3RD NATIONAL SYMPOSIUM ON COMPLEMENTARY & ALTERNATIVE GERIATRIC HEALTH CARE

INTEGRATIVE PAIN MANAGEMENT

AND THE 24TH ANNUAL GERIATRIC RESEARCH, EDUCATION & CLINICAL CENTER SYMPOSIUM

WELCOME TO
LOGAN COLLEGE OF CHIROPRACTIC

3RD NATIONAL SYMPOSIUM ON COMPLEMENTARY AND ALTERNATIVE GERIATRIC HEALTH CARE
INTEGRATIVE PAIN MANAGEMENT
AND THE 24TH ANNUAL GERIATRIC RESEARCH, EDUCATION & CLINICAL CENTER SYMPOSIUM

September 24-25, 2009

Acknowledgements:

This educational activity is sponsored by the following:
Logan College of Chiropractic
Saint Louis University School of Medicine
Gateway Geriatric Education Center OF Missouri & Illinois
Veteran Integrated Service Network 15 GRECC

Conference Overview & Objectives:

The unique diagnostic and treatment features of pain presentation in older adults often pose a challenge for the clinician. Pain lowers the quality of life in the older adult by decreasing function and amplifying the stresses of aging. Pain management may optimize the quality of life in the elderly population if it is multidisciplinary and integrative and characterized by the clinical objectives of preservation and restoration of function.

This symposium will provide a unique multidisciplinary educational experience that promises to advance the clinician's skill and understanding of the diagnostic and integrative treatment of pain in older adults. Complementary and integrative approaches to pain management will be emphasized. Lectures with illustrative case study presentations, and a discussion panel will help facilitate the delivery of these learning objectives:

- Overview the unique challenges posed by the elderly patient experiencing pain
- Review the anatomical and neurophysiological principles underlying pain processing
- Present the unique role of the Biopsychosocial Model of pain management in adults
- Review the functional neuroimaging models of complementary and integrative techniques of pain management
- Discuss the differential diagnosis of common pain syndromes in older adults
- Present the range of pain assessment tools for use in elderly patients
- Demonstrate how complementary and integrative techniques as well as medical therapeutics are used for pain management in older adults (guided imagery, acupuncture, clinical nutrition, spinal manipulation, rehabilitation, pharmacologic)
- Use pain case studies to illustrate integrative pain management

Planning Committee:

Norman W. Kettner, D.C., Chair, Department of Radiology, Logan College of Chiropractic
Nina Tumosa, Ph.D., GRECC Health Educational Specialist, St. Louis Veterans Affairs Medical Center
Elizabeth Goodman, D.C., Ph.D., Interim Dean of Admissions, Logan College of Chiropractic
Carl Saubert, Ph.D., Associate Vice President, Logan College of Chiropractic
Glenn Bub, D.C., Chief of Staff, Logan College of Chiropractic
Fawn Knoll, Assistant to the Associate Vice President for Public Relations and Web-site Coordinator**,** Logan College of Chiropractic
Erica Collier, Administrative Assistant, Department of Radiology, Logan College of Chiropractic
John E. Morley, MB, BCh, St. Louis VAMC VISN 15 and Saint Louis University
Alicia Yochum, R.N., Student, Logan College of Chiropractic

Accreditation/Approval

American Nurses Credentialing Center (ANCC)

Saint Louis University School of Nursing is an approved provider of continuing nursing education by the Missouri Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation. Missouri Nurses Association provider # 109-VII. California State Board Provider #13123.

American Medical Association (ACCME)

Saint Louis University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Saint Louis University maintains responsibility for the program. A certificate of attendance will be awarded to participants and accreditation records will be on file at the Saint Louis University CME office. In order to receive a certificate, participants must sign in at the beginning of this activity, complete an evaluation, attend 100% of the program, and pick up their own certificate at the conclusion of the program (certificates will not be mailed). Saint Louis University cannot issue certificates for less than 100% participation as required by accrediting body regulations.

Continuing Education Credits

Doctors of Chiropractic (DC)

Missouri is approved for 12.5 hours (12.5 general or 7.5 general, 1 chiropractic principles, 3 differential diagnosis, & 1 acupuncture).

Illinois is approved for 12.5 hours.

Arkansas is approved for 12.5 hours.

Kentucky is approved for 12.5 hours.

Iowa is approved for 12.5 hours.

Texas is approved for 12.5 hours.

Indiana is approved for 12.5 hours.

Kansas: is approved for 12.5 hours.

American Nurses Credentialing Center (ANCC)

Saint Louis University School of Nursing designates this educational activity for 12.25 contact hours in continuing nursing education.

American Medical Association (ACCME)

Saint Louis University School of Medicine designates this activity for a maximum of 12.25 AMA PRA Category I Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity. Continuing Education Certificates will be mailed only to those participants who have requested and paid for them. The certificates will be mailed to the participants by November 1. Should you need verification of your attendance before this date, please see the attendant at the registration booth prior to your

Missouri Board of Nursing Home Administrators

The Division of Geriatrics at Saint Louis University is approved as a Training Agency (TA-064-408) by the Missouri Board of Nursing Home Administrators. This program is being reviewed for a maximum of 12.25 clock hours including a maximum of 10.25 hours that could be patient care hours. For your convenience, each presentation has been assigned the number of proposed patient care and/or administrative hours being reviewed by the Missouri Board of Nursing Home administrators. Continuing Education Certificates will be available at the registration booth prior to your departure from the conference. Copies of the sign-in/sign-out sheets will be forwarded to the Missouri Board of Nursing Home Administrators indicating those people who have paid for continuing education credits. This information will be sent within 30 days of the conclusion of the conference. In order to receive continuing education credit, participants must complete an evaluation for all sessions attended. Contact St. Louis University representative for NHA, Nina Tumosa at tumosan@slu.edu for questions related to NHA credit.

AMERICANS WITH DISABILITIES ACT POLICY:

In compliance with the Americans with Disabilities Act, if you need special assistance to participate in this meeting, please contact Erica Collier at (636) 227-2100 extension 1830. Notification 48 hours prior to the meeting will enable Logan to make reasonable arrangements to ensure accessibility to this meeting. {28 CFR 35.102-35.104 ADA Title II}

DISCLOSURE POLICIES:

It is the policy of Saint Louis University School of Medicine to insure balance, independence, objectivity, and scientific rigor in its continuing medical education program. Faculty and planning committee members participating in these activities are required to disclose to the audiences prior to the activity the following:

1. The existence of any significant financial or other relationship with the manufacturer of any commercial product or provider of any commercial service discussed.
2. Their intention to discuss a product that is not labeled for the use under discussion.
3. Their intention to discuss preliminary research data.

Saint Louis University School of Medicine will review this activity's disclosures and resolve all identified conflicts of interest, if applicable.

FACULTY DISCLOSURE POLICY

It is the policy of Saint Louis University School of Medicine to insure balance, independence, objectivity and scientific rigor in all its educational programs. All faculty participating in these activities are expected to disclose to the program audiences (1) any real or apparent conflicts of interest related to the content of their presentations, and (2) if their presentation will include any information regarding unapproved uses of pharmaceuticals or (3) ongoing research (preliminary data).

FACULTY DISCLOSURES

All faculty have indicated no disclosures.

SAINT LOUIS UNIVERSITY SCHOOL OF MEDICINE POLICY FOR RELATIONSHIPS WITH COMMERCIAL ENTITIES

The purpose of continuing medical education (CME) is to enhance the Physician's ability to care for patients. It is the responsibility of the accredited sponsor of a CME activity to assure that the activity is designed primarily for that purpose.

Accredited sponsors often receive financial and other support from non-accredited commercial organizations. Such support can contribute significantly to the quality of CME activities. The purpose of these guidelines is to describe appropriate behavior of accredited sponsors in planning, designing, implementing, and evaluating certified CME activities for which commercial support is received.

-Preamble: ACCME Standards for Commercial Support of CME

COMMERCIAL SUPPORT MAY BE ACCEPTED FOR AN EDUCATIONAL ACTIVITY UNDER THE FOLLOWING CONDITIONS

("Accredited sponsor" refers to Saint Louis University School of Medicine CME):

Statement of Purpose: The program must be for scientific and educational purposes only and will not promote the commercial entity's products, directly or indirectly.

Letter of Agreement: The accredited sponsor and the commercial entity must agree in writing (see Letter of Agreement) to abide by the ACCME Standards for Commercial Support of Continuing Medical Education and the FDA guidelines regarding same.

Design of Activity: In designing educational activities, the accredited sponsor (CME) must assure that the activities have the following characteristics: They must be free of commercial bias for or against any product; If the activities are concerned with commercial products, they must present objective information about those products, based on scientific methods generally accepted in the medical community. Full disclosure of potential conflicts of interest with industry must be made by all participating faculty members (see SLU Policy on Conflict of Interest and Disclosure form), and must be disclosed to the audience of the program through the publicity, in course syllabi, and/or in the introductions of presenters.

Independence of Accredited Sponsors: The design and production of educational activities shall be the ultimate responsibility of the accredited sponsor. Commercial supporters of such activities shall not control the planning, content or execution of the activity. To assure compliance with this standards, the following requirements must be adhered to.

Assistance with Preparation of Educational Materials: The content of slides and reference materials must remain the ultimate responsibility of the faculty selected by the accredited sponsor. A commercial supporter may be asked to help with the preparation of conference related educational materials, but these materials shall not, by their content or format, advance the specific proprietary interests of the commercial supporter.

Assistance with Educational Planning: An accredited sponsor may obtain information that will assist in planning and producing an educational activity from any outside source whether commercial or not. However, acceptance by an accredited sponsor of advice or services concerning speakers, invitees or other educational matters, including content, shall not be among the conditions of providing support by a commercial organization.

Marketing of CME Activities: Only the accredited sponsor may authorize a commercial supporter to disseminate information about a CME activity to the medical community. However, the content of such information is the responsibility of the accredited sponsor, and any such information must identify the educational activity as produced by the accredited sponsor.

Activities Repeated Many Times: If commercially supported educational activities are offered that repeat essentially the same information each time they are given, then it must be demonstrated that every iteration of that activity meets all of the Essentials and Standards of the ACCME.

Educational Activities or Materials Prepared by Proprietary Entities: When educational activities consisting of concepts or materials are prepared by proprietary entities, such activities must adhere to the Essentials and Standards in all respects, especially with regard to the provisions concerning the independence of the accredited sponsor in planning, designing, delivering and evaluating such activities.

Policy for Relationships With Commercial Entities

Enduring Materials: The accredited sponsor is responsible for the quality, content, and use of enduring materials for purposes of CME credit. (For the definition, see ACCME "Standards for Enduring Materials.")

Identifying Products, Reporting on Research, and Discussing Unlabeled Uses of Products

a. Generic and Trade Names: Presentations must give a balanced view of therapeutic options. Faculty use of generic names will contribute to this impartiality. If trade names are used, those of several companies should be used rather than only that of a single supporting company.

b. Reporting Scientific Research: Objective, rigorous, scientific research conducted by commercial companies is an essential part of the process of developing new pharmaceutical or other medical products or devices. It is desirable that direct reports of such research be communicated to the medical community. An offer by a commercial entity to provide a presentation reporting the results of scientific research shall be accompanied by a detailed outline of the presentation which shall be used by the accredited sponsor to confirm the scientific objectivity of the presentation. Such information must conform to the generally accepted standards of experimental design, data collection and analysis.

c. Unlabeled Uses of Products: When an unlabeled use of a commercial product, or an investigational use not yet approved for the purpose is discussed during an educational activity, the accredited sponsor shall require the speaker to disclose that the product is not labeled for the use under discussion or that the product is still investigational.

Exhibits and Other Commercial Activities:

Exhibits: When commercial exhibits are part of the overall program, arrangements for these should not influence planning nor interfere with the presentation of CME activities. Exhibit placement should not be a condition of support for a CME activity. If exhibits are included as a part of an activity, exhibitors should represent a diversity of companies/products rather than those of a single company.

Representatives from the exhibiting companies may not act in a manner which could be interpreted as interfering with the educational activity (e.g., actively pursing the participants for the purpose of promoting a product).

Continuing medical education activities are not trade shows and must not give the appearance that the primary intent is marketing of product.

Commercial Activities During Educational Activities: No commercial promotional materials shall be displayed or distributed in the same room immediately before, during, or immediately after an educational activity certified for credit.

Commercial Supporters at Educational Activities: Representatives of commercial supporters may attend an educational activity, but may not engage in sales activities while in the room where the activity takes place.

Management of Funds from Commercial Sources:

Independence of the Accredited Sponsor in the Use of Contributed Funds: The ultimate decision regarding funding arrangements for CME activities must be the responsibility of the accredited sponsor. Funds from a commercial source should be in the form of **an educational grant made payable to the accredited sponsor** for the support of programming (see also Saint Louis University School of Medicine Guidelines for Continuing Medical Education Activities). The terms, conditions and purposes of such grants must be documented by a signed agreement between the commercial supporter and the accredited sponsor. All support associated with a CME activity, whether in the form of an educational grant or not, must be given with the full knowledge and approval of the accredited sponsor. No other funds from a commercial source shall be paid to the director of the activity, faculty, or others involved with the supported activity.

Payments to Faculty: Payment of reasonable honoraria and reimbursement of out-of-pocket expenses for faculty is customary and proper. **Payments to the faculty must be from the accredited sponsor, NOT the commercial supporter. As outlined above, "funds from a commercial source should be in the form of an educational grant made payable to the accredited sponsor…" Under no circumstances should a commercial supporter pay a faculty member directly.**

Policy for Relationships With Commercial Entities

Acknowledgement of Commercial Support: Commercial support must be acknowledged in printed announcements and brochures, however, reference must not be made to specific products.

Accountability for Commercial Support: Following the CME activity, upon request, the accredited sponsor should be prepared to report to each commercial supporter and other relevant parties, and each commercial supporter to the accredited sponsor, information concerning the expenditures of funds each has provided. Likewise, each commercial supporter should report to the accredited sponsor information concerning their expenditures in support of the activity.

Commercially Supported Social Events: Commercially supported social events at CME activities should not compete with, nor take precedence over, the educational events.

Policy on Disclosure of Faculty and Sponsor Relationships:

a. Disclosure Policy for All CME Activities: An accredited sponsor shall have a policy requiring disclosure of the existence of any significant financial interest or other relationship a faculty member or the sponsor has with the manufacturer's) of any commercial product's) discussed in an educational presentation. All certified CME activities shall conform to this policy (see Saint Louis University Faculty Disclosure Policy).

b. Disclosure in Conference Materials: CME faculty or sponsor relationships with commercial supporters shall be disclosed to participants prior to educational activities in brief statements in conference materials such as brochures, syllabi, exhibits, poster sessions, and also in post-meeting publications.

c. Disclosure for Regularly Scheduled Activities: In the case of regularly scheduled events, such as grand rounds, disclosure shall be made by the moderator of the activity after consultation with the faculty member or a representative of the supporter. Written documentation that disclosure information was given to participants shall be entered in the file for that activity.

Financial Support for Participants in Educational Activities:

a. Use of funds: In connection with an educational activity offered by an accredited sponsor, the sponsor may not use funds originating from a commercial source to pay travel, lodging, registration fees, honoraria, or personal expenses for non-faculty attendees. Subsidies for hospitality should not be provided outside of modest meals or social events that are held as part of the activity.

b. Scholarships for Medical Students, Residents and Fellows: Scholarship or other special funding to permit medical students, residents, or fellows to attend selected educational conferences may be provided, as long as the selection of students, residents or fellows who will receive the funds is made either by the academic or training institution or by the accredited sponsor with the full concurrence of the academic or training institution.

   Funding for medical students, residents or fellows is acceptable, however, the selection of those individuals must be unrestricted and should be the choice of the accredited sponsor and not the commercial organization, with the full concurrence of the academic or training institution.

Program Schedule

Thursday, September 24, 2009

8:00 a.m.	Registration
8:25 a.m.	Welcome/Introductions
8:30 a.m. – 10:00 a.m.	Keynote Speaker Aging Successfully with Pain, John Morley, MB, BCh
10:00 a.m. – 10:15 a.m.	Morning Break
10:15 a.m. – 11:15 a.m.	Physiology of Pain: From the Periphery to the Cortex, Norman Kettner, DC
11:15 a.m. – 12:15 p.m.	Biopsychosocial Models of Pain, Rodger Tepe, PhD
12:15 p.m. – 1:15 p.m.	Lunch (on your own)
1:15 p.m. – 2:15 p.m.	Neuroimaging of CAM Techniques, Vitaly Napadow, PhD
2:15 p.m. – 3:15 p.m.	Clinical Presentation and Differential Diagnosis of Geriatric Pain Syndromes, Jeffrey Kamper, DC
3:15 p.m. – 3:30 p.m.	Afternoon Break
3:30 p.m. – 4:30 p.m.	Using the Instruments of Pain Assessment, Fredric Metzger, PhD
4:30 p.m.	Evaluation, Staff
4:45 p.m.	Adjournment

Friday, September 25, 2009

8:00 a.m.	Registration
8:30 a.m.-9:30 a.m.	Chiropractic Management of Lumbar and Cervical Spine Stenosis, Paul Dougherty, DC
9:30 a.m. – 10:30 a.m.	Interrupting the Cycle of Musculoskeletal Pain: Acupuncture for Older Adults, Linda Smith, DC
10:30 a.m. – 10:45 a.m.	Morning Break
10:45 a.m. – 11:45 a.m.	Guided Imagery for Pain Management, Jane Hart, MD
11:45 a.m. -12:45 p.m.	Lunch (on your own)
12:45 p.m. – 1:45 p.m.	The Chemistry of Inflammation and Nociception: Insights into Nutritional Modulation, David Seaman, DC
1:45 p.m.-2:45 p.m.	Identifying and Treating Pain Among Older Patients, Joseph Flaherty, MD
2:45 p.m. – 3:00 p.m.	Afternoon Break
3:00 – 4:00 p.m.	Panel Discussion: Dr. Norman Kettner will facilitate case study discussions of diagnosis, management and treatment of pain in older persons. Panelists: Drs. Dougherty, Hart, Flaherty, Seaman, and Smith
4:00 p.m.	Evaluation, Staff
4:15 p.m.	Adjournment

LECTURE NOTES

Aging Successfully With Pain

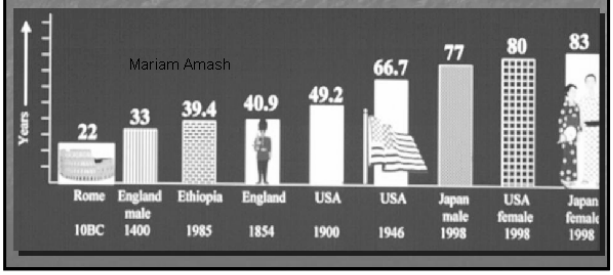
John E. Morley, MB, BCh

Aging Successfully With Pain

Gateway Geriatric Education Center | Department of Veterans Affairs | Saint Louis University Division of Geriatric Medicine

Lifespan is Increasing

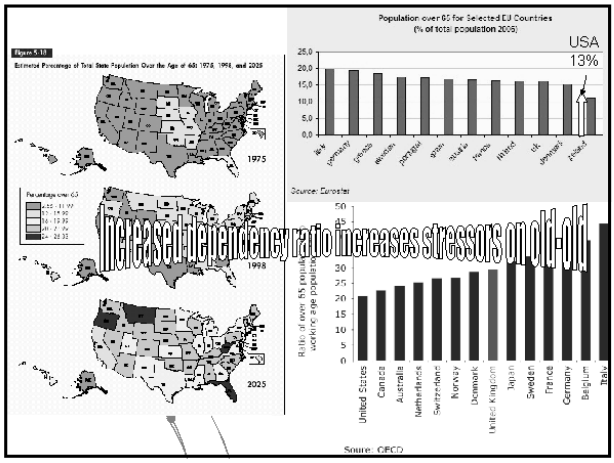
Jeanne Calment

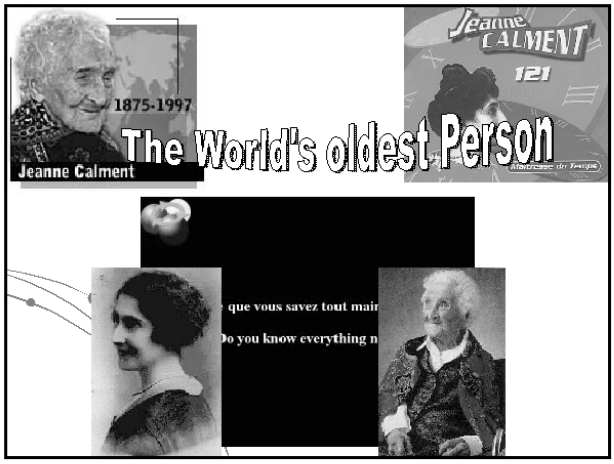


Female vs Male mortality

- Lonely X
- Hormones…critical period for estrogen
- Risk Taking
- Smoking/alcohol
- Health compliance
- Immune differences

WOMEN HAVE MORE ILLNESSES AND DISABILITY





Michelangelo and the Pietas

- **1500**
- **Age 25**

1550 – 1555
Completed at 80

Successful Aging (Genes)

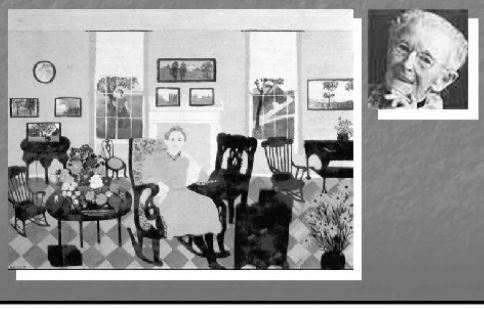
or

Aging Successfully (Fortitude)

20 – 30 % of aging due to genes

Most of this effect is seen in persons over 60 years of age

Grandma Moses produced her last painting at age 103.



