pain perception,
Immune function

Implications to Holistic Dental Societies

- Many modern ailments will require complex integrated therapies to be successful. The influence of jaw orthopedic disturbances have to be given greater recognition with regard to:
 - Cavitations
 - Heavy metal toxicities
 - Galvanic influences



Sensory modulation

- Peripheral (spinal) sensory modulation (i.e. pain, neuropathies, etc)
 - a. thalamic modulation
 - b. descending opiate pathway
 - c. Limbic modulation
- Modulation of smell, hearing, taste
- Glossopharygeal, C1-C3, and Vagus sensory modulation (nucleus caudalis)
- Trigeminal is primary influence on Substance P levels
- Modulation of vision and oculomotor

- Gastroenterology. 2008 Mar;134(3):747-55. Links
 - **Substance P as a novel anti-obesity target.**
 - [Karagiannides I](#), [Torres D](#), [Tseng YH](#), [Bowe C](#), [Carvalho E](#), [Espinoza D](#), [Pothoulakis C](#), [Kokkotou E](#).
 - Gastrointestinal Neuropeptide Center, Gastroenterology Division, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA.
 - BACKGROUND & AIMS: Substance P (SP) is an 11-amino acid peptide that belongs to the tachykinin family of peptides. SP acts in the brain and in the periphery as a neuropeptide, neurotransmitter, and hormone affecting diverse physiologic pathways, mainly via its high-affinity neurokinin-1 receptor (NK-1R). Its presence in the hypothalamus and other areas of the brain that regulate feeding as well as in the stomach and small intestine prompted us to investigate its role on appetite control and energy balance. METHODS: CJ 012,255 (CJ), a SP antagonist that binds to NK-1R, was injected into lean, diet-induced obese (DIO), and genetically obese (ob/ob) mice, and its effects on body weight, adiposity, and insulin sensitivity were investigated. RESULTS: CJ administration prevented weight gain and accumulation of fat after 2 weeks of high-fat feeding, whereas similar CJ treatment in obese mice (following 3 months of high-fat diet) resulted in weight loss, reduction in adiposity, and improvement of insulin sensitivity, in part because of inhibition of food intake. The effects of SP in the control of energy balance are, at least in part, leptin independent because CJ treatment was also effective in leptin-deficient mice. Peripheral SP administration resulted in a mild, dose-dependent increase in food intake, evident 3 hours post-SP injection. CONCLUSIONS: CJ reduces appetite and promotes weight loss in mice. **We speculate that NK-1R antagonists, already tested in clinical trials for various diseases, may represent a potential target against obesity.**
 - PMID: 18325388

Limbic modulation

Trigeminal has major influence on limbic brain

- Modulates neuro-immune complex
- Modulates emotions
- Short term memory

Pathological Consequences:

Mood disorders

Eating disorders

Hyper and hypo immune function

Repetitive infections

Autoimmune disorders

Cognitive decline

- Sheng Li Ke Xue Jin Zhan. 2005 Oct;36(4):289-94.Links
 - **[Involvement of amygdala in the emotional processing of pain]**
 - [Article in Chinese]
 - [Huang J](#), [Kang XZ](#), [Luo P](#).
 - Neuroscience Research Institute, Peking University, Beijing 100083.
 - This review will discuss the recent studies about the role of amygdala in pain processing. Pain has a strong emotional component, and the amygdala plays a major role in emotional behaviours. An increasing number of evidences implicated the amygdala in the process of pain encoding and modulation. Amygdala may integrate the nociceptive information from the spinal cord and the trigeminal nucleus with information of other sensory modalities from thalamic and cortical areas, and generate the emotional reactions and the behavioral responses of pain. On the other hand, amygdala may also be involved in pain modulation through connections with periaquiductal gray (PAG) , rostral ventromedial medulla (RVM), and other brain stem areas.
 - PMID: 16408764

- Neuroscientist. 2004 Jun;10(3):221-34. Links
 - **The amygdala and persistent pain.**
 - [Neugebauer V](#), [Li W](#), [Bird GC](#), [Han JS](#).
 - Department of Anatomy & Neurosciences, University of Texas Medical Branch, Galveston, 77555-1069, USA. voneugeb@utmb.edu
 - **A reciprocal relationship exists between persistent pain and negative affective states such as fear, anxiety, and depression.** Accumulating evidence points to the amygdala as an important site of such interaction. Whereas a key role of the amygdala in the neuronal mechanisms of emotionality and affective disorders has been well established, the concept of the amygdala as an important contributor to pain and its emotional component is still emerging. This article will review and discuss evidence from anatomical, neuroimaging, behavioral, electrophysiological, pharmacological, and biochemical data that implicate the amygdala in pain modulation and emotional responses to pain. The latero-capsular division of the central nucleus of the amygdala is now defined as the "nociceptive amygdala" and integrates nociceptive information with poly-modal information about the internal and external bodily environment. Dependent on environmental conditions and affective states, the amygdala appears to play a dual facilitatory and inhibitory role in the modulation of pain behavior and nociceptive processing at different levels of the pain neuraxis. Only recently, electrophysiological, pharmacological, and biochemical neuroplastic changes were shown in the nociceptive amygdala in persistent pain. It is conceivable, however, that amygdala plasticity plays an important role in emotional pain behavior and its modulation by affective state.
 - PMID: 15155061

Mesencephalic nucleus

Only primary sensory cell bodies in the brain!