Renoir, 1915
Blonde a la rosa

Model: DeeDee

Henri Matisse (1869 – 1954)

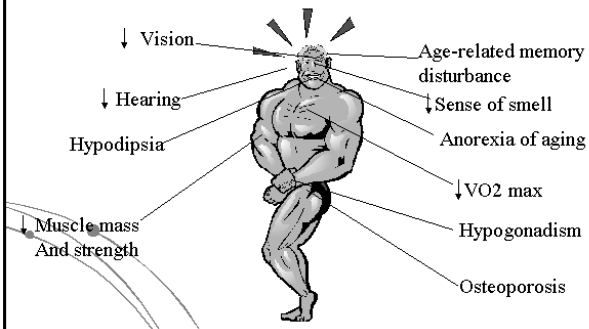
Monet

1899

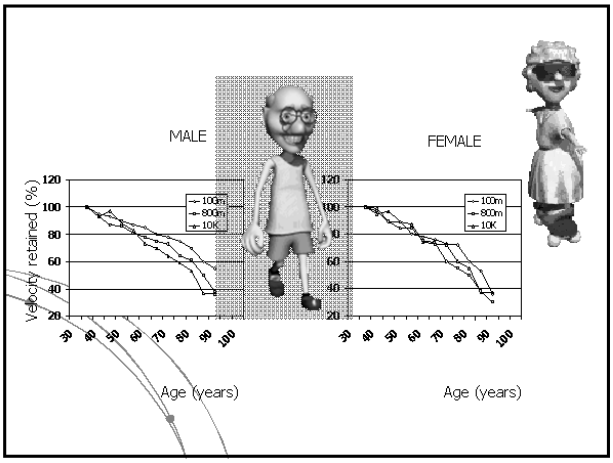
1900

1923

Tithonusism

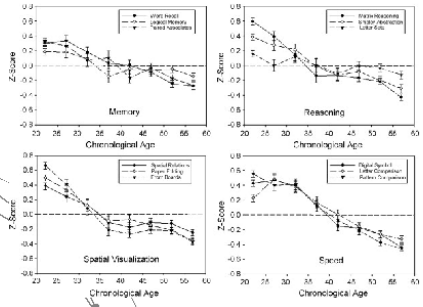


Physiological changes of Aging

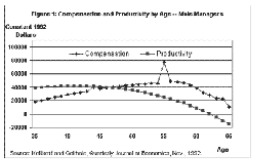


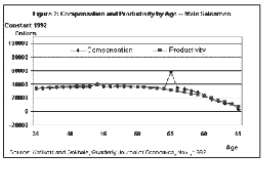
Memory Declines from a Young Age

Salthouse, Neurobiology of Aging 2009



Productivity Declines with Age





HERTFORDSHIRE COHORT STUDY
SARCOPENIA ORIGINATES AT BIRTH

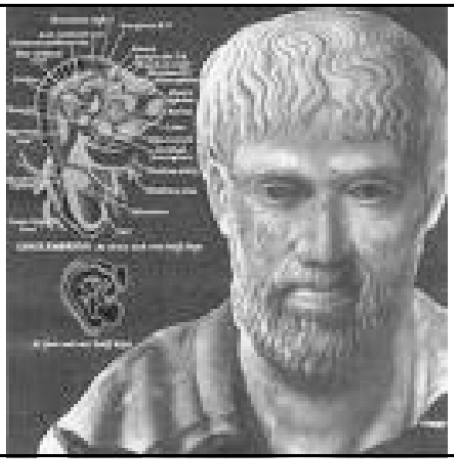
Sayer et al J Gerontol A 59:930,2004

730 men 673 women
Known weight at birth and one year

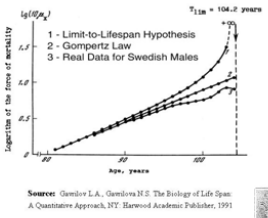
GRIP STRENGTH CORRELATES WITH
BIRTH WEIGHT
NOT INFANT GROWTH

Paternal Smoking And Obesity

- Males who smoke before 11 years of age have obese offspring
- Animal studies suggest that this may be an epigenetic effect due to abnormal methylation



Mortality at Advanced Ages



Source: Gavrilov L.A., Gavrilova N.S. The Biology of Life Span: A Quantitative Approach, NY: Harwood Academic Publisher, 1991

Roger Bacon

(c.1214-1294)

- Controlled diet
- Proper rest
- Exercise
- Moderation life style
- Good hygiene
- Inhaling the breath of a young virgin


Roger Bacon (1214-1294)


Manage crises well


Don't abuse alcohol


Enjoy a stable marriage


Watch your weight

Get some exercise

Do not smoke

To Age Successfully

Health Behaviors and Aging Successfully
EPIC-Norfolk Study

Khaw et al, PLOS Medicine 2008,5:e2

- Non-smoking
- Not physically inactive
- Moderate alcohol intake (1 – 14/week)
- Fruit and Vegetable 5 servings/daily (vitamin C >50 mmol)

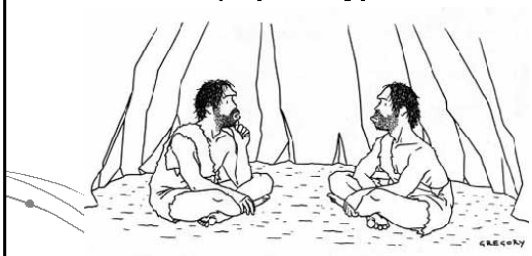

Age 42

Estimated 14 year improvement in physiological age

FRANS HALS

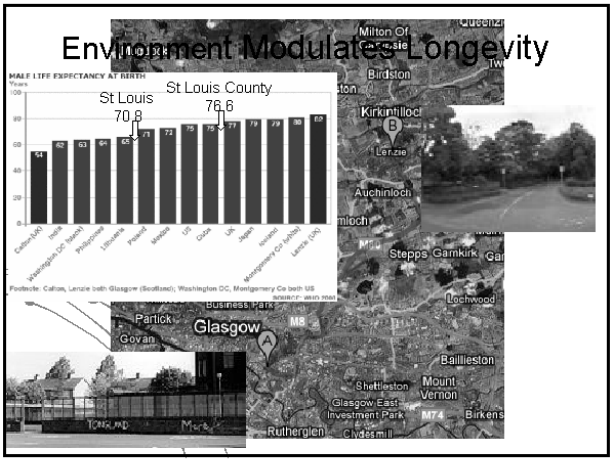

Age 63

Does environment interact with physiology?

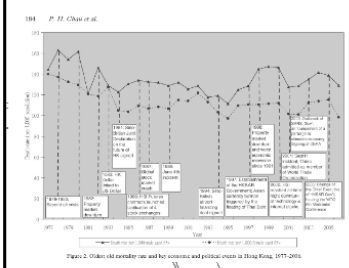


"Something's just not right—our air is clean, our water is pure, we all get plenty of exercise, everything we eat is organic and free-range, and yet nobody lives past thirty."

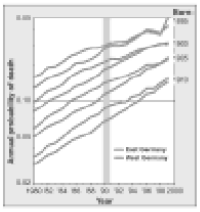
Environment Modulates Longevity



Stressful Social Events increase Mortality in oldest-old males in Hong Kong



After the fall of the Berlin Wall East Germans rapidly developed a survival equivalent to West Germans



High dietary intake or high blood concentrations of antioxidant vitamins are associated with a reduced risk of cardiovascular disease and cancer at several community sites

….Nutrition 14:513,1998

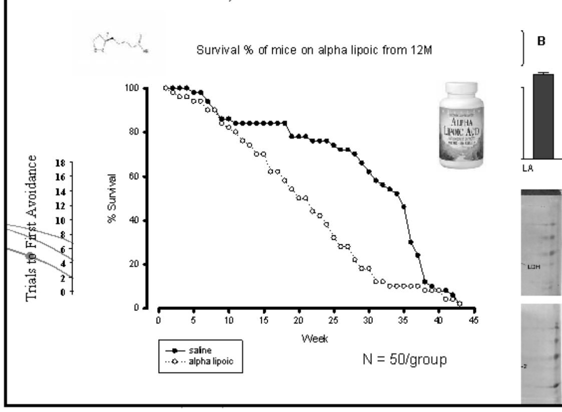
Vitamin Supplements Fail to Improve Outcomes

Table 3. Events, Annualized Percentages, and Multivariable Adjusted[a] Relative Risks of Cardiovascular Disease (CVD) by Multivitamin Use in the Women's Health Initiative (CTs and OS)

Category of Multivitamin Use	MI[b] No. (%)[e]	MI[b] HR (95% CI)	MI[b] P Value	Stroke[c] No. (%)[e]	Stroke[c] HR (95% CI)	Stroke[c] P Value	Venous Thromboembolism[d] No. (%)[e]	Venous Thromboembolism[d] HR (95% CI)	Venous Thromboembolism[d] P Value	Total Mortality No. (%)[e]	Total Mortality HR (95% CI)	Total Mortality P Value
Any multivitamin			.27			.75			.84			.48
No	2528 (0.38)			2173 (0.30)			364 (0.10)			5911 (0.80)		
Yes	1765 (0.36)	0.96 (0.89-1.03)		1427 (0.28)	0.99 (0.91-1.07)		204 (0.10)	[illegible]		3864 (0.77)	1.02 (0.97-1.07)	
Type of multivitamin			.10			.63			.35			.69
None	2528 (0.38)			2173 (0.30)			364 (0.10)			5911 (0.80)		
Multivitamin	176 (0.40)	1.08 (0.91-1.28)		140 (0.32)	1.10 (0.91-1.33)		21 (0.12)	[illegible]		372 (0.83)	[illegible]	
Multivitamin with minerals	1497 (0.35)	0.96 (0.89-1.03)		1201 (0.28)	0.98 (0.90-1.06)		173 (0.10)	1.07 (0.86-1.32)		3335 (0.77)	1.02 (0.97-1.07)	
Stress multivitamins	84 (0.22)	0.75 (0.58-0.99)		86 (0.22)	0.97 (0.72-1.29)		8 (0.05)	[illegible]		181 (0.61)	0.94 (0.80-1.10)	

Abbreviations: CI, confidence interval; CTs, clinical trials; HR, hazard ratio; MI, myocardial infarction; OS, observational study.
[a] All HRs from a proportional hazards model adjusted for the characteristics listed in Table 1 and stratified according to age (5-year groups), hormone therapy trial randomization assignment or study enrollment (active conjugated equine estrogen [CEE] plus medroxyprogesterone acetate [MPA], placebo CEE plus MPA, active CEE, placebo CEE, not randomized), dietary modification trial randomization (intervention, control, not randomized), or OS enrollment.
[b] Includes fatal and nonfatal MI. In addition to the adjustments listed in footnote a, the models were adjusted for a family history of MI and a personal history of MI.
[c] Includes fatal and nonfatal stroke. In addition to the adjustments listed in footnote a, the models were adjusted for a family history of stroke and a personal history of stroke.
[d] Clinical trials only; includes venous thromboembolism and pulmonary embolism; the outcomes were not adjudicated for the OS. In addition to the adjustments listed in footnote a, the models were adjusted for a history of venous thromboembolism and a history of pulmonary embolism.
[e] Annualized percentage of cases.

ALPHA-LIPOIC ACID, SAMP8 AND PROTEIN OXIDATION



THE WORLD IS MORE COMPLEX THAN WE WANT
Dali's Galatea

Is it Food that Protects us ?

- Cruciferous foods such as broccoli decrease cancer risk though there are individual genetic variants

  Higden Pharmacol Res 2007;55:224

- Sulforaphane from broccoli modulates NrF-2 resulting in decreased oxidative stress

The New England
Journal of Medicine

Volume 323 JULY 5, 1990 Number 1

Effects of Human Growth Hormone in Men over 60 Years Old

Daniel Rudman, M.D., Asaf G. Feller, M.D., Hoskote S. Nagraj, M.D., Gregory A. Gergans, M.D., Pardee Y. Lalitha, M.D., Allen F. Goldberg, D.D.S., Robert A. Schlenker, Ph.D., Lester Cohn, M.D., Inge W. Rudman, B.S., and Dale E. Mattson, Ph.D.

Clinical Endocrinology (1993) 39, 417-425

Carpal tunnel syndrome and gynaecomastia during growth hormone treatment of elderly men with low circulating IGF-I concentrations

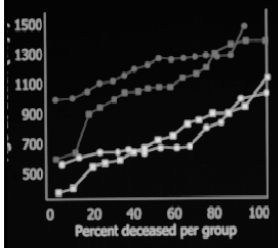
Lester Cohn, Axel G. Feller, Michael W. Draper, Inge W. Rudman and Daniel Rudman
Department of Medicine, Medical College of Wisconsin and Medical Service, Veterans Administration Medical Center, Milwaukee, WI; Department of Medicine, Chicago Medical School and Medical Service, Veterans Affairs Medical Center, North Chicago, IL; and Eli Lilly and Co., Indianapolis, IN, USA

(Received 16 November 1992; returned for revision 15 January 1993; finally revised 5 April 1993; accepted 28 April 1993)

Increased from the range 0.10 – 0.35 units/ml into the range 0.5 – 2.5 units/ml. Among the 18 men who completed 12 months of hGH treatment without experiencing one of the three above-noted presumed hGH side-effects, mean and peak plasma IGF-I during treatment were significantly lower than among the 13 men who experienced carpal tunnel syndrome or gynaecomastia (one subject had both) while on hGH. With one exception, neither carpal tunnel syndrome nor gynaecomastia occurred in any individual with a mean IGF-I level less than 1.0 units/ml during hGH treatment. Twelve months of hGH treatment [illegible] caused an

Growth Hormone and Mortality
"Of Mice and Men"

Ames Dwarf Mice
Brown-Borg *et al*, Nature 364:3, 1996



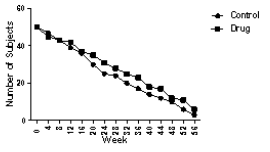
Paris Prospective Study
Maison *et al*, BMJ 316:1132, 1998

Mortality

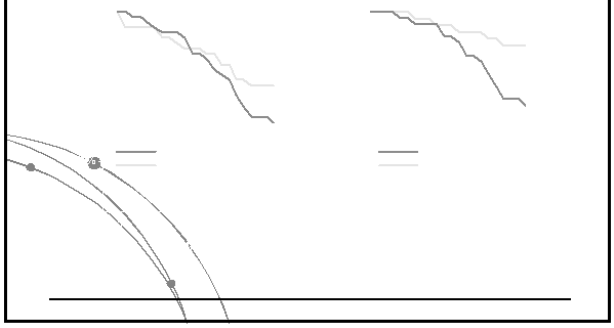
	Hazard Ratio	p
All causes		
2h GH	2.54	0.002
Fasting GH	1.50	0.009
Cardiovascular		
Fasting GH	1.79	0.05
Malignancy		
2h GH	2.59	0.04

Is survival dependent on slowing down?

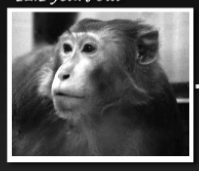
GHRH Antagonist Slows Mortality
MZ-5-156
SAMP8



Does CR in monkeys extend lifespan?

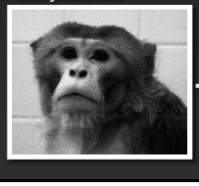


CONTROL [78005]
12.1 years old



30.1 years old

DR [ss42]
14.3 years old



32.3 years old

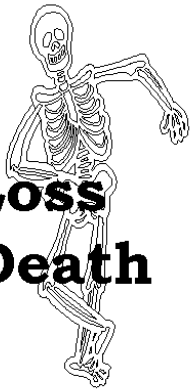
Caloric Restriction Lowers oxidative metabolism and prolongs life

"Against diseases known,
the strongest fence
is the defensive virtue
abstinence"
Benjamin Franklin

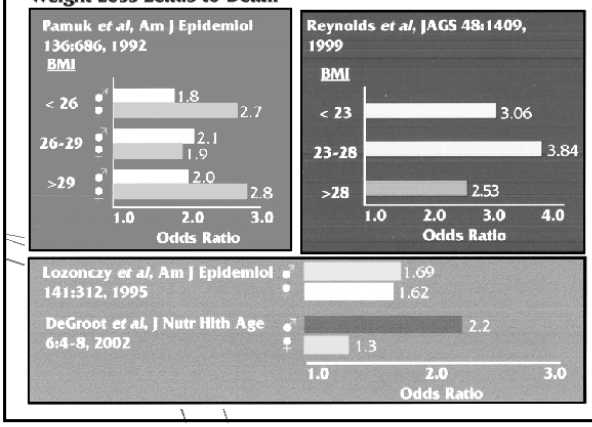
"To eat only enough to sustain life"

Louis Cornaro
1464-1566

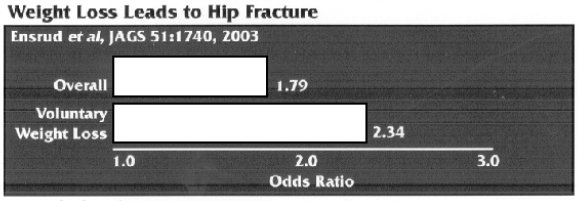
Weight Loss Leads to Death



Weight Loss Leads to Death



Weight Loss Leads to Hip Fracture



HIGH TOTAL ENERGY EXPENDITURE LEADS TO INCREASED LONGEVITY

Rate of Living
(Rubner 1908;
Pearl 1922)

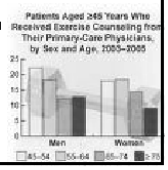
Toxic By-Products of Metabolism
(Metchnikoff, 1908)

Can this be explained by uncoupling leading to less free radical generation ?

Exercise and incident dementia in persons 65 years and older

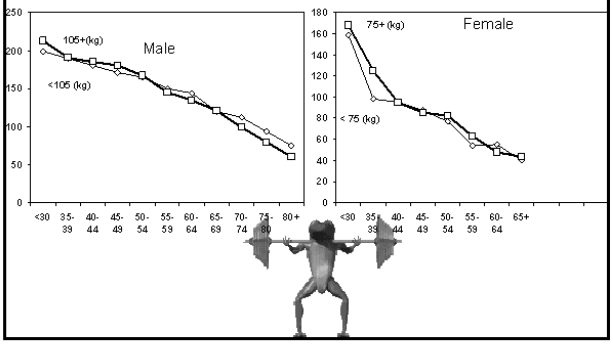
Larson et al, Ann Int Med 2008;144:73

- 1740 older persons who scored above 25th percentile cognitively
- Follow-up 6.2 years
- Exercise 3 times/week: 13.0 per 1000
- Exercise less: 19.7 per 1000
- OR 0.62 (0.44 – 0.86, p = 0.004)

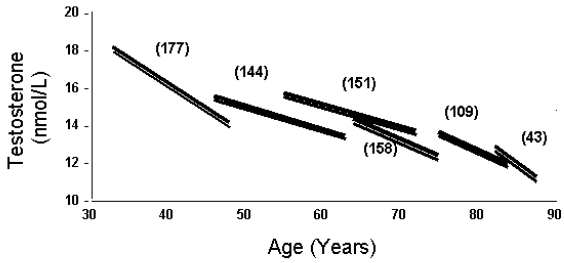


World Clean and Jerk Weight Lifting Records

www.mastersweightlifting.org

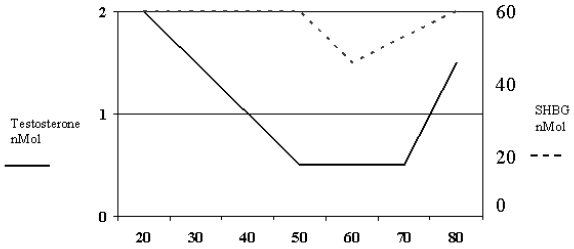


Longitudinal Changes in Testosterone

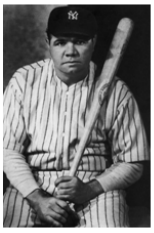


Adapted from Harman SM, et al. *J Clin Endocrinol Metab*. 2001;86:724-731.

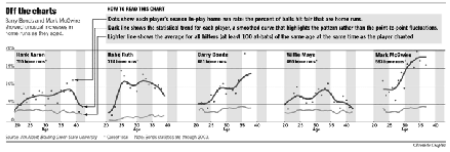
Female Changes in Testosterone over Lifespan

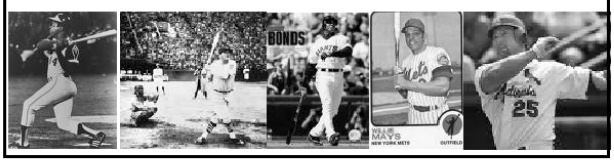


STEROIDS ENHANCE PERFORMANCE



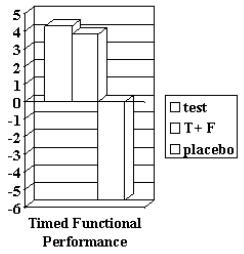
Steroid use enhances older baseball players performance



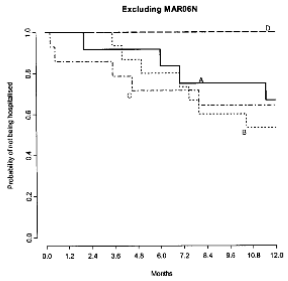


Testosterone IM and Physical Performance Page et al,JCEM 90:1502,2005

- Age 75,36 months
- T(n=24),T+F(n=24), Placebo(n=22)
- Improved TFP(chair rising,walking,stair climbing,opening/closing door)
- Improved LBM



Risk of non-elective hospital admission
Testosterone, Caloric Supplement or Combination

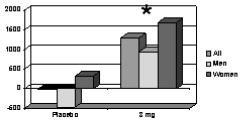


← Combined treatment

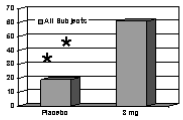
← No treatment

GTx SARM (Ostarine) n=120, Mean age 64.8 yrs

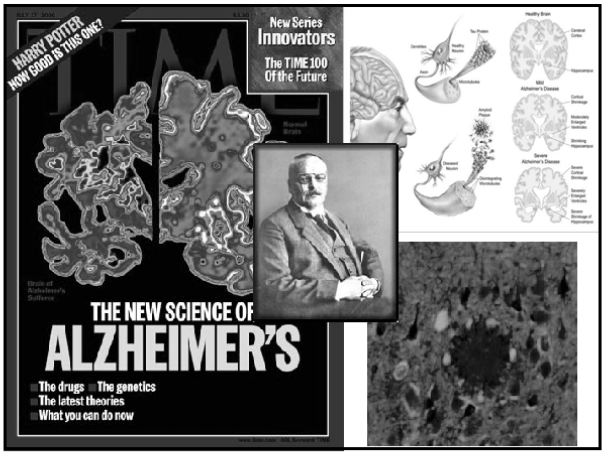
Fat Free Mass (Dexa)

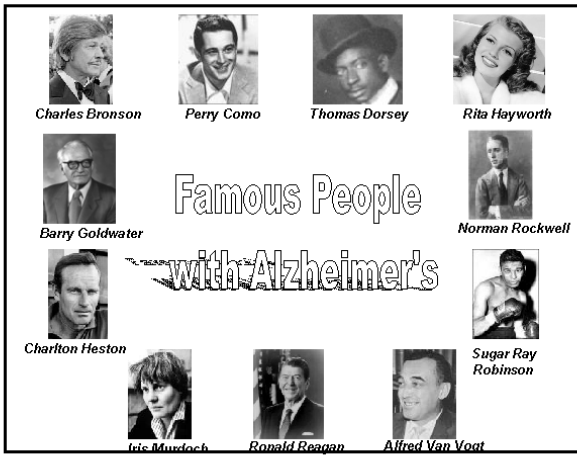


Stair Climb Power (Watts)

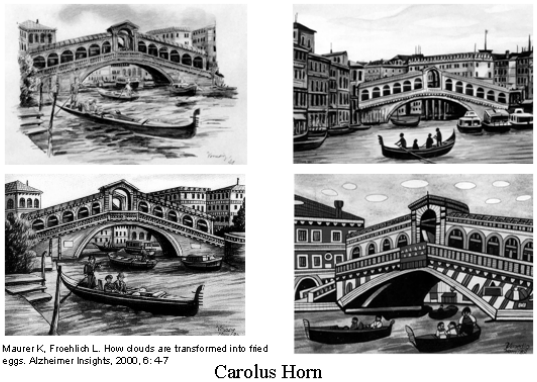


Aging : The physiology - disease continuum





How clouds are transformed into fried eggs



Maurer K, Froehlich L. How clouds are transformed into fried eggs. Alzheimer Insights, 2000, 6: 4-7

Carolus Horn

Effect of Alzheimers Disease on Survival

AGE (years)	SEX	AD (years)	REST (years)
70	Female	8	16
	Male	4.4	9.3
85	Female	3.9	6
	Male	3.3	4.7

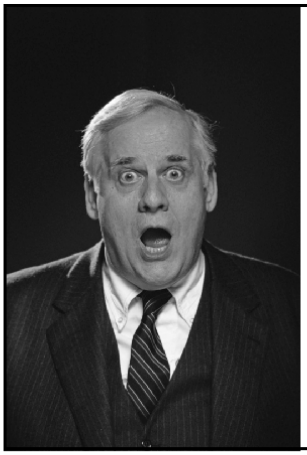
Factors affecting mortality in patients with Dementia

- Greater functional impairment (ADLs or FAST)
- Inability to walk without assisstance (death within 6 months)
- Medical co-morbidities
- Recent hospitalisation
- Incontinence
- Pressure ulcers

These are not necessarily different from non-demented nursing home residents

Neuropsychiatric factors affecting mortality in dementia

- Vascular Dementia
- Very rapid decline in mental status
- ? Lower education
- Hallucnations
- Behavior Disturbances including wandering
- Antipsychotics including atypicals



The use of antipsychotics may increase mortality risk 1.6-1.7 times…..

Antipsychotics for Alzheimer's Disease

Tariot et al NEJM 2006; 355:1525

	Olanzapine	Quetiapine	Resperidone	Placebo
Discontinuation (weeks)	8.1	5.3	7.4	8.0
Intolerability (%)	24	16	18	5
Improvement (%)	32	26	29	21

Effectiveness of Cholinesterase Inhibitors and Memantine for Treating Dementia : Evidence Review for a Clinical Guideline

- **Treatment of dementia with cholinesterase inhibitors and memantine can result in statistically significant (cognition and global assessment) but CLINICALLY MARGINAL IMPROVEMENT**

Raina et al, Annals Int Med 148:379, 2008

Spirituality and Vitality

- Multiple studies have shown that church attendance (social support) and spirituality (coping skills) enhance function and decrease mortality

Pain
The 5th Vital Sign

”To life,which is the place of pain…”

-Bhagawad Gita
Chapter VII

- PAIN IS GOD’S MEGAPHONE

…….C.S.Lewis

“I’m just pain covered in skin”

…….Mrs WILSON

The Grapes Of Wrath
John Steinbach

Pain Pathways

Nerve

⇩

Spinal Cord

⇩

Descending Pathway ⇦ / ⇩

Midbrain

⇩

Thalamus

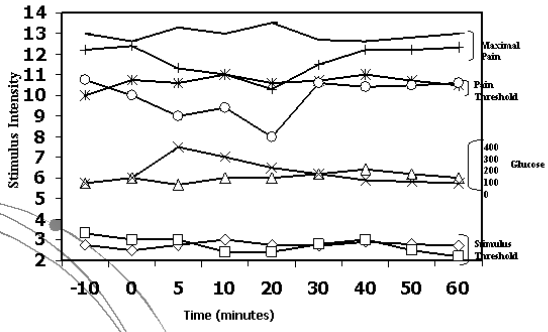
⇩

Cortex

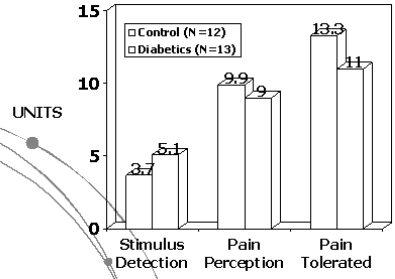
Pain Types

- Nociceptive
  - Trauma
  - Pressure
  - Inflammation
  - Ischemia
- Neuropathic
  - Peripheral
  - Central
    - thalamic
    - radiculopathies

Nonspecific
Headaches
Psychological
Somatization

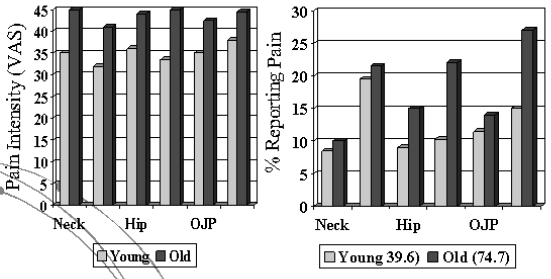


Comparison of Stimulus Detection, Pain Perception and Pain Threshold in Diabetics and Controls



Pain Frequency by Age

NHANES



Site of Chronic Pain

Frequency of Acute Pain

Steinbach (1986)

	Age (years) 18-24 (%)	64+ (%)
Headache	85	50
Backache	63	49
Muscle	62	42
Joint	41	71
Stomach	62	31
Dental	36	14

Pain-Related Disability and Veterans

- High……27%
- Moderate…….43%
- Low……30%
- Depressive increased effect of pain

The Biopsychosocial Pain Model

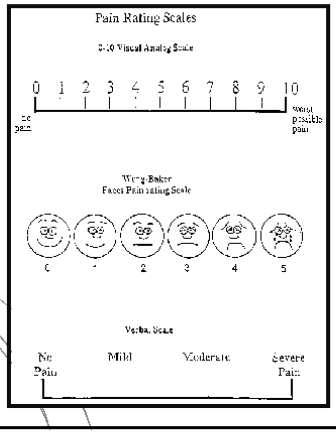
- Physical
  - disease
  - repetitive biomechanical strain
  - depression
  - deconditioning
- Psychological
  - dependency needs
  - anger
  - coping skills
  - lack of trust of health professionals
  - medication seeking

Social
relationships
job stress
family reinforces behavior
worker's compensation
poorly coordinated health care

Pain Assessment Principles

An ABCDE Mnemonic

- **A** sk about the pain regularly
- **A** ssess pain systematically
- **B** elieve patient and family reports of pain and what relieves it
- **C** hoose pain control options appropriate for the patient, family and setting
- **D** eliver interventions in a timely, logical and coordinated fashion
- **E** mpower the patients and their families
- **E** nable them to control the course of their lives to the greatest extent possible

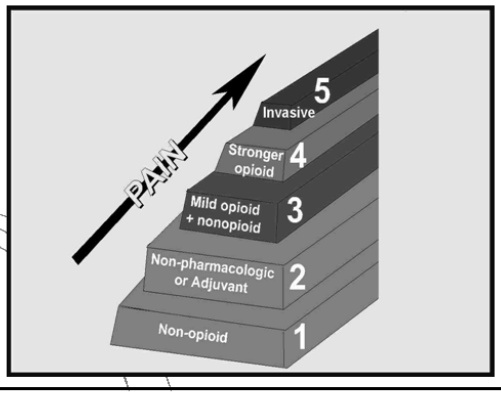


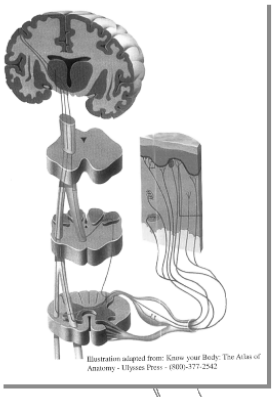
P ain is real. (believe the patient!)
A sk about pain regularly
I solation (psychological and social problems)
N otice non-verbal pain signs
E valuate pain characteristics
D oes pain impair function?

O nset
L ocation
D uration

C haracteristics
A ggravating factors
R elieving factors
T reatments previously tried

The Analgesic Pyramid





Nonpharmacological Pain Management Strategies

Distraction therapy

- Movies
- Laughter
- Art therapy
- Music therapy

Behavioral modification

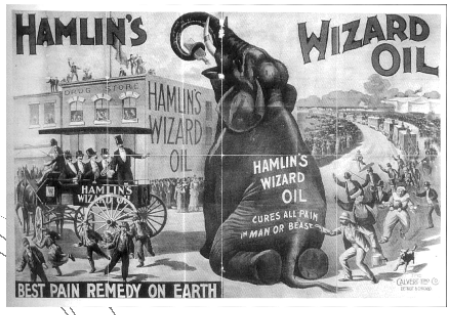
- Imagery/meditation
- Relaxation techniques
- Hypnosis
- Biofeedback

Physical therapy

- Massage
- Ultrasound
- Hot/cold therapies
- Exercise

Neurostimulation

- Transcutaneous nerve stimulation (TENS)
- Acupuncture



Analgesic Use

- One-fifth (1/5) of older Americans take OTC analgesics several times a week.
- "The desire to take medicine is one feature that distinguishes man,the animal from his fellow creatures" Sir William Osler

Principles of Pharmacological Management

- Choose the appropriate analgesic
- Use the simplest regimen
- Oral route preferable
- Consider cost
- Treat round-the-clock, not PRN
- Use additional doses for breakthrough pain
- Provide written pain management plan
- Use sorbitol/lactulose for constipation

END OF LIFE CARE PALLIATIVE CARE

- DRONABINOL
- Appetite stimulant
- Antinausea
- Decreases pain
- Enhances general wellbeing
- THE IDEAL DRUG FOR PALIATION

DRONABINOL
Dosing in Elderly

- Start with 2.5 mg prior to bedtime
- After one week move to 2.5mg before supper
- After 2 weeks if no response 2.5mg before supper and lunch

Morpheus
the god of sleep

Paracelsus, who first made a paste of alcohol and opium, called tincture laudanum (praiseworthy)

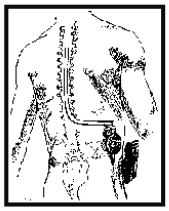
Sertuerner, German pharmacist who extracted opium from the poppy in the 19th century

Severe Pain

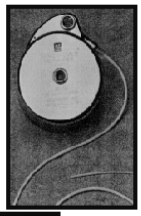
- Morphine
- Oxycodone
- Fentanyl (Duragesic)
- Methadone
- Hydromorphone
- **AVOID MEPERIDINE (DEMEROL)**

Invasive Modalities

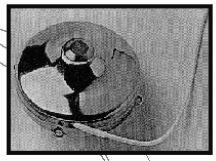
A



B



C



D

Conclusion

- Pain needs to be taken seriously and treated in a timely manner.
- Depression needs to be treated.
- Non-pharmacological as well as pharmacological modalities should be used to treat pain.
- Pain medicine works better when given continuously. Avoid PRNs.
- Use of opiates for uncontrolled pain is appropriate.

Aging Successfully : Conclusions

- **Genetics account for 20-30% of successful aging**
- **Epigenetics and prenatal events also play a role**
- **Enviroment and the individual response to stressors play a clear role**
- **Disease interacts with physiology to accelerate deterioration**
- **Fortitude (psychological adaptability) allows aging successfully**
- **Community support (from church to health care) can have a positive effect**

Physiology of Pain: From the Periphery to the Cortex

Norman W. Kettner, DC, DACBR

Physiology of Pain: From the Periphery to the Cortex

Norman W. Kettner, DC, DACBR, FICC
Chair, Department of Radiology
Logan College of Chiropractic
Chesterfield, Missouri

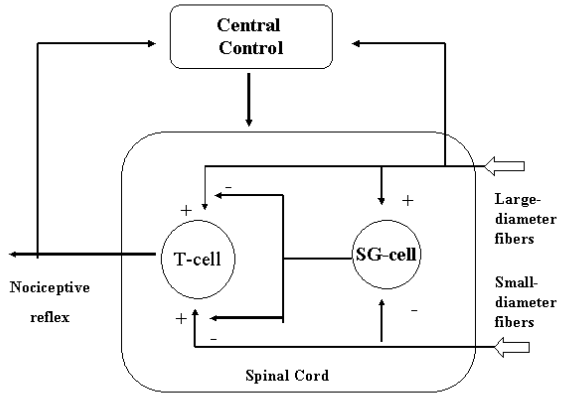
Course Outline

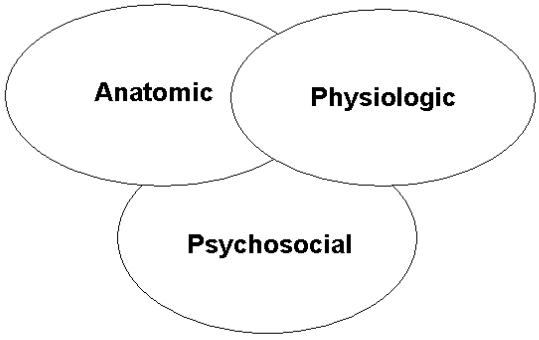
- Introduction to Pain Processing
- Pain in the Aged
- Language of pain
- Peripheral pain mechanisms
  - Transduction
  - Transmission
  - Modulation
  - Perception
- Spinal pain mechanisms
  - Dorsal horn
- Ascending system
- Descending system
- Supraspinal pain processing
- Psychological aspects of pain
- Placebo effects
- Pain neuroplasticity in the CNS

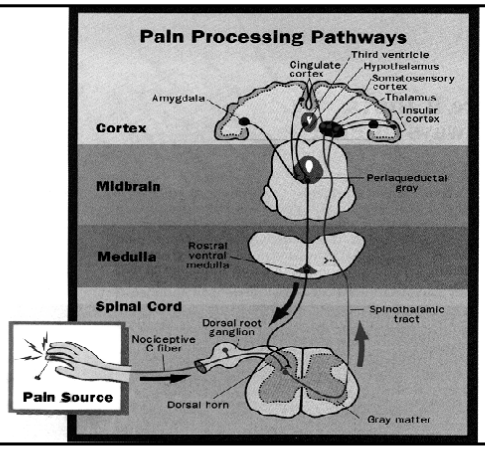
The Pain Revolution

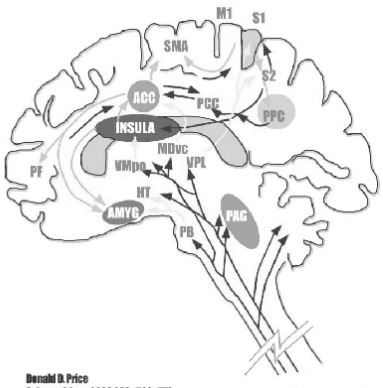
Melzack R, Wall PD:
Pain mechanisms: a new theory.
Science. 1965 Nov 19;150(699):971-9

Engel GL:
The need for a new medical model: a challenge for biomedicine.
Science. 1977 Apr 8;196(4286):129-36

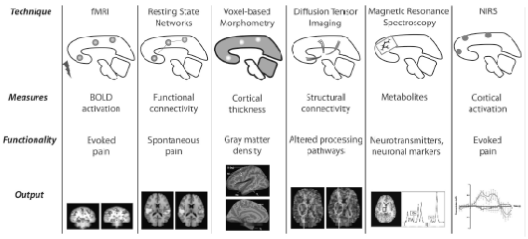




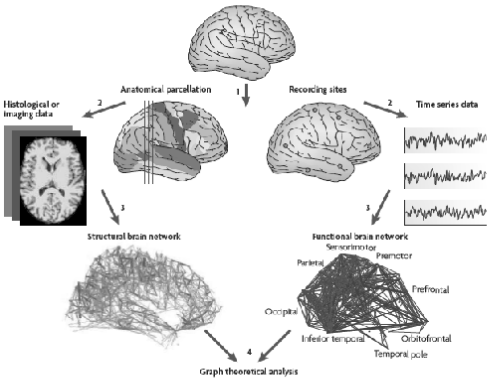




Donald D. Price
Science 9 June 2000 288: 1769-1772



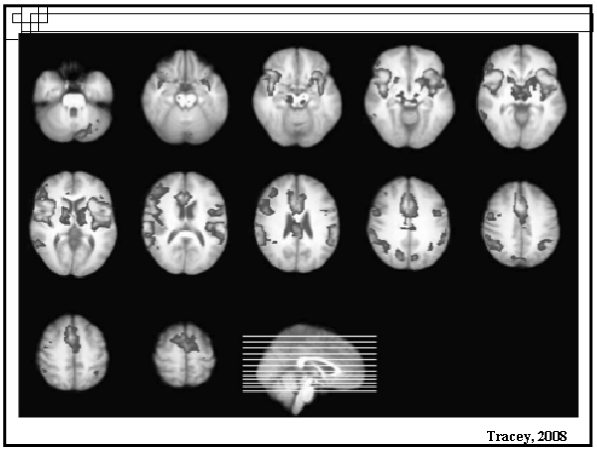
Sava et al, 2009



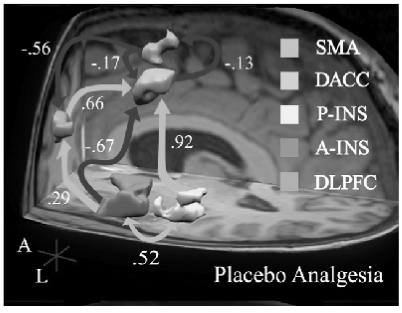
Bullmore 2009

Pain Neuromatrix

$$D=\begin{bmatrix} Dxx & Dxy & Dxz \\ Dxy & Dyy & Dyz \\ Dxz & Dyz & Dzz \end{bmatrix} \quad P=\begin{bmatrix} S2 & ACC & amygdala \\ thalam & insula & PAG \\ S1 & PFC & BG \end{bmatrix}$$



Tracey, 2008



Craggs, 2007

Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

Pain in the Aged

- Pain is the most common symptom in older patients although often under reported, (as high as 80% in long term facilities)
- Pain medications are the second most frequent prescription after cardiac-renal.
- Functional impairment, sleep disturbance, anxiety, depression, and social isolation exacerbate pain and reduce homeostatic reserve in the CNS, autonomic and immune systems.

Pain in the Aged

- Non-pharmacologic treatment options help lower drug effects.
- Two-thirds of patients suffering from arthritis pain and other MSK disorders have utilized integrative techniques (complementary) such as spinal manipulation, acupuncture and herbal preparations (Rao et al, 1999).

Pain in the Aged

- The role for integrative techniques in the palliative care for the hospice patient has not been adequately defined, but preliminary studies have been encouraging for pain, xerostomia, nausea and vomiting reduction and mood improvement.

Pain in the Aged

- Aging is associated with a global decline in cognitive functions such as attention, working memory and information processing. Age related changes in pain processing also promote disability.

Pain in the Aged

- Pain is an integrative experience dependent on excitatory and inhibitory mechanisms.
- Peripheral nerves, cortical neurons and their neurotransmitters decline with age, and damaged and degenerated nerves increase in number altering the balance of pain excitation and inhibition.

Pain in the Aged

- Pain processing regions of the brain that decline with age especially impact descending inhibition (gate theory).
- In AD, the medial pain system (motivational and autonomic) is affected before the lateral (sensory-discriminative) reducing the affective response to pain.

Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

The Language of Pain

Pain

- An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Nociception

- Transduction by thermal, mechanical or physical energy impinging on specialized neural receptors. Nerves (nociceptors) convey sensory information about tissue damage to the central nervous system.

Acute Pain

- Pain elicited by the injury of body tissues and activation of nociceptive transducers at the site of local tissue damage. Local injury alters the response characteristics of nociceptors, their central connections and the autonomic nervous systems in the region.
- The state of acute pain lasts for a limited time and remits when the underlying pathology resolves.

Case Study

- A 26 y/o male injured his knee playing volleyball. Lateral knee pain and swelling were immediate and prominent. An MRI was obtained to exclude internal derangement.

Chronic Pain

- Usually elicited by an injury, it is perpetuated by factors that are remote from the originating cause. Chronic pain extends for long periods of time, has low levels of underlying pathology that do not explain the presence and extent of pain or both.

Chronic Pain

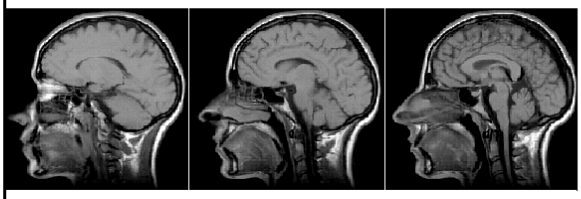
- This type of pain prompts patients to seek health care but treatment is rarely effective. Its persistence suggests environmental and affective factors interact with tissue damage and contribute to the persistence of pain and illness behaviors.

Chronic Pain

- As the brain is modified by experience, it may alter the processing of noxious information to reduce or augment its effectiveness on subjective awareness (neuroplasticity).

Case Study

- A 60 y/o female has experienced daily headaches and memory impairment for several months following a snowmobile accident. She did not recollect head impact and wore a helmet. Neurological exam was normal. Cervical radiography, CT and MRI of the head within days of the accident were unremarkable.



Central Pain

- Pain initiated by a primary lesion or dysfunction in the central nervous system. Also known as thalamic pain, or central post-stroke pain.

Neurogenic Pain

- Pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation in the peripheral or central nervous system.

Psychogenic Pain

- Report of pain attributable to psychological factors usually in the absence of objective physical pathology that could account for pain. This term is commonly used in a pejorative sense.

Central Sensitization

- An increase in the excitability and responsiveness of neurons in the spinal cord and brain. This mechanism is likely an etiological factor in chronic pain disorders such as fibromyalgia, CRPS and chronic low back pain.

Neuroplasticity

- Nociceptive input leading to structural and functional neural changes that may cause altered perceptual processing and contribute to pain chronicity.

Allodynia

- Pain arising from a stimulus that does not normally provoke pain.

Hyperalgesia

- An increased response to a stimulus that is normally painful.

Placebo

- A substance or procedure without therapeutic effect that is provided as a treatment. It is frequently used to control for patient expectations in testing a treatment.

Placebo Effects

- Refers to the positive benefits (pain relief) from a placebo preparation or procedure that is generally achieved only with an active treatment. Cognitive and affective processes likely interact to produce this effect.

Nocebo

- Negative treatment effects (pain) induced by a substance or procedure containing no toxic or detrimental substance. The inverse of placebo.

Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain Neuroplasticity in the CNS

Receptors and Peripheral Nerves

Lloyd/Hunt System	Diameter (μm)	Letter System	Conduction Velocity (m/sec)	Myelin	Receptor/ending types
Ia	12-20	—	70-120	+	Muscle spindle primary endings
Ib	12-20	—	70-120	+	Golgi tendon organs
—	12-20	A-α	70-120	+	Muscle efferents (extrafusal)
II	6-12+	A-β	30-70	+	Encapsulated endings (Meissner, Ruffini, Pacinian); Merkel intraepithelial; muscle spindle secondary endings
—	2-10	A-γ	10-50	+	Muscle efferents (intrafusal)
III	1-6	A-δ	5-30	+	A-δ specific nociceptors; A-δ polymodal receptors; cold receptors; most hair receptors; some visceral receptors
—	<3	B	3-15	+	Preganglionic autonomic
IV	<1.5	C	0.5-2.0	No	C-nociceptors; C-polymodal receptors; some visceral receptors; warmth receptors; some mechanoreceptors; postganglionic autonomic; enteric nerve fibers

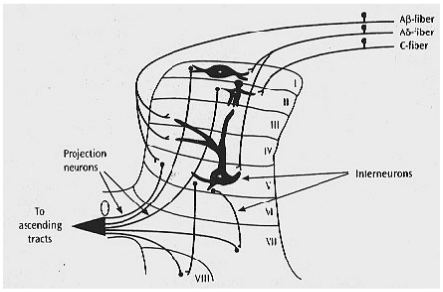
Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

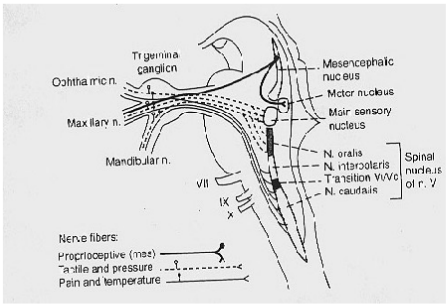
Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

Neuroanatomy of the Dorsal Horn



Bonica, 2001

Neuroanatomy of the Trigeminal System



Bonica, 2001

Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

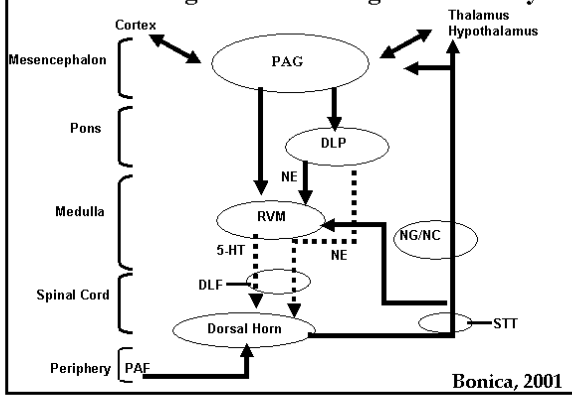
Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

The Ascending and Descending Pain Pathways



Bonica, 2001

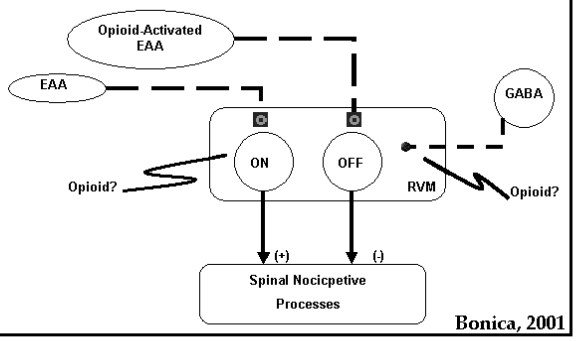
Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

Rostroventral Medulla

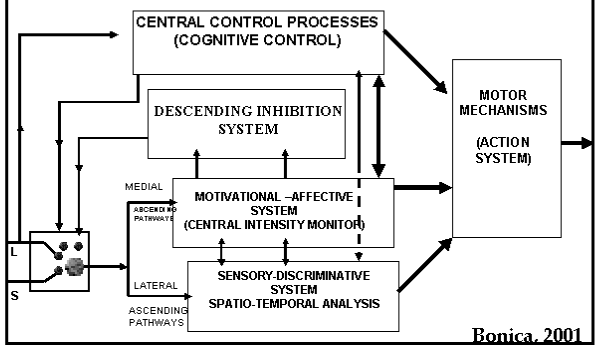


Bonica, 2001

Supraspinal Targets of Nociception

Functional Correlation	Cortical Area	Possible Functions
Pain intensity	Primary somatosensory cortex Secondary somatosensory cortex	Sensory discrimination, stimulus localization, sensory integration, (touch, pain, visual) spatially directed attention, visceral sensory, visceral motor, limbic integration
Temperature sensation	Insula	
Pain threshold	Right frontal inferior cortex Left thalamus Right	Response selection, motor suppression, attention, affect
Pain unpleasantness	Left Anterior cingulate cortex	
Pain intensity	Right posterior cingulate cortex Brainstem/peri-ventricular gray Prefrontal cortex	Affect, memory

Sensory, Motivational, and Cognitive Pain Modulation



Bonica, 2001

Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

Cognitive Factors Influencing Pain

attention
imagery
expectancy
memory
meaning

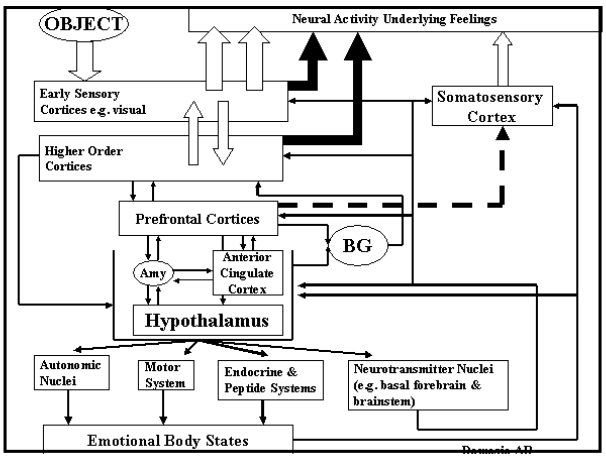
PERCEPTION

Pain

THINKING

planning and forecasting
decision making & classification
mental computation
language and self-talk
knowledge building

Bonica, 2001



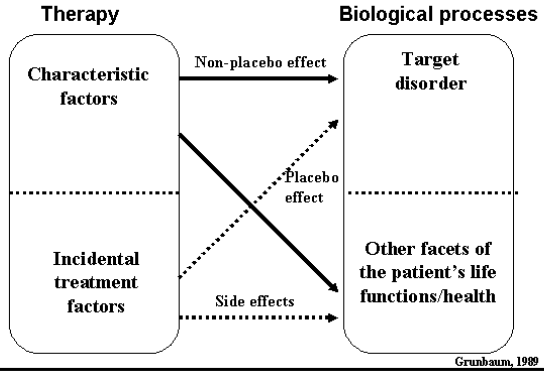
Course Outline

Introduction to Pain Processing
Pain in the Aged
Language of pain
Peripheral pain mechanisms
- Transduction
- Transmission
- Modulation
- Perception

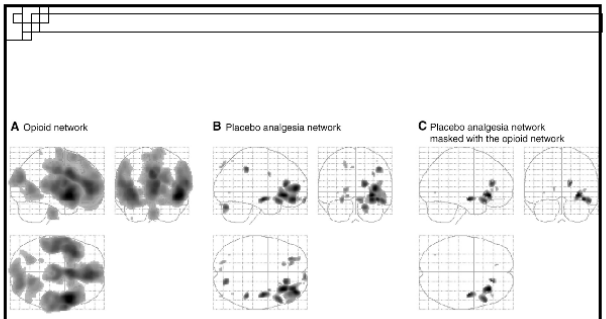
Spinal pain mechanisms
- Dorsal horn

Ascending system
Descending system
Supraspinal pain processing
Psychological aspects of pain
Placebo effects
Pain neuroplasticity in the CNS

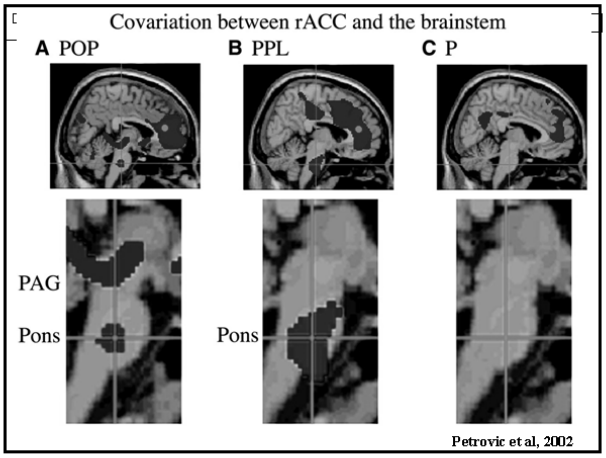
Placebo Effects



Grunbaum, 1989



Petrovic, P. et al,



Petrovic et al, 2002

Course Outline

- Introduction to Pain Processing
- Pain in the Aged
- Language of pain
- Peripheral pain mechanisms
  - Transduction
  - Transmission
  - Modulation
  - Perception
- Spinal pain mechanisms
  - Dorsal horn
- Ascending system
- Descending system
- Supraspinal pain processing
- Psychological aspects of pain
- Placebo effects
- Pain Neuroplasticity in the CNS

Immunology Cognitive Changes Autonomic Nervous System

Functional Structural

Supraspinal

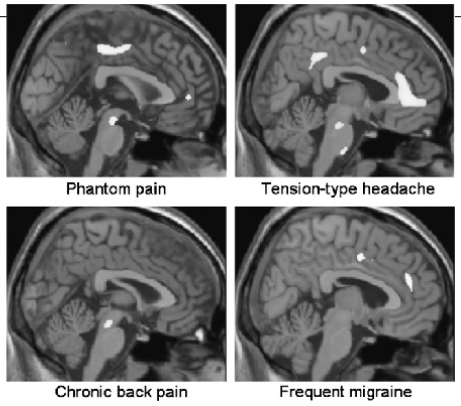
Modulation and modification of nociceptive and antinociceptive synaptic transmission

Spinal

Peripheral

Peripheral sensitization, denervation, ectopic activity

May, 2008



May et al, 2008

Chronification of Pain

Acute pain (transient)	→	Chronic pain (spontaneous)
Bio	→	Psychosocial
Peripheral	→	Central sensitization
Objective findings	→	Subjective reports
Structural injury	→	Functional syndrome
Components	→	Inter-relationships (systems biology)

Neural Correlates of Chronic Pain

- **Spontaneous pain intensity is encoded in cortical and subcortical sites:**

hedonic and emotional learning
(medial PFC, rACC, orbitofrontal cortex)

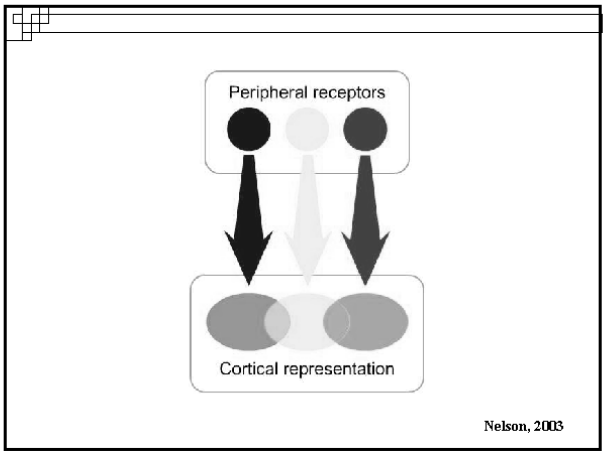
reward and goal direction
(striatum)

fear behavior
(amygdala)

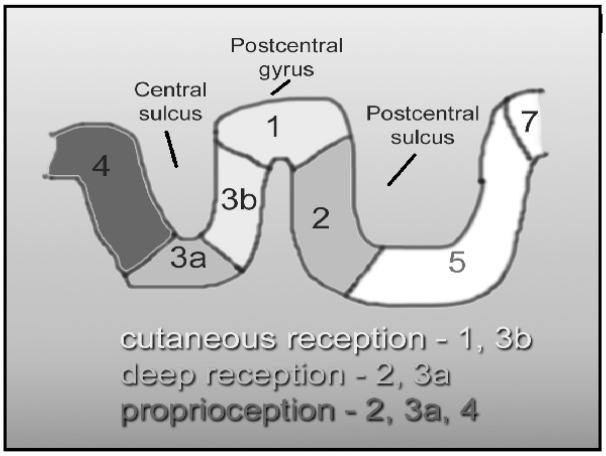
Apkarian, 2008

Pain Management Using CNS Neuroplastic Reorganization

Propriospinal	Sensory Discrimination	Counter Stimulation	Electromagnetic Stimulation	Cognitive Therapy

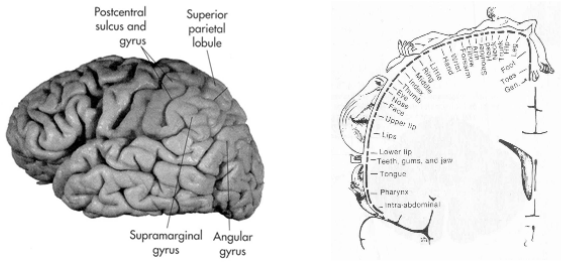


Nelson, 2003



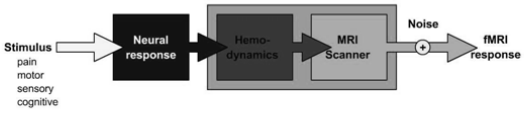
Digital Mapping – S1 Somatotopy

- The somatotopic digit homuncular organization in the human primary somatosensory cortex (S1) was originally mapped by Penfield in 1937.

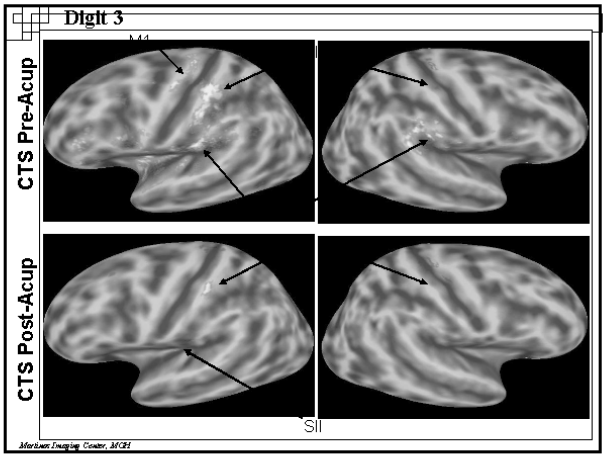


Martinos Imaging Center, MGH

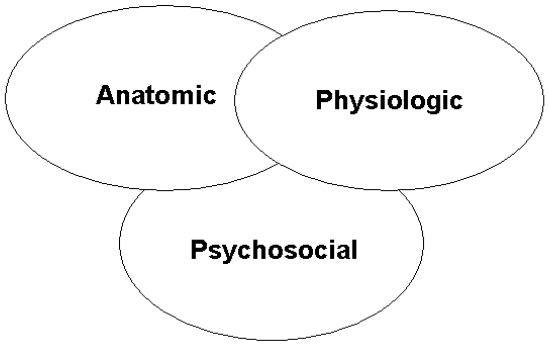
What is fMRI?

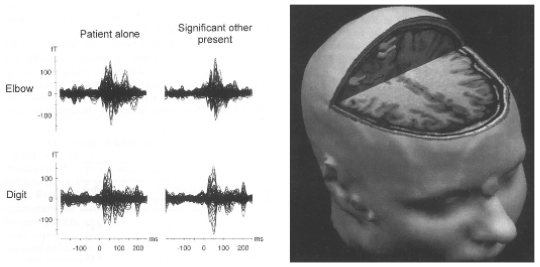


Huettel, 2004



Martinos Imaging Center, MGH





Montoya et al, 2004

Neuromechanisms of Pain Empathy

NOCICEPTIVE INPUTS ⟷ COGNITIVE RESONANCE

Neuromechanisms of Pain Empathy

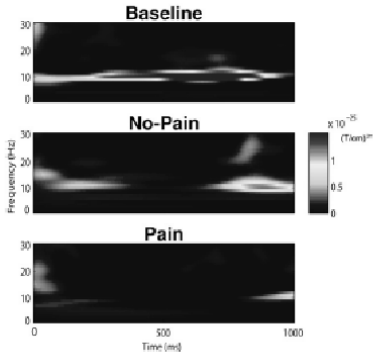
- The emotional and cognitive resources necessary for empathy are linked to pain processing networks and likely the mirror-neuron system (neurons activated by the action of self or others).
- Even the observation of analgesia in others can produce a learned placebo analgesia. (Colloca and Benedetti 2009).

Neuromechanisms of Pain Empathy

- The perception of pain occurring in others requires the formation of a representative image of pain in oneself. The neural systems recruited in observing pain overlap with systems generating the personal experience of pain (empathy).

Neuroimaging of Pain Empathy

- Neuroimaging of pain empathy assesses cognitive, emotive and behavioral responses to observed pain. MEG 10 Hz concentrates over central sulcus (S1) and will decrease while watching pain pictures (Cheng et al, 2007).



Cheng et al, 2008

Course Outline

- Introduction to Pain Processing
- Pain in the Aged
- Language of pain
- Peripheral pain mechanisms
  - Transduction
  - Transmission
  - Modulation
  - Perception
- Spinal pain mechanisms
  - Dorsal horn
- Ascending system
- Descending system
- Supraspinal pain processing
- Psychological aspects of pain
- Placebo effects
- Pain neuroplasticity in the CNS

Collaborators

Athinoula A. Martinos Center for Biomedical Imaging (MGH/HMS/MIT)

B. Rosen	K. Hui
N. Makris	K. Kwong
V. Napadow	J. Liang
P. Dhond	M. Li

Spaulding
A. Ryan
J. Audette

MIT
C. Moore
A. Nelson

Biopsychosocial Models of Pain

Rodger Tepe, PhD

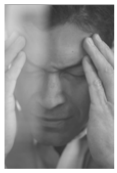
LOGAN
UNIVERSITY PROGRAMS
COLLEGE OF CHIROPRACTIC

Biopsychosocial Models of Pain

"It's just a sprain. But let me put a cast on it so you won't look like an idiot for screaming like a freakin' schoolgirl."

Rodger Tepe, PhD
Dean of Research and Development
Logan College of Chiropractic

Overview



- Pain Epidemiology and Costs
- What is Pain?
- Primitive Pain Model
- Gate Control Theory
- Neuroplasticity
- Central Sensitization
- Biopsychosocial Model
- Geriatric Pain

Chronic Pain Quick Facts

- Estimated incidence of pain: 76.2 million people in the U.S.

National Center for Health Statistics. Health, United States, 2006 With Chartbook on Trends in the Health of Americans. Hyattsville, MD: 68-71.

- The annual cost of chronic pain in the U.S. including healthcare expenses, lost income, and lost productivity, is estimated to be $100 billion.

National Institutes of Health. NIH Guide: New Directions in Pain Research I. September 4, 1998.

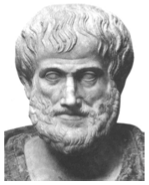
Learning Objective

- Formulate a working definition of pain.

What is Pain?

What is Pain?

"We cannot learn without pain." -Aristotle



"Before we make love my husband takes a pain killer." - Joan Rivers

Pain Definition

- *Pain is whatever the experiencing person says it is, existing whenever he says it does*. - Margo McCaffery, RN

Pain Definition

- Pain: An uncomfortable frame of mind that may have a physical basis in something that is being done to the body, or may be purely mental, caused by the good fortune of another. - Devil's Dictionary Published 1906 by Ambrose Bierce

Pain Definition

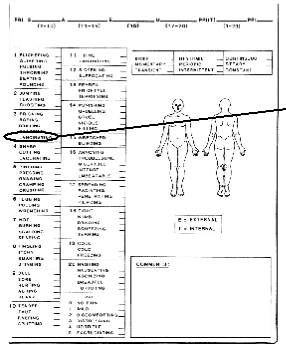
World Health Organization

- *An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage* - World Health Organization

What is Pain?

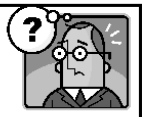
Allodynia
Central Pain
Causalgia
Neurogenic Pain
Anesthesia Dolorosa
Hypoalgesia
Hyperesthesia
Anesthesia Dolorosa
Hyperpathia
Neuropathic Pain
Hyperalgesia
Analgesia
Hypoesthesia
Dysesthesia
Peripheral Neuropathic Pain
Neuralgia
Neuropathy
Peripheral Neurogenic Pain
Neuritis
Nociceptor
Pain Tolerance Level
Noxious Stimulus
Pain Threshold
Paresthesia

McGill Pain Questionnaire



Lancinating???

Section Question



- Which of the following describes the modern WHO definition of pain?

A. The good fortune of another

B. An unpleasant sensory and emotional experience

C. An automatic response to external stimuli

D. Joan Rivers in a bikini

Take Home Message

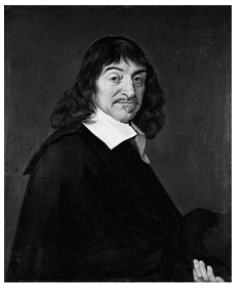
- Pain is complex and multifactorial (more to come later!)

Learning Objective

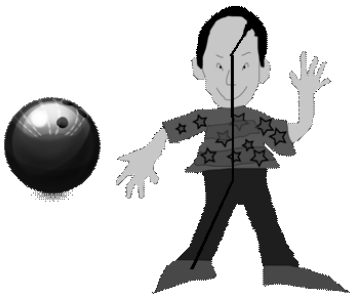
- Understand how Gate Control Theory differs from previous models of pain.

Primitive Pain Models

- Pain is a direct response to a stimulus, a one-way "alarm system" (René Descartes).



Primitive Pain Models



Gate Control Theory

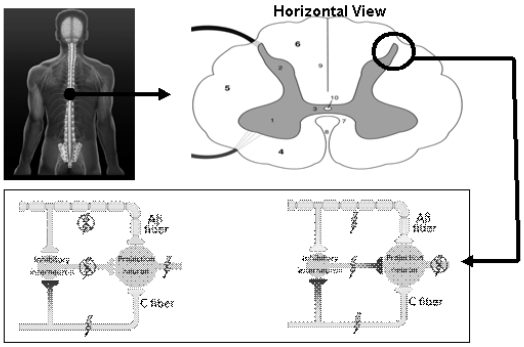
- Ronald Melzack and Patrick David Wall – 1962
- Activation of nerves which **do not** transmit pain signals, can interfere with signals from pain fibers, thereby **inhibiting pain**.

Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965; 150(699): 971-9.

Gate Control Theory

- Stimulation of Aβ (mechanoreception) pathways can "block out" C (chronic nociceptive) pain.
- Aβ stimulation
  - GABA release – inhibits C fiber conduction
  - Excites brain areas which send out descending fibers that secrete GABA at the cord level (Descending Inhibition)

Gate Control Theory
Dorsal Horn of the Spinal Cord



Gate Control Theory

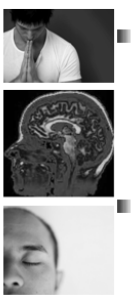
- *"The theory forced the medical and biological sciences to accept the brain as an active system that filters, selects and modulates inputs.*
- *The dorsal horns, too, were not merely passive transmission stations but sites at which dynamic activities* (inhibition, excitation and modulation) *occurred."*
  - Ronald Melzack

Support For Gate Control Theory
Dorsal Horn Stimulation

- Dorsal horn nociceptive signaling decreases during TENS application.
- These findings are consistent with the gate control theory – mechanoreception blocks C nociception.

Garrison DW, Foreman RD. Effects of prolonged transcutaneous electrical nerve stimulation (TENS) and variation of stimulation variables on dorsal horn cell activity in cats. *Eur J Phys Med Rehab*, 1996; 6: 87-94.

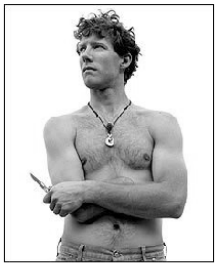
Support For Gate Control Theory
Descending Inhibition



- A meta-analytic study examining the analgesic effect of hypnosis for pain reduction found that hypnoanalgesia offered considerable non-endorphin mediated pain relief for 75% of the populations included in the analysis.
- Hypnosis may activate descending pathways that inhibit c pain fibers.

Montgomery, GH, DuHamel, KM, Redd, WH. A meta-analysis of hypnotically induced analgesia: How effective is hypnosis? *International Journal of Clinical and Experimental Hypnosis*, 2000 48, 138–153.

Descending Inhibitory Pathway



- "Pain was just one more thing I had to do, and it was, in some sense, a very beautiful feeling, too. … It was liberation."

-Aron Ralston

Gate Control Theory: Clinical Applications

Deep Tissue Massage

TENS

Spinal Manipulation

Spinal Cord Stimulation

Therapeutic Exercise

Hypnotically Induced Analgesia

Section Question

- Gate Control Theory explains:

A. Pain is the result of tissue damage

B. Pain signals originate in the brain

C. Pain signals can be inhibited in the CNS

D. The CNS is constantly remodeling

Take Home Messages

- Gate Control Theory - pain perception is not simply automatic neural transmission.
- Pain signals are modulated by the brain and in the dorsal horns of the spinal cord.

Learning Objective

- Understand the relationship between neuroplasticity and pain perception.

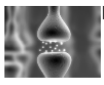
Neuroplasticity

- Changes that occur in the organization of the central nervous system as a result of experience.

"I never heard of anyone pulling a muscle while thinking."

DeFelipe J. Brain plasticity and mental processes: Cajal again. *Nat Rev Neurosci.* 2006; 7(10):811-7.

Neuroplasticity and Pain



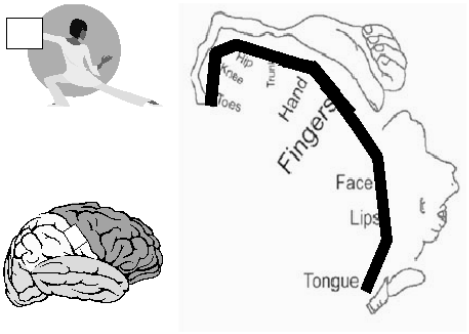
- Ongoing pain is associated with widespread neuroplastic changes at multiple levels within the nervous system.

Boal RW, Gillette RG. Central neuronal plasticity, low back pain and spinal manipulative therapy. *J Manipulative Physiol Ther* 2004;27(5):314–26.

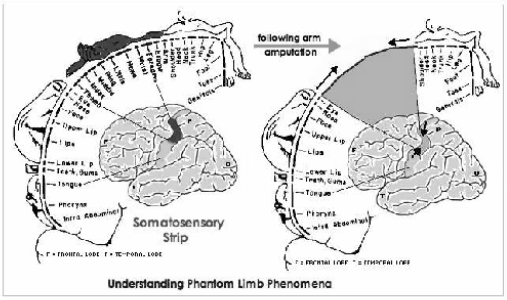
- Functional reorganization of somatosensory cortex has been documented in chronic pain.

Flor H. Cortical reorganization and chronic pain implications for rehabilitation. *J Rehabil Med* 2003 (Suppl. 41): 66–72.

Phantom Limb Pain: Classic Neuroplasticity



Phantom Limb Pain: Classic Neuroplasticity



Section Question:

- Which is an example of neuroplasticity?

A. A man regains the ability to move in his arm after a stroke.

B. Rubbing an achy muscle offers some relief.

C. When playing golf for the first time, Michael Jordan shot par.

D. When taking a test, a student uses an earlier question to help formulate the correct answer.

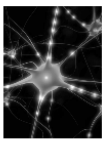
Take Home Messages

- Neuroplasticity - the nervous system has the ability to change based various stimuli.
- Pain has been shown to induce neuroplastic changes which modifies subsequent pain perception.

Learning Objective

- To understand how central sensitization involves both Gate Control Theory and neuroplasticity.

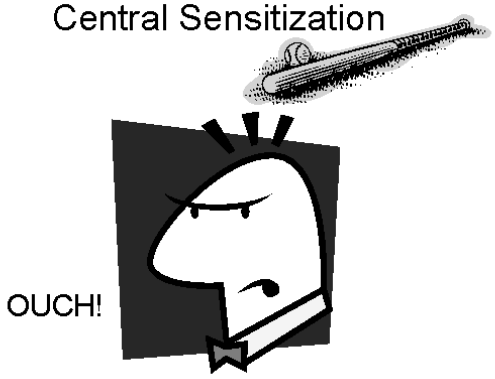
Central Sensitization: An Example of Neuoplasticity



"when peripheral sensory neuron activity drives central spinal systems that amplify and prolong the incoming sensory messages. Consequently, this is a mechanism whereby the final sensation of pain becomes dissociated from peripheral activity"

Dickenson AH. Gate control theory of pain stands the test of time. *Br J Anaesth* 2002;88(6):755-7.

Central Sensitization

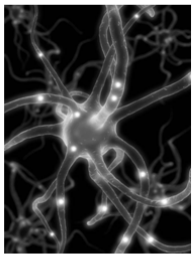


Allodynia - Central Sensitization

- Pain from a non-painful stimulus.
- How does this happen?
- Through neuroplastic changes, the CNS has become sensitized.

Central Sensitization: Modern Gate Control Theory

- In many ways, central sensitization, a CNS process by which injury signals induce an amplified nociceptive message
- Is the modern version of Gate Control Theory.



Basbaum, A. Gate control theory: Is it relevant to pain management in the 21st century? *Pain Practice,* 2007; 7 Supplement 1:3.

The Gate Held Open: Chronic Pain

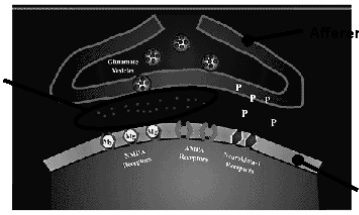
- Chronic/persistent pain is not long lasting acute pain.
- Chronic pain depends on the generation of an altered dorsal horn, one that amplifies and prolongs "pain" signals, one that can alter the perception of non-noxious as well as noxious stimuli.

Basbaum, A. Gate control theory: Is it relevant to pain management in the 21st century? Pain Practice, 2007; 7 Supplement 1:3.

Mechanisms of Central Sensitization:

Dorsal Horn of the Spinal Cord

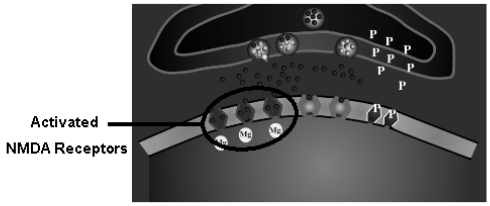
- After injury, release of glutamate (the major transmitter in afferent A- and C-fibers) increases.



Dickenson AH. Gate control theory of pain stands the test of time. *Br J Anaesth* 2002; 88(6): 755-7.

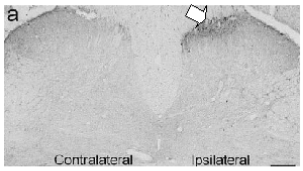
Mechanisms: Central Sensitization

- Increased glutamate then leads to enhanced activation of the receptors for glutamate, especially the N-methyl-D-aspartate (NMDA) receptor implicated in central sensitization.



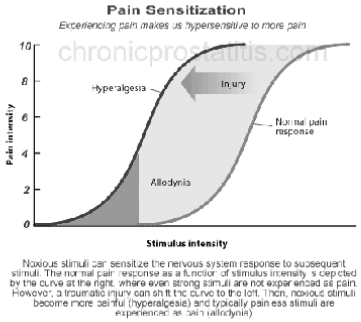
Central Sensitization

- Prolonged unilateral injection of capsaicin (burning agent) into a rat's hindpaw induces ERK phosphorylation in L5 dorsal horn.
- ERK activated by NMDA receptor stimulation.



Ji RR, Woolf CJ. Neuronal plasticity and signal transduction in nociceptive neurons: implications for the initiation and maintenance of pathological pain. *Neurobiol Dis* 2001;8(1):1–10.

Central Sensitization



Noxious stimuli can sensitize the nervous system response to subsequent stimuli. The normal pain response as a function of stimulus intensity is depicted by the curve at the right, where even strong stimuli are not experienced as pain. However, a traumatic injury can shift the curve to the left. Then, noxious stimuli become more painful (hyperalgesia) and typically pain-less stimuli are experienced as pain (allodynia).

Central Sensitization May Explain:

- Pain can be experienced after its original "cause" no longer exists - Although a herniated disc may be removed from a pinched nerve, pain may continue as a memory of the nerve compression.

Goulet JA, Senunas LE, DeSilva GL, Greenfield ML: Autogenous iliac crest bone graft: complications and functional assessment. *Clin Orthop* 1997, 339:76–81.

- Persistent non-cardiac chest pain after a single episode of acid infusion into the lower esophagus.

Sarkar S, Aziz Q, Woolf CJ, Hobson AR, Thompson, TG. Contribution of central sensitisation to the development of noncardiac chest pain. The Lancet 2000; 356: 1127-1128.

Section Question:

- Central sensitization is:

A. best explained by Gate Control Theory

B. the same as neuroplasticity

C. the opposite of neuroplasticity

D. a type of neuroplasticity

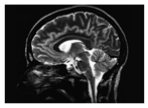
Take Home Messages

- Central sensitization involves changes in the CNS that amplify afferent signals.
- Pain stimuli can activate CNS pain receptors that remain active even after the source of affectation disappears. Consequently, pain becomes entirely central.

Take Home Messages

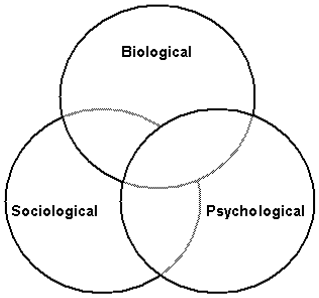
- Pain is modulated by the CNS. (Gate Control Theory)
- Experience changes nervous system organization. (Neuroplasticity)
- Prolonged stimulation can result in pain that that is entirely central. (Central Sensitization)
- Prolonged stimulation = CNS change = Chronic pain

Biopsychosocial Model



- Chronic pain changes CNS so…
- Reciprocal, cybernetic need something visual that shows the feedback loops
- How does the CNS affect pain?

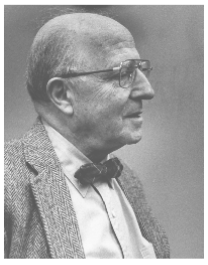
Biopsychosocial Model: A More Complete Understanding



Learning Objective:

- Understand the three main aspects of the biopsychosocial model and the differences between disease and illness.

Biopsychosocial



- George Engel (1977) new system that questioned the dualistic approach: mind and body function separately.

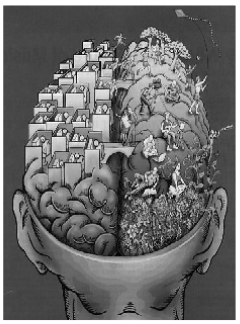
Engel, GL. The need for a new medical model. *Science*; 196:129–136, 1977.

Biopsychosocial

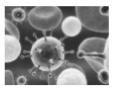
- Pain is the result of three distinct factors:

1. Biological
2. Psychological
3. Social

The model also differentiates disease from illness.



Biopsychosocial



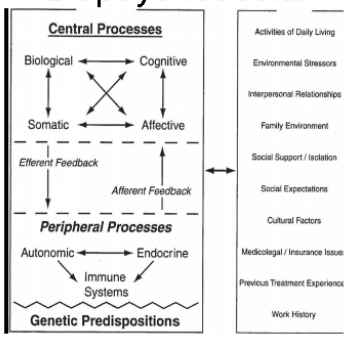
- Disease: a biological event that results in the disruption of a specific structure or organ system of the body due to anatomical, pathological or physiological insult.

Gratchel, RJ. Comorbidity of chronic pain and mental Health disorders: The biopsychosocial perspective. *American Psychologist*; 58:795–805, 2004.

Biopsychosocial

- Illness: the individual subjective experience of how the individual and their family/social context respond to the symptoms or their disability.

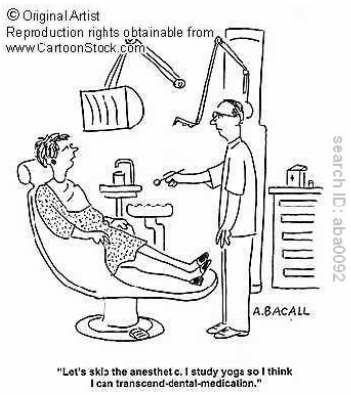
Biopsychosocial



RJ Gatchel, YB Peng, ML Peters, PN Fuchs, DC Turk. The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological Bulletin*, 2007 133(4) 581–624.

Biopsychosocial Model: Example

- Joe experiences acute low back pain that would typically resolve in 3 weeks but the next day…
- He goes on a diet of Mountain Dew and cheese puffs (Bio).
- He gets fired (Social) and his wife leaves him (Psycho).
- Acute low back pain evolves into chronic, centrally sensitized pain syndrome over time.



Section Question:

- The biopsychosocial model is best described as:

A. Reductionistic

B. Dualistic

C. Cybernetic

D. Mechanistic

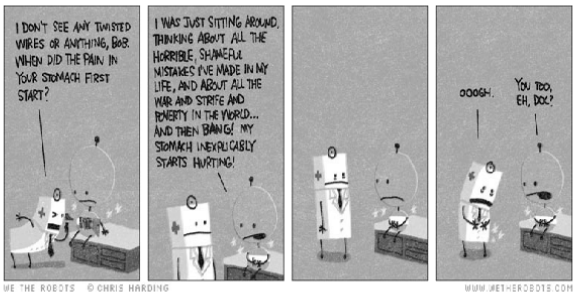
Take Home Message:

- Pre Gate Theory models of pain are linear, considering pain to be only the result of tissue damage.
- The biopsychosocial model is cybernetic, taking into account the interaction between numerous factors that contribute to pain.

Learning Objective:

- Understand how the biopsychosocial model explains pain.

Biopsychosocial

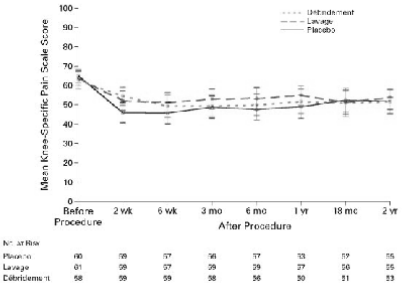


Biopsychosocial

- Methods: 180 patients with knee osteoarthritis were randomly assigned to receive:
  1. Arthroscopic débridement
  2. Arthroscopic lavage
  3. Placebo surgery (skin incisions and simulated débridement without insertion of the arthroscope.)
- Results: The intervention and placebo groups reported similar pain and function.

Moseley JB, Malley MO, Petersen NJ, Menke. Controlled Trial of Arthroscopic Surgery for Osteoarthritis of the Knee. *New England Journal of Medicine*, 2002, 347:81-88.

Biopsychosocial



Moseley JB, Malley MO, Petersen NJ, Menke. Controlled Trial of Arthroscopic Surgery for Osteoarthritis of the Knee. *New England Journal of Medicine*, 2002, 347:81-88.

Biopsychosocial

- Certain cognitive styles and personality traits have been associated with amplification and extension of pain experience in the absence of tissue damage.

Meeus, M. & Nijs, J. Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. *Clin Rheumatol* 2007; 26:465–473.

Biopsychosocial

- Adults being treated for leg wounds

- Delayed wound healing was 4 times more common in patients who scored in the upper 50% of the Hospital Anxiety and depression Scale as in patients who scored in the lower 50%.

Cole-King A, Harding KG, Psychological factors and delayed healing in chronic wounds. Psychosomatic medicine, 2001; 63:216-220

Biopsychosocial




- In patients with acute or subacute low back pain, measures of emotional distress are associated with the future development of chronic pain and disability. Catastrophizing, fear-avoidance beliefs and low self-efficacy are predictors of chronicity.

Hurwitz EL, Morgenstern H, Yu F. Cross-sectional and longitudinal associations of low-back pain and related disability with psychological distress among patients enrolled in the UCLA Low-Back Pain Study. J Clin Epidemiol 2003;56(5):463–71.
Dionne CE. Psychological distress confirmed as predictor of long-term back-related functional limitations in primary care settings. J Clin Epidemiol 2005;58(7):714–8.
Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. Spine 2002;27(5):E109–20.

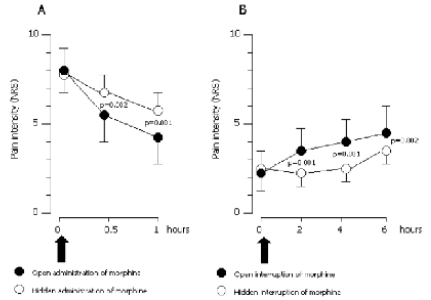
Biopsychosocial: Fear Avoidance



- After an episode of acute low back pain, patients often remain sedentary because of fear that movement will cause pain.
- Such behavior is particularly detrimental since decreased recreational activity leads to deconditioning, which further impacts emotional and physical well being.

Hurwitz EL, Morgenstern H, Chiao C. Effects of recreational physical activity and back exercises on low back pain and psychological distress: findings from the UCLA Low Back Pain Study. *Am J Public Health* 2005;95(10):1817–24.
Grotle M, Vollestad NK, Veierod MB, Brox JI. Fear-avoidance beliefs and distress in relation to disability in acute and chronic low back pain. *Pain* 2004;112(3):343–52.

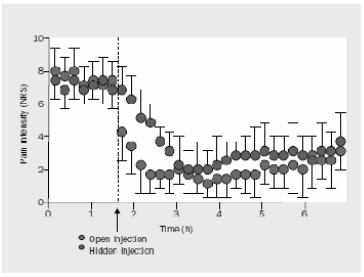
Biopsychosocial



Benedetti F, Maggi G, Lopiano L, et al. Open versus hidden medical treatments: the patient's knowledge about a therapy affects the therapy outcome. *Prevention & Treatment* 2003:6.

Biopsychosocial

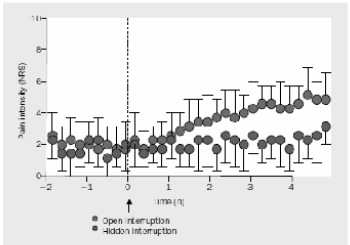
- Open vs. hidden administration of morphine treatment for postoperative pain.
- Broken line indicates time of injection.
- Open group knew when they received their morphine.
- Hidden group did not know when morphine was given.



Benedetti F, Maggi G, Lopiano L, et al. Open versus hidden medical treatments: the patient's knowledge about a therapy affects the therapy outcome. *Prevention & Treatment* 2003:6.

Biopsychosocial

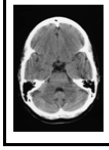
- Open versus hidden interruption of a morphine treatment.
- Broken line shows the time of morphine interruption.
- Note the early relapse of pain in the open group but not in the hidden one.



Benedetti F, Maggi G, Lopiano L, et al. Open versus hidden medical treatments: the patient's knowledge about a therapy affects the therapy outcome. *Prevention & Treatment* 2003:6.

Biopsychosocial





- Design: An 8-week mindfulness meditation program for older adults with CLBP.
- Results: Three-month follow-up suggested sustained benefit from the program as measured by continued meditation by program participants and sustained improvement in physical function and pain acceptance.
- Conclusion: Mind–body therapies such as the MBSR program are a promising non-pharmacologic adjunct to current pain treatment for older adults.

Morone NE, Greco CM, Weiner DK. Mindfulness meditation for the treatment of chronic low backpain in older adults: A randomized controlled pilot study. *Pain* 2008; 134 (3), 310-319.

Biopsychosocial

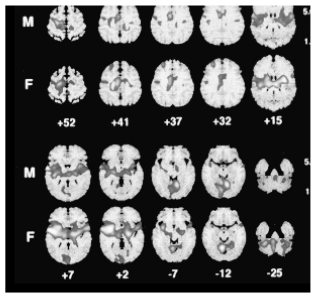
- Increased likelihood of pain reporting:
- Lower levels of education
- Lower income
- Being unemployed

R.S. Roth, M.R. Punch and J.E. Bachman, Educational achievement and pain disability among women with chronic pelvic pain, *J Psychosom Res* 51 (2001), pp. 563–569.

R.K. Portenoy, C. Ugarte, I. Fuller and G. Haas, Population-based survey of pain in the United States: differences among white, African–American, and Hispanic subjects, *J Pain* 5 (2004), pp. 317–328.

Biopsychosocial

- Male (M) and Female (F) responses to repetitive noxious heat stimulation.
- Females reported more intense stimulation than males.
- Female subjects had greater stimulation of thalamus and anterior insula.



Paulson PE, Minoshima S, Marrow TJ, Casey KLGender, Differences in pain perception and patterns of cerebral activation during noxious heat stimulation in humans, *Pain*, 1998; 76 p. 227.

Section Question:

- According to the biopsychosocial model, who is most likely to experience chronic pain?

A. A high school football player with a fractured clavicle

B. An infant with torticollis

C. A woman who drives race cars in her spare time

(D) A man who recently lost his job and spouse but has no observable pathology

Take Home Message

- When treating a chronic pain patient treatment protocols should address all factors that contribute to pain: biological, psychological and social. The bio-psycho-social model argues for inter-disciplinary treatment. Age, gender, mood, attitude, health knowledge, nutrition, exercise, personality, stress, culture, social context, support resources, and financial resources all contribute to the experience of pain.

Learning Objectives:

- Recognize the subfield of geriatric pain.
- Understand biopsychosocial models' specific implications for the geriatric population.

Geriatric Pain

Pain Differences in Older Individuals

- Emergence of a subfield: Pain and Aging
- From 1987-2007:
  - Pain publications increased 3.5xs
  - Pain and aging publications increased 6xs

Gaglise L. Pain and Aging: The Emergence of New Subfield of Pain Research. *J* of *Pain* 2009; 10(4):343-353.

Geriatric Pain
Pain Differences in Older Individuals

- Older individuals have an increased vulnerability to prolonged sensitization after injury.

Gaglise L. Pain and Aging: The Emergence of New Subfield of Pain Research. *J* of *Pain* 2009; 10(4):343-353.

Geriatric Pain
Pain Measures

- Visual Analog Scale problematic for:
  - Increased age
  - Psychomotor dysfunction
  - cognitively impaired
- Consider:
  - McGill Pain Questionnaire
  - Numeric Rating Scale
  - Verbal Descriptor Scale

Gaglise L. Pain and Aging: The Emergence of New Subfield of Pain Research. *J* of *Pain* 2009; 10(4):343-353.

Biopsychosocial: Geriatric Considerations
Support for the Model among Geriatrics

- Pain reporting in older adults is widely variable for similar conditions.
- E.g. some individuals with advanced disease reported severe pain while others reported no pain.

Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: Relationship to age, gender, and performance status in 1,000 patients. *Supportive Care Cancer* 2000; 8: 175-179.

Biopsychosocial: Geriatric Considerations

- Geriatric biopsychosocial pain factors:
  - Comorbidities
  - Widowhood
  - Cognitive Function
  - Drug Reactions

Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: Clinical, research, and policy implications of a core geriatric concept. J *Am Geriatr Soc* 2007; 55:780-791, 2007

Geriatric Considerations

- Minimize the expression of pain.
- Pain is sometimes ignored in elderly.

Stein et al. Cancer pain in the elderly hospice patient. *J Pain Symptom Manage* 1993; 8: 474-482.

Section Question:

- Which is correct?

A. Depression and pain are unrelated in the elderly

B. Pain at 13 years old is the same as pain at 70 years old

C. Older individuals are more likely to experience chronic pain

D. The biopsychosocial model is more applicable for the elderly than for younger individuals

Summary

- Pain is complex and multifactorial.
- Pain is modulated by the CNS.
  (Gate Control Theory)
- Experiences change nervous system organization.
  (Neuroplasticity)
- Prolonged stimulation can result in pain that that is entirely central.
  (Central Sensitization)
- Prolonged stimulation = CNS change = Chronic pain

Summary

- The biopsychosocial model takes into account the numerous factors that contribute to pain and the interaction between these factors.
- When treating a chronic pain patient treatment protocols should address the many factors that contribute to pain.
- Geriatrics may experience pain differently than younger people and they are more likely to develop chronic pain.

Resources

- American Pain Foundation: http://www.painfoundation.org/
- American Pain Society: http://www.ampainsoc.org/
- Central Sensitization Video: www.bayareapainmedical.com/wGABA.html
- The International Association for the Study of Pain: http://www.iasp-pain.org
- NIH Pain Consortium: http://painconsortium.nih.gov/

Neuroimaging of CAM Techniques

Vitaly Napadow, PhD

Neuroimaging of CAM Techniques

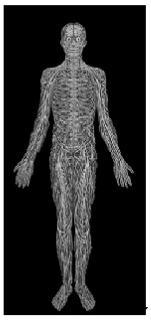
Vitaly Napadow, Ph.D. LicAc
Martinos Center for Biomedical Imaging, Dept Radiology, MGH,
Harvard Medical School, Boston, MA
Dept. Radiology, Logan College of Chiropractic, Chesterfield, MO

Overview

- Neuroimaging technologies and common CAM brain networks
- Placebos and endogenous modulation of pain
- Meditation / Hypnosis
- Neurofeedback
- Acupuncture

Human Brain

hypothesis: brain response to CAM therapies is a common denominator amongst various disparate therapies

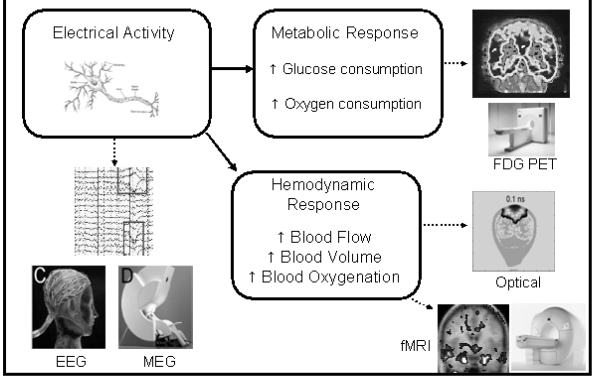


- 2% body weight
- 20% blood supply
- 20-30% body's energy consumption
- Most protected organ in the body:
  - skull
  - 3 membranes: dura, arachnoid, pia
  - cerebrospinal fluid (CSF)
  - blood-brain barrier: restricts passage of most substances to the brain

Must be important! – How Can We Study Brain Function?

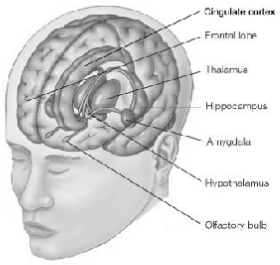
Functional Neuroimaging:

Hemodynamics, Metabolism, Electrophysiology, Neurochemistry



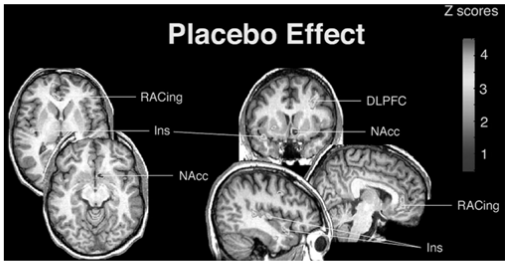
The Limbic System: A brain target for CAM modalities

- The limbic system brain regions are involved in regulation of autonomic, neuro-endocrine and sensorimotor systems, as well as the affective and cognitive aspects of pain.



PET Opioid Binding & Placebo Analgesia

- Placebo effects for analgesia have been attributed to several affective / cognitive brain regions: rACC, DLPFC, insula etc.

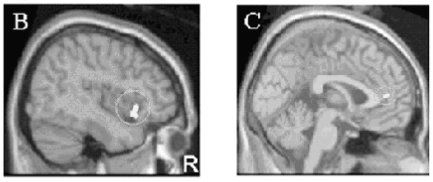


Zubieta et al. J Neurosci. 2005 25(34):7754-62.

fMRI & Placebo Analgesia with Streitberger Needle

• Pain processing post- versus pre- Streitberger Needle treatment.

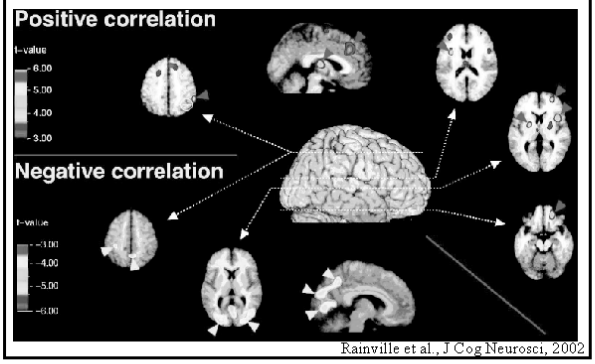
insula rACC



Kong et al. J Neurosci. 2006

PET imaging of brain correlates of hypnotic absorption

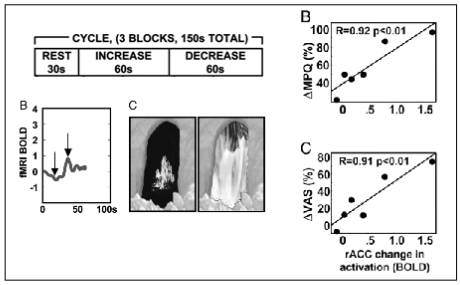
• Increasing absorption correlates with ACC, anterior insula, OFC



Rainville et al., J Cog Neurosci, 2002

ACC fMRI Biofeedback for Chronic Pain Analgesia

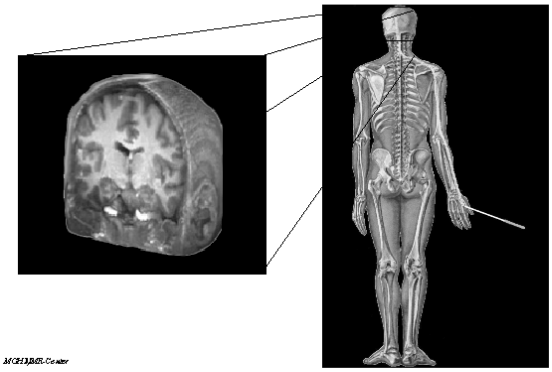
• Realtime fMRI focused on ACC used to reduce pain ratings in refractory chronic pain patients.



deCharms, PNAS. 2005 Dec 20;102(51):18626-31

Martinos Imaging Center, MGH

Acupuncture Neuroimaging



MGH/MGH-Center

Using fMRI neuroimaging to study the brain and potential Acupuncture mechanisms of action

Functional MRI (fMRI):
- non-invasive
- good spatial and temporal resolution for investigating brain activity

Siemens MRI Scanner

acupuncture applied with subject inside the MRI scanner

Martinos Center for Biomedical Imaging

Using fMRI to Study Acupuncture Effects on Brain Function



Response to Challenge → Acupuncture → Response to Challenge

pre-Acup — post-Acup

characterization studies

brain response *to* acupuncture stimuli

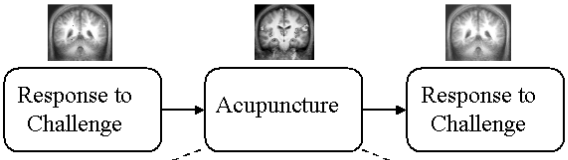
vs.

look at different:
- stimulation styles
- acupoints
- patient cohorts etc. etc.

innocuous — noxious

resting state — cognitive task — pain

Characterization of Brain Response to Acupuncture Stimuli using healthy subjects

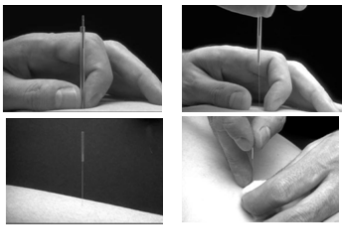


characterization studies
date back to the mid-1990's
at MGH and UC-Irvine

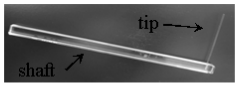
important to tease apart physiological response to distinct components of acupuncture thought to be clinically active

Acupuncture Methods for fMRI

- Verum ACUP: needle (pure silver or titanium, 0.20mm) twisting at 1Hz

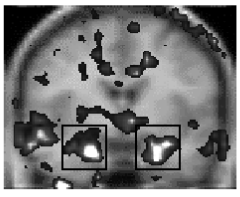


- **SHAM acupuncture:** fake insertion through guide-tube with 5.88 von Frey monofilament … then tapping stimulation at 1Hz

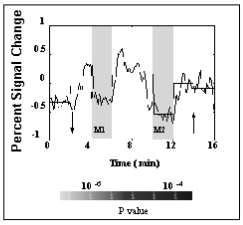


Acupuncture modulates the limbic system

(Characterization Studies: Block Design fMRI)



Amygdala



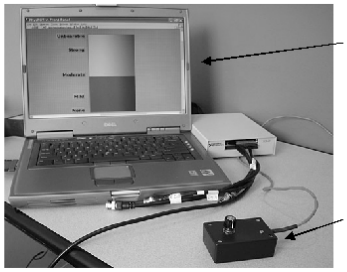
Hui et al. **HBM** 2000

Stimulus associated de-activation of limbic brain regions

Evaluate Brain Correlates of Acup Sensation

- Does needle stimulation = deqi sensation?
- If not, how would this affect results of fMRI analysis? Is this a source of variability in previous acupuncture fMRI studies?
- Acupuncture sensation has been linked to clinical efficacy in texts, studies, etc.

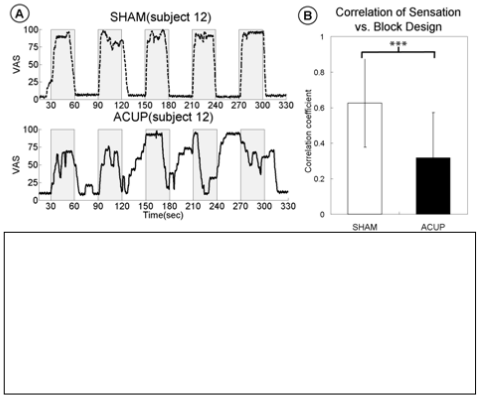
Percept-related fMRI: rating sensation on-line with fMRI



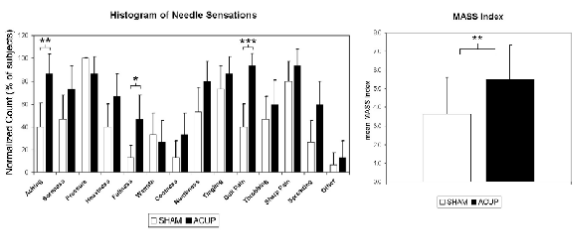
Visual rating projected to subject inside MRI scanner

Rating dial held in right (dominant) hand

Online Psychophysics



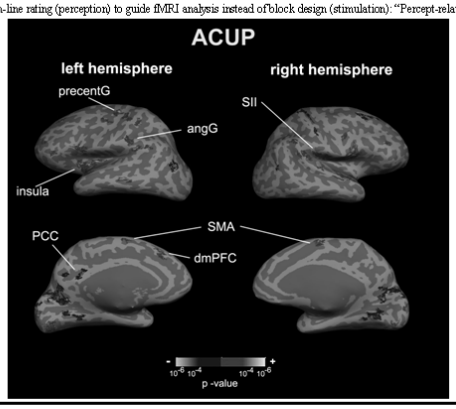
Psychophysics Results – MASS



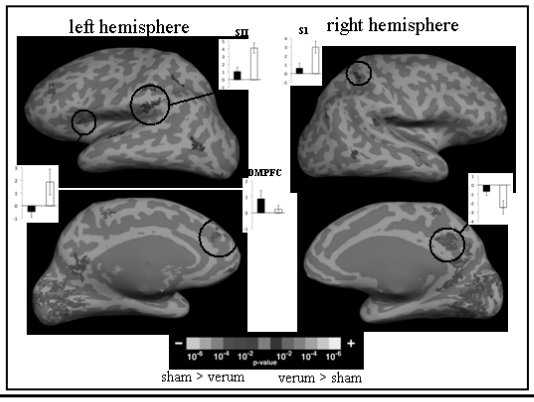
- Retrospective analysis demonstrated that ACUP induced stronger overall deqi sensation which more frequently included aching, fullness, and dull pain.

Percept-related fMRI Results

- Use on-line rating (perception) to guide fMRI analysis instead of block design (stimulation): "Percept-related fMRI"



Percept-related fMRI Difference Map: ACUP - SHAM

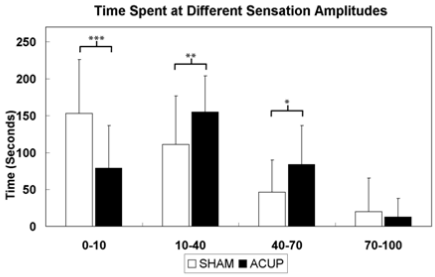


Summary of Percept-related fMRI: ACUP vs. SHAM

- SHAM produced greater activation in sensory-discriminative brain regions (SI, SII, insula)
- SHAM produced more robust deactivation than ACUP in Default Mode Network (vmPFC, PCC, precuneus, IPL) – a network of brain regions associated with internal mentation, and which is commonly deactivated with any externally focused task (visual, auditory, cognitive, somatosensory etc.).
- ACUP produced greater activation than SHAM in dmPFC (BA 9/10)
- Less differences in limbic regions between ACUP and SHAM compared to other acupoints (LI-4, ST-36). Perhaps due to:
  1. we used "percept-related fMRI"
  2. greater sensitivity of this location (note: perhaps for PC-6 our "SHAM" approximated *acupressure*?? at PC-6, cutaneous pressing is used to control motion sickness)?

Why did SHAM produce more robust SI/SII & DMN response?

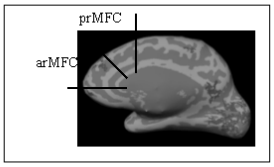
- Subjects experiencing ACUP spent more time rating low (10-40) and medium (40-70), and less time rating minimal/nil (0-10) sensations

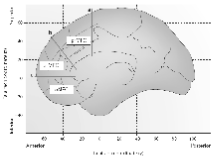


- Thus, SHAM was associated with more distinct transitions between existent and non-existent sensations → clear brain switching between task (SI/SII) and non-task (DMN) states

Why did ACUP produce more robust activity in dmPFC?

- ACUP was associated with less clear transitions between existent and non-existent sensations, and thus greater cognitive load
  - prMFC monitors sensation and evaluates possible behavior, arMFC is associated with emotional and interoceptive processing
  - ACUP sensation comes from deep receptors, is more ambiguous and more difficult to rate compared to SHAM (cutaneous receptors) → hence greater arMFC and prMFC activation than SHAM
  - ***The relative ambiguity and novelty for ACUP sensations may in fact be a salient feature of acupuncture***

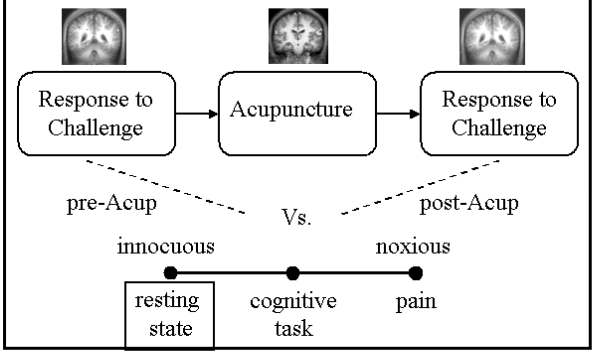




Amodio et al. 2006

Is Needle Sensation related to a Potential Acupuncture Mechanism of Action?

Part III: Effects of acupuncture on brain response to a challenge (pre-acup vs. post-acup)

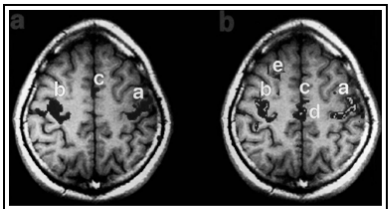


Motivation for the Study of Resting State Connectivity in Intrinsic Networks

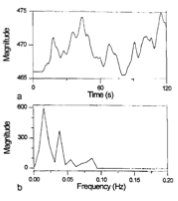
- The brain is 2% of our body weight but consumes 20% of body energy
- Task related increase in metabolism is small (<5%) when compared to this large resting (and much less studied) energy metabolism…
- fMRI fluctuations at rest are NOT random or chaotic, but instead correlate across distant brain regions.
- Resting State Network (RSN) analysis is a growing field of study in neuroimaging

Resting State: Sensorimotor Network (SMN)

- One of the first reports of connectivity in low frequency dominated resting state fMRI data - sensorimotor network
- Similar to brain activation attributed to a motor task using a block design protocol



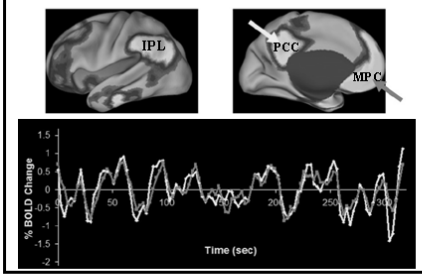
motor task resting state



Biswal et al., 1995

Default Mode Network and Resting BOLD Signal

- Anatomically defined brain regions which are more active at rest (internal focus) than during externally focused tasks (e.g. visual, motor, somatosensory, etc.)
- Includes inferior parietal lobule (IPL), posterior cingulate cortex / precuneus (PCC), medial prefrontal cortex (MPC)



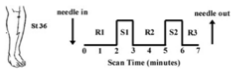
Shulman et al., 1997; Fox et al. 2005

Can RSN's be influenced by State? Evaluating the Effects of Acupuncture on Resting State Connectivity

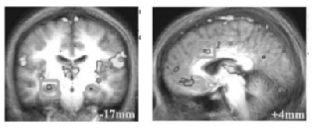
Dhond RP, Yeh C, Park K, Kettner N, Napadow V. Acupuncture Modulates Resting State Connectivity in Default and Sensorimotor Brain Networks. *Pain*. 2008, 136(3):407-18.

Neuroimaging Acupuncture Effects

- Event-related & Block Design paradigms can evaluate ***immediate*** brain response to acupuncture stimulation.



DMN ↓ SMN ↑

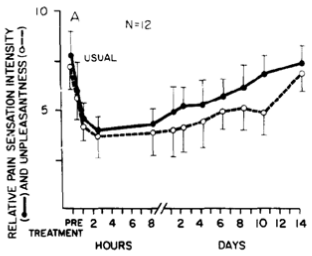


Napadow et al., 2005

- …in contrast
- RSN analysis can evaluate sustained effects of acupuncture ***after*** active stimulation.

Sustained Clinical Effects of Acupuncture

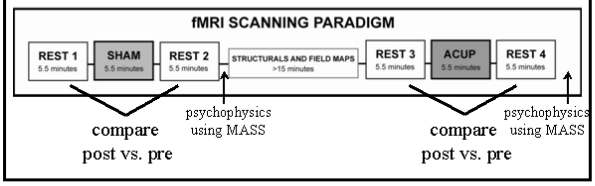
- Acupuncture analgesic effect (VAS of chronic low back pain) is maximal ***several hours*** to 2 days after treatment
- Experimental Question: What is the brain doing not ***during*** but ***after*** active acupuncture stimulation?



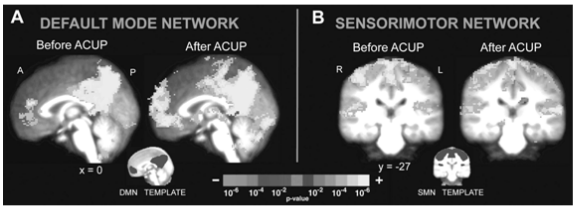
Price et al., 1984

Overview of Scanning Session

- N=15 healthy adult subjects
- Rest fMRI → cross hair (+) fixation for 5.5minutes
- Siemens Trio 3T, 12-channel coil
  - TR/TE = 3sec / 40msec, coronal slices, whole brain coverage (3.13 x 3.13 x 3.6mm)



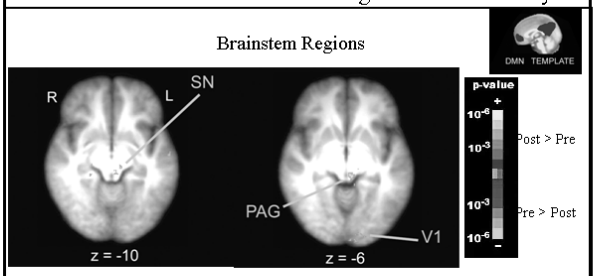
fMRI Results: Group Maps (n=15) for Resting DMN and SMN Connectivity



- Good match between group maps and template
- Can qualitatively see more extensive connectivity for DMN post- vs. pre-acupuncture.

ACUP Increases Extent of Resting DMN Connectivity

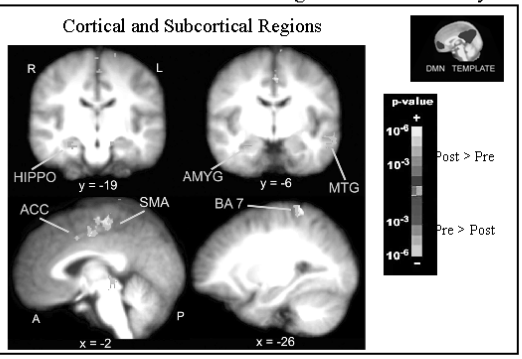
Brainstem Regions



- Increased DMN connectivity with pain and anti-nociceptive related brain regions post-ACUP: periaqueductal gray (PAG) and substantia nigra (SN)

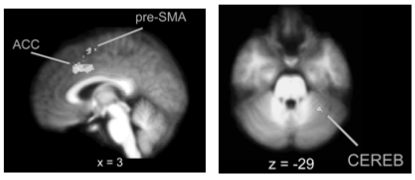
ACUP Increases Extent of Resting DMN Connectivity

Cortical and Subcortical Regions

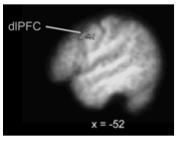


Acupuncture Effects on Resting SMN Connectivity

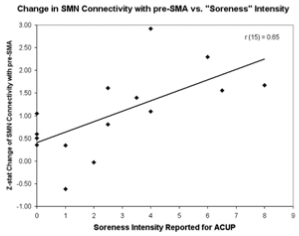
ACUP



SHAM



Sensation Intensity Correlates with Increasing SMN Connectivity to the pre-SMA in post-hoc Analysis



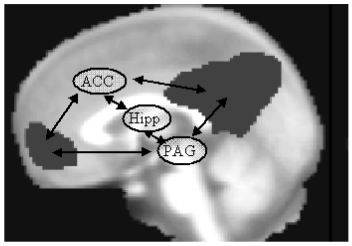
- Greater soreness elicited by ACUP leads to greater connectivity between SMN and the pre-SMA, a region known to be important for motor planning
- Acupuncture stimulation leads to increased somatosensory-motor binding?

Conclusions

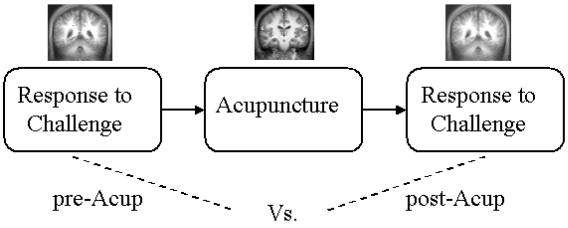
- Verum but not sham acupuncture increases resting state DMN and SMN connectivity with memory, affective, anti-nociceptive and pain processing brain regions – suggesting that these RSN's may be not only trait, but state dependent
  - Differences between verum and sham may have been due to differences in psychophysics
  - Increased functional connectivity may be explained by anatomical connectivity: the DMN is comprised largely of cortical "association areas" - extensive connections not only with primary sensory areas but also subcortical regions involved in pain processing, affect, and memory.

Is Increased Connectivity a Mechanism for Acup Analgesia?

- Speculation: Is increased functional connectivity between endogenous anti-nociceptive brain regions (PAG) and brain regions that process pain signals (ACC → pain affect), via the DMN, a mechanism for acupuncture analgesia?



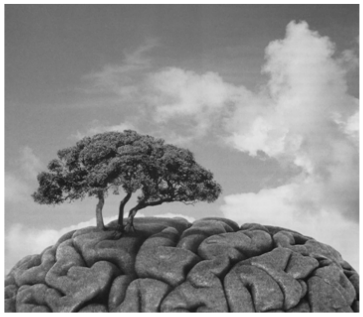
Long-term effects of acupuncture on brain response to a challenge (pre-acup vs. post-acup)



pre-Acup Vs. post-Acup

combining neuroimaging with a longitudinal trial

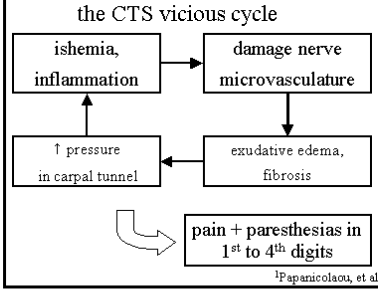
Neuroplasticity in Carpal Tunnel Syndrome treated by Acupuncture

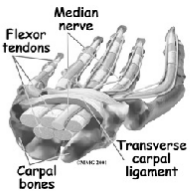


Acupuncture and CTS - Introduction

- Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy → U.S. prevalence 3.72%[1].

the CTS vicious cycle

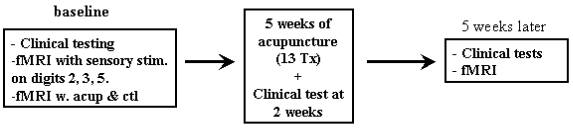




[1]Papanicolaou, et al. J Hand Surg. 2001; 26(3):460-6

Methods

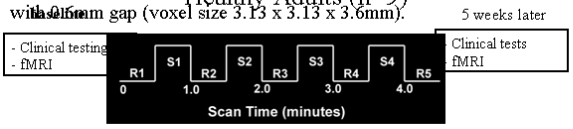
CTS (n=10)



fMRI Stimulation: 100Hz electro-stimulation on digits 2, 3, and 5 (pseudo-random order); just below pain sensitivity threshold.

Imaging: 3.0 T, TE/TR = 30msec/3sec, 38 sagittal slices, 3mm thick with 0.5mm gap (voxel size 3.13 x 3.13 x 3.6mm).

Healthy Adults (n=9)



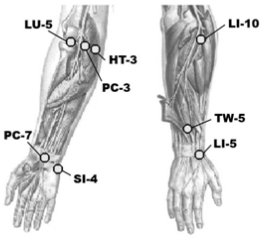
Acupuncture Design

"Semi-Individualized" Protocol
3x/week for 3 weeks + 2x/week for 2 weeks = 13x over 5 wks:

Needles: 38 guage (0.18mm), 30mm

Common Points (every subject): unilateral TW-5 (*interosseous*) to PC-7 (*median*), 2Hz EA, low intensity.

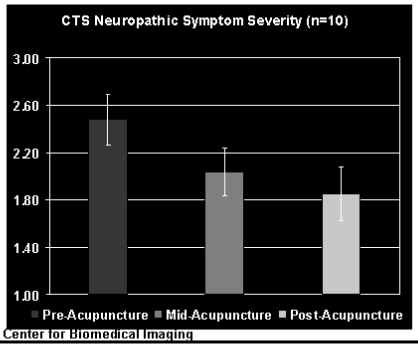
Variable Points (symptom based): acupuncturist chooses 3 of 6 based on diagnosis: HT-3 (*antebrachial cutaneous*), PC-3 (*median*), SI-4 (*ulnar*), LI-5 (*radial*), LI-10 (*radial*), LU-5 (*radial*); manual even needle technique.



Martinos Center for Biomedical Imaging

Clinical Results (subjective): Boston CTS Questionnaire

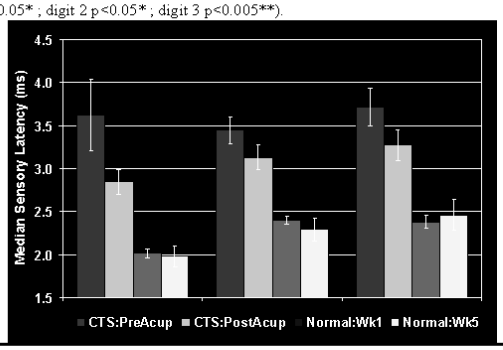
- Acupuncture diminished neuropathic symptom severity, as measured by the Boston CTS Questionnaire (paired t-test: $p<0.005$***).



Martinos Center for Biomedical Imaging

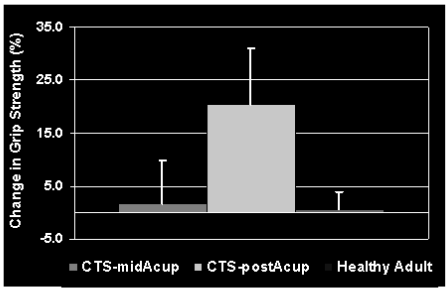
Clinical Results (objective): Median n. Sensory Latency

- CTS had a significantly greater sensory latency than control ($p<.001$)
- After acupuncture, median n. latency was significantly reduced (paired t-test: digit 1 $p<0.05$* ; digit 2 $p<0.05$* ; digit 3 $p<0.005$**).



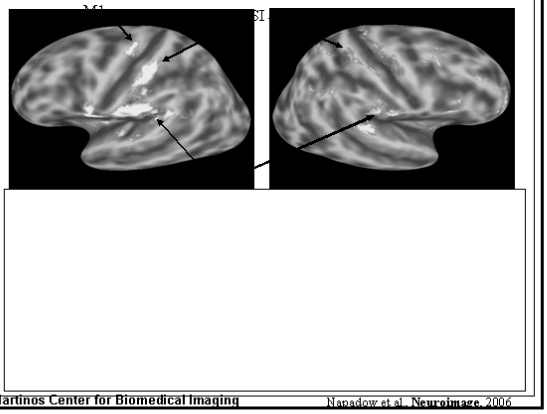
Clinical Results (functional): Grip Strength

- Acupuncture improved grip strength (paired t-test $p<0.05$ *). No significant change in healthy adults.



Martinos Center for Biomedical Imaging

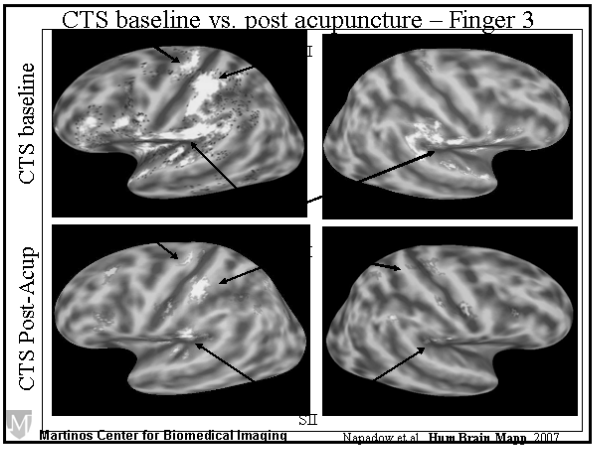
CTS vs. Healthy Adults – Finger 3



Martinos Center for Biomedical Imaging

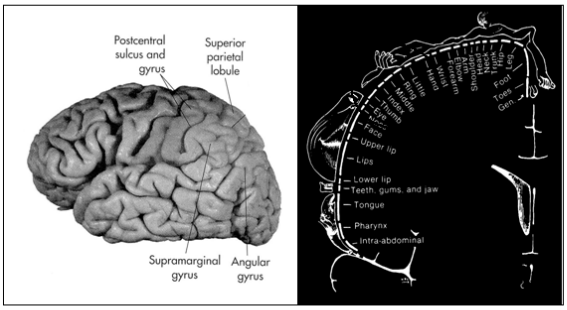
Napadow et al. **Neuroimage**. 2006

CTS baseline vs. post acupuncture – Finger 3



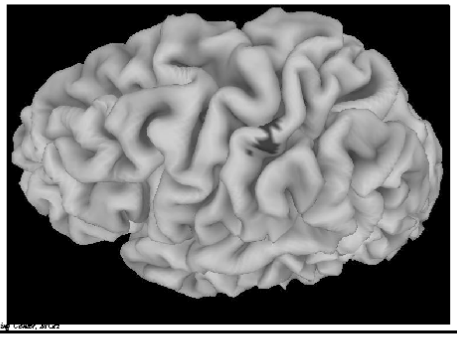
Finger Mapping in SI - Somatotopy

- The somatotopic humuncular organization in the primary somatosensory cortex, SI (Penfield, 1937).



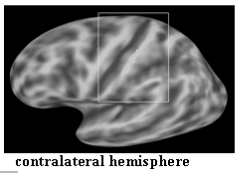
fMRI Digit Representations

- **fMRI activation was observed in contralateral BA 1 for digits 2, 3, and 5 in most subjects, with digit 2 most ventral and digit 5 most dorsal, demonstrating distinct finger separation.**

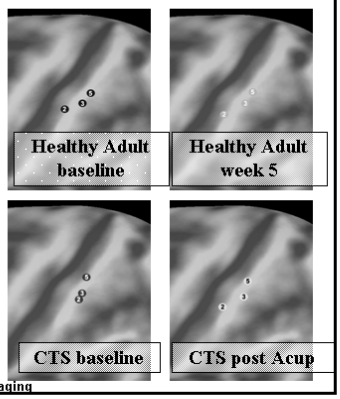


Group Map SI Somatotopy

- D2 & D3 were closer together for CTS patients than healthy adults
- D2 & D3 were more separated post-acup



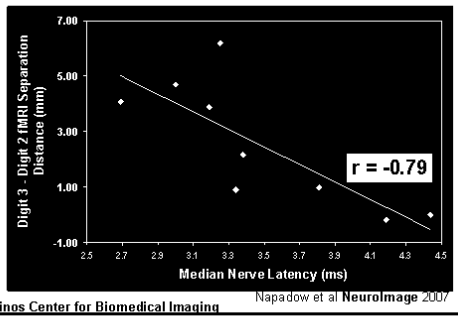
contralateral hemisphere



Martinos Center for Biomedical Imaging

Somatotopic Separation Correlates with Peripheral Pathology in CTS patients

- Negative correlation between digit 3/2 separation distance and D2 nerve conduction delay ($p<0.05$).

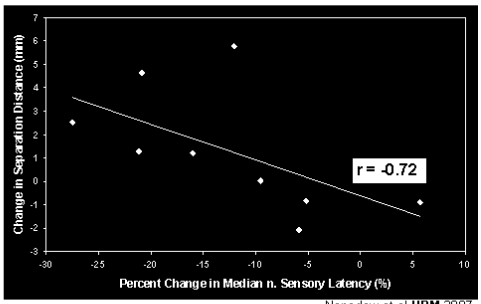


Napadow et al **NeuroImage** 2007

Martinos Center for Biomedical Imaging

Change in Somatotopic Separation Correlates with Improvement in Peripheral Pathology

Negative correlation between change in D3/D2 separation and improvement in D3 conduction delay ($p<0.05$).



Napadow et al **HBM** 2007

Martinos Center for Biomedical Imaging

CTS – A Central Manifestation of Peripheral Nerve Dysfunction

Carpal Tunnel Syndrome

pain + paresthesias

more frequent and abnormal nerve traffic to brain

more simultaneous signaling from affected digits

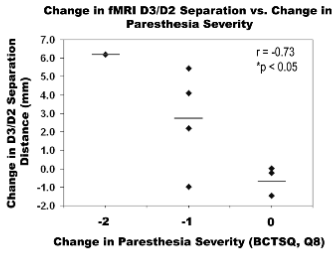
disinhibition

Hebbian plasticity mechanisms

more extensive, wider digit representations in cortex

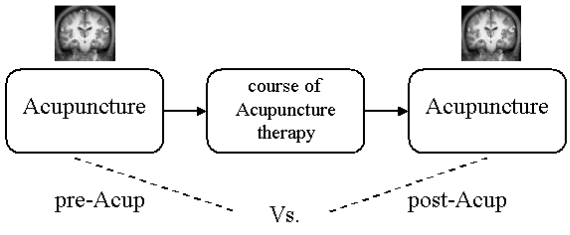
less separated, blurred digit representation in cortex

Improvement in Paresthesias Correlates with Improvement in Somatotopy



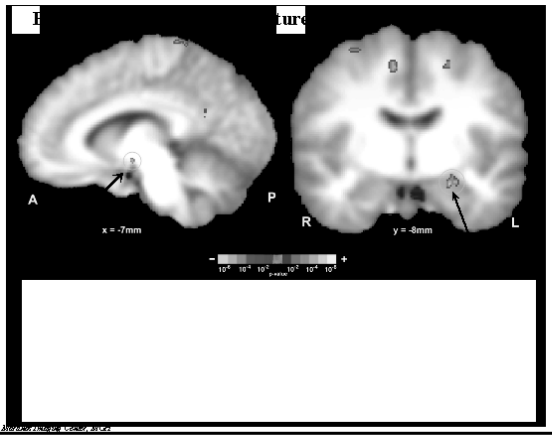
• ***Future Studies (*behavioral correlate):** Do blindfolded CTS patients mis-attribute D2 stimulation with D3?

Coupling Characterization with a Longitudinal Trial

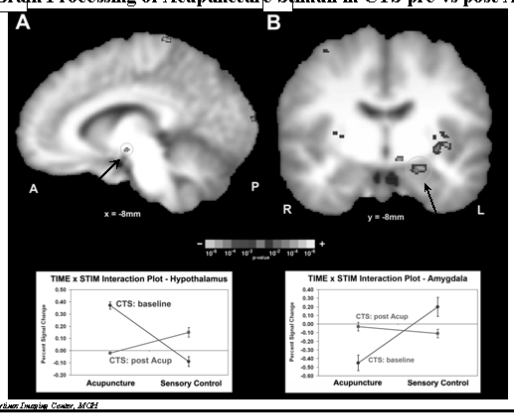


combining characterization with a longitudinal trial

Q: Do the brains of patients respond to Acupuncture needling the same way as brains of healthy adults?



Brain Processing of Acupuncture Stimuli in CTS pre vs post Acup



Martinos Imaging Center, MGH

CONCLUSIONS

Acknowledgements

Martinos Center for Biomedical Imaging, MGH, Boston, MA

Polly Dhond
Bruce Rosen
Lauren LaCount
Mark Vangel

Logan College of Chiropractic, Chesterfield, MO

Norman Kettner

Dept Biomedical Engineering, Kyunghee University, Yongin, Korea

Kyungmo Park
Jieun Kim
Jeungchan Lee

Osher Institute, Harvard Medical School, Boston, MA

Ted J Kaptchuk

Spaulding Rehabilitation Hospital, Medford, MA

Joseph Audette

NCCAM

Center of Excellence for Research in CAM (P01-AT002048), R01AT004714, K01-AT002166, F05-AT003770

Clinical Presentation and Differential Diagnosis of Geriatric Pain Syndromes

Jeffrey R. Kamper, DC, DCBCN

CLINICAL PRESENTATION AND DIFFERENTIAL DIAGNOSIS OF COMMON GERIATRIC PAIN SYNDROMES

Jeffrey R. Kamper, DC, DCBCN
Logan College of Chiropractic
Chesterfield, MO

Epidemiology of Pain in the Geriatric Population

- According to the American Geriatric Society pain is highly prevalent and under treated
- Clinical Journal of Pain reported the presence of acute pain remains the same across adult life span, but there is an age related increase in the prevalence of chronic pain
- According to the National Age Research Institute the prevalence of persistent pain often exceeds 50% of community-dwelling older persons and up to 80% of nursing home residents

Pain Characteristics in Elderly

- Pain is a complex, subjective and unpleasant sensation derived from sensory stimuli and modified by memory, expectations and emotions
- These modifying entities tend to be accentuated in the elderly
- Because pain is very common among the elderly, and is often underreported, it is vitally important to routinely ask geriatric patients about pain

Common Presenting Complaints in the Geriatric Patient Population

- Headache
- Back/neck pain
  - neuromusculoskeletal vs. organic referral
- Extremity
  - neuropathic
  - extraskeletal joint
  - radiating/referred
  - primary pathology
  - vascular
- Abdominal
- Chest

Common Syndromes Seen by First Contact Health Care Providers

- Hip/knee arthritis
- Myofascial pain
- Deep vein thrombosis
- Thunderclap headache
- Vascular claudication

Common Syndromes Seen by First Contact Health Care Providers

- Hip osteonecrosis/fracture
- Diabetic neuropathy
- Rotator cuff disease
- Spinal compression fractures
- Chronic pain

Potential Challenges in the Clinical Assessment of Older Individuals

- Cognitive impairment
- Decreased mentation from drugs
- Dementia
- Hearing difficulties
- Intoxication
- Psychiatric disorders

Case Study

Sudden Onset Headache

Headache

- Headache is a common condition, accounting for 2% of all emergency department visits, but a challenging symptom to work up in primary care. While most are benign, the rare serious cases are devastating if missed. The challenge to the physician is to differentiate those patients requiring only symptomatic management from those requiring further diagnostics.

Headache Demographics and Pathological Diagnosis Rates

- According to the National Hospital Ambulatory Care Survey for the years 1992-2001 non-traumatic headache accounted for 2.1 million ED visits a year or 2.2% of visits.
- Migraine or vascular headaches accounted for 63% of all patients
- Pathological diagnosis overall was 2%, however patients 50 and over had a 6% rate of pathological findings
- On multivariable analysis the odds ratio for patients over 50 to receive a pathological diagnosis is 3.3

Headache Differential Considerations

- Common causes
  - Tension headache
  - Migraine
  - Cervical discopathy
  - Ocular, including refractive errors
  - Sinusitis
  - Rebound headache from analgesia overuse
  - Iatrogenic headache, m/c nitrates and Ca channel blockers
- Pathological
  - CNS infection
  - Stroke
  - Transient ischemic attack
  - Intracerebral hemorrhage
  - Subarachnoid hemorrhage
  - Aneurysm
  - Glaucoma
  - Benign intracranial HTN
  - Temporal arteritis
  - hypertensive encephalopathy

Red Flag Signs and Symptoms

- Thunderclap headache or worst headache ever
- Visual loss
- New onset headache in elderly
- Positional exacerbation or increase with valsalva
- Morning headaches
- Hx of carcinoma
- Neurological deficits
- Trauma, intoxication, or anticoagulation

Symptomatically Paradoxical Headache

An expanding intracranial mass will present as a relatively mild unremitting headache

Extraskeletal Pain Syndromes

- General Syndromes
  - Osteoarthritis
  - Neuropathic
  - Vascular
  - Referred Pain
  - Pathological
  - Neuropathic
- Regional
  - Hip
  - Shoulder

Osteoarthritis

- Must differentiate osteoarthritis from pathological inflammatory and malignant processes
- Accomplished through history, exams, and investigations
- Contemporary definitions of OA consider it more of a syndrome with multiple etiologies rather then a single disease entity

Osteoarthritis Risk Factors

- Female gender
- Age
- Family history
- Excess weight
- Past history of joint trauma
- Joint misalignment
- Repetitive joint loading tasks

Clinical Features of Osteoarthritis

- Joint pain following activity
- Transient stiffness in the AM and after rest
- Reduced ranges of motion
- Joint crepitus and/or periarticular swelling
- Pain described as aching or throbbing with periodic activity-related episodes of sharp shooting pain
- Generally insidious in onset

Features That May Suggest Alternative Diagnosis

- Age<40
- Mono-articular involvement
- Marked inflammatory signs in the affected joint
- Systemic features eg. fever, weight loss, rash
- Raised inflammatory markers
- Acute pain with sudden onset
- Pain limited to spine
- Family history of autoimmune diseases

Radiological Characteristics of Osteoarthritis

- Radiological disease apparent in approximately 75% aged 60-70 years
- Up to 40% with advanced radiological changes are symptom free
- Standard radiographs may be normal in some symptomatic individuals with defects in cartilage and bone only seen on MRI
- Limited correlation between radiological disease and the presence pain and impaired function

Pathological Features of Osteoarthritis

- Early features
  - Focal areas of damage to articular cartilage
  - Changes in subchondral and marginal bone
  - Variable synovitis and marginal thickening
- More advanced disease
  - Narrowing of joint space
  - Osteophytes
  - Changes in subchondral bone

Case Study

Diabetic Peripheral Neuropathic Pain

Diabetic Peripheral Neuropathy

- According to the National Institute of Kidney Disease in Bethesda, MD 18% of persons older than 65 in the US have diabetes, representing 40% of all persons with the Dz
- One of the leading causes of visits to primary care physicians on Medicare

Diabetic Neuropathy Characteristics

- Results from nerve ischemia as the result of microvascular changes, effects of hyperglycemia on neurons, and intracellular metabolic impairment of nerve function
- Stocking-glove distribution
  - Symmetric polyneuropathy is most common and affects the distal feet and hands
- Includes small-fiber neuropathy, large fiber neuropathy, and radiculopathies

Clinical Features of Diabetic Neuropathies

- Small-fiber neuropathy
  - Pain, numbness, loss of temperature sensation with vibration and position sense being preserved
  - Patients are prone to foot ulcerations and neuropathic joint degeneration (Charcot's)
- Large-fiber neuropathy
  - Muscle weakness, loss of position and vibration, and lack of DTRs
  - Atrophy of intrinsic foot muscles and foot drop

Clinical Features of Diabetic Neuropathy

- Radiculopathies
  - Commonly misdiagnosed and managed as solely spondylogenic
  - Most often affect the proximal L2-L4 nerve roots resulting in pain, weakness, and atrophy of the LE (diabetic amyotrophy)
  - Also commonly affect proximal T4-T12 nerve roots causing abdominal pain (thoracic Polyradiculopathy)

Case Study

Vascular Pathology

Vascular Pathology in Pain Syndromes

- Deep vein thrombosis
- Peripheral artery disease
  - Intermittent claudication
    - Vasculogenic
    - Neurogenic
  - Other forms

Deep Vein Thrombosis

- 250,000 hospitalized yearly in US for DVT
- Prompt dx and tx to prevent short term sequelae of pulmonary embolism (frequency of silent pulmonary embolism is 40-50%) and death as well as long term complications of recurrent venous thromboembolism and post-thrombotic syndrome
- Occurrence rates increase with age from .5% at 50 yo to 10.7% at 80 yo
- Mortality rates increase exponentially with age

Risk Factors in HX for DVT

- Recent surgery, trauma, or immobilization
  - Representative of 50% of patients with DVT
- Limited mobility without immobilization
- Hx of DVT or pulmonary embolism
- 60 yo or older
- Male gender
- Congestive heart failure
- Systemic lupus erythematosis
- Peripheral artery disease

Clinical Features of DVT

- Signs and symptoms
  - Pain and tenderness
  - Edema, calor, and erythema
  - Homan's sign
    - Elicitation of calf or popliteal pain after forceful dorsiflexion of the ankle
  - These findings are generally unilateral

Peripheral Arterial Disease

- 8 million Americans affected
- Common but under diagnosed and under treated disorder with substantial morbidity and mortality
- Estimated prevalence is 14-29% in >70 yo
- Intermittent claudication is only present in 10% of the patients with PAD
- 50% have atypical symptoms, 40% are asymptomatic
- This heterogeneity of clinical presentations may explain why only 25% of affected persons are diagnosed and treated

Clinical Features of PDA Not Classifies As Intermittent Claudication

- Lower extremity muscular pain
- Hair loss extremities cool to palpation
- Poorly palpable pulses
- Patient in high risk groups
  - >70 yo, African American, Diabetes mellitus, smoker, Hyperlipidemia, impaired renal function

Signs Suggestive of PAD

- Elevation skin pallor within 60 secs of passive elevation of feet to 60 degrees
- Dependent rubor and/or onset of erythema more then 15 secs after sitting upright following leg elevation

Diagnostic Testing for PDA

- Contrast angiography is the criterion standard
  - Risks include bleeding, arterial dissection,infection, and contrast-induced nephropathy
- Ankle-brachial pulse index
  - Non-invasive. Can quantify the severity and predict the risk of future cardiovascular events
  - Can be combined with treadmill testing to determine functional baselines and responses to care
- Computed tomographic angiography and magnetic resonance angiography should be employed if considering revascularization

Intermittent Claudication

- Defined as pain, fatigue,discomfort that involves specific limb muscle groups during exertion due to exercise induced ischemia
- Progresses over time
- Functional decline; pain occurs earlier and is more sever with same activity
- Present in 3-10% of those over 50

Failure to Diagnose PAD

Dx of PDA Can Be Missed in Over 90% of Afflicted If Clinicians Rely Solely on Classic IC Symptoms

Differentiating IC by Type

- Neurogenic and vasculogenic hx and exam are very similar however vasculogenic affects calf, thigh or buttock where neurogenic is more diffuse
- Neurogenic generally requires a longer resting period to resolve
- Treadmill testing can differentiate as ABPI decreases with vasculogenic but not with neurogenic claudication

Differential Diagnosis of Hip Pain

- Osteoarthritis
- Osteonecrosis
- Fracture
- Bursitis
- Referred or inaccurately reported location of pain with the sacroiliac joint typically as the pain generator

Hip Osteoarthritis

- Common site for OA affecting 10-25% of population over 55 yo
- Radiographs represent the current gold standard for diagnosing hip OA
  - Radiographic findings must be correlated with reported pain levels and examination findings
  - Findings include joint space narrowing, osteophytes, bony changes at joint margins, and alterations of subchondral bone

Examination Findings of Hip OA

- Capsular pattern of joint restriction
  - Unique pattern suggestive of OA consisting of gross limitation in internal rotation,flexion, and abduction
- Abnormal end feels at the end ranges of passive motion
  - Early capsule end feel, a spasm end feel, bone- to- bone
- Provocative tests
  - Patrick's test, scour test, hip flexion test, squat test

Clinical Prediction Rule for Presence of Hip OA

- 3 of the 5 listed predictor variables resulted in a post-test probability of 29-68% likelihood of hip OA
- 4 of the 5 this to 91%
- Predictor variables include
  - Self-reported squatting as an aggravating factor
  - Active hip flexion causing lateral hip pain
  - Scour test with adduction causing lat hip or groin pain
  - Active hip extension causing pain passive internal rotation of less than 25 degrees
  - Active hip extension causing pain

Hip Fractures

- Hip fractures are the leading cause of morbidity and mortality in the geriatric population
- Significant trauma usually not present in patient's history with most fractures caused by stumbling or tripping on level ground indoors
- On x-ray look for 90% of fractures to occur in the femoral neck and intertrochanteric regions (equal distributions) with subtrochanteric accounting for the other 5-10%

Shoulder Pain Syndromes

- Rotator cuff tears can be classified as acute or chronic and may be full or partial tears
- Result in significant upper extremity pain and dysfunction
- Physical exam reveals signs of supraspinatus tendinitis and weakness on active abduction and external rotation
- Imaging includes MRI with high sensitivity and specificity and diagnostic Musculoskeletal ultrasound