Mesencephalic nucleus of trigeminal= proprioceptors of muscles of mastication

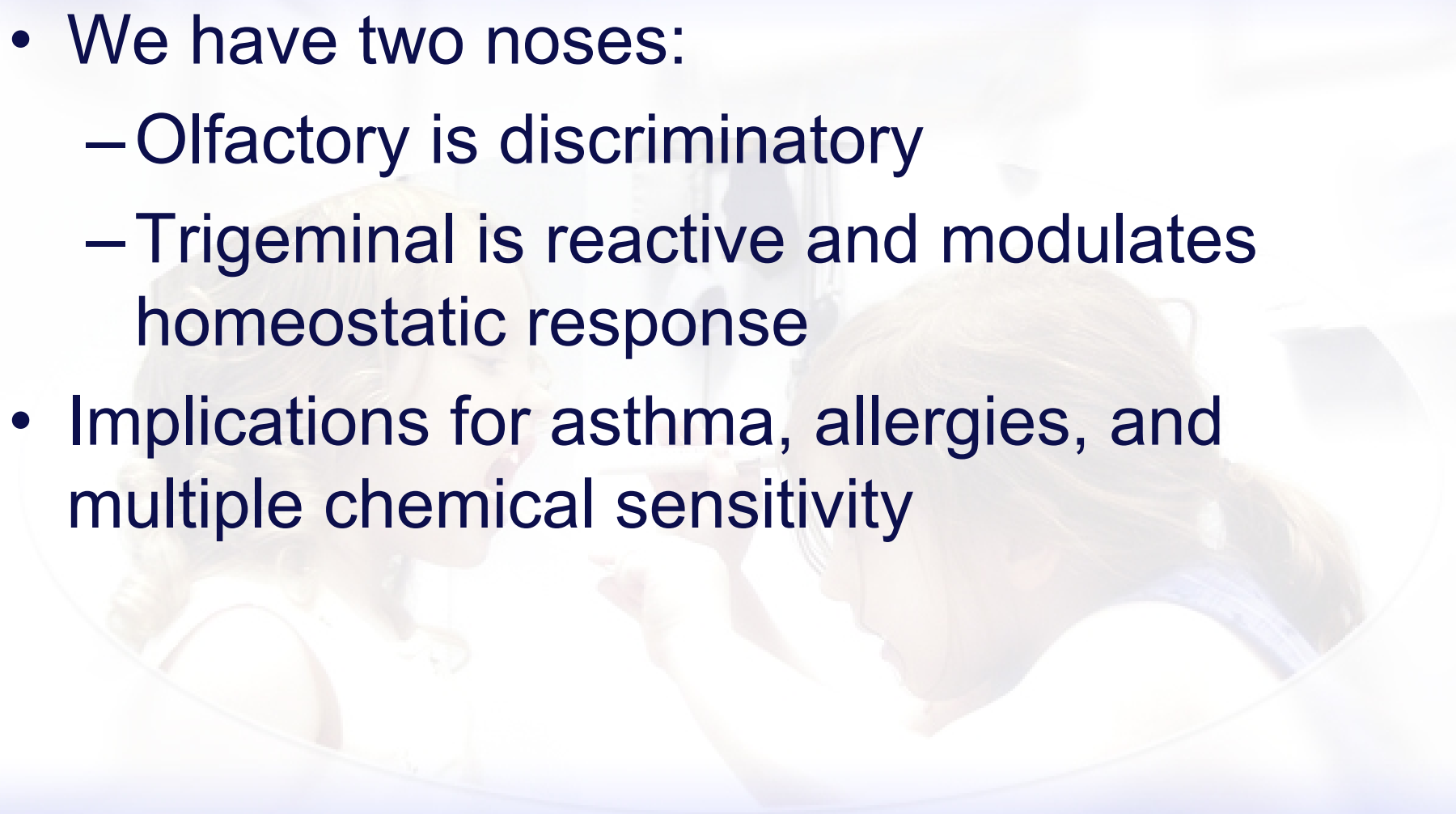
- Mesencephalic nucleus modulates golgi tendon apparatus systemically
- Effects muscle strength systemically
- Modulates enteric plexus
- Modulates adrenal function
- Modulates pigmentation in skin
- Modulates pineal gland

Vestibular influence

- In conjunction with cervical sensory input, it contributes a massive amount of sensory information to vestibular function and gait
- Dizziness often a symptom of cranio-mandibular dysfunction
- Chronic wear of dentition is a cause of vestibular dysfunction in the elderly

Chemoreceptors in the nose

- We have two noses:
 - Olfactory is discriminatory
 - Trigeminal is reactive and modulates homeostatic response
- Implications for asthma, allergies, and multiple chemical sensitivity



Generalized Hypersensitivity Syndrome

- Long term trigeminal hypertonicity causes systemic hypersensitivity
- Results in central hypersensitivity
- Patient becomes hypersensitive to any and all sensory input
- Result: chronic illness



In summary: 3 CRITICAL CONCEPTS

- Systemic influence of trigeminal system
- Biomechanical principles of occlusion
- Need for integration of medical information into orthodontic treatment



Neurological basis necessitating orthopedic precision

- Vast neurological disturbances with jaw orthopedic and occlusal discrepancies
- Hypersensitization a sequella of trigeminal disturbance
- Leads to high medical utilization
- Behooves us to approach this system with our best efforts

Discussion



A dramatic landscape photograph featuring a low sun on the horizon, creating a strong orange and yellow glow that illuminates the sky and the silhouettes of distant mountains. The sky is filled with layers of clouds, some of which are dark and heavy, while others are thin and catch the light from the sun. The overall mood is somber and final. The text "THE END" is centered in the lower half of the image in a white, bold, sans-serif font.

THE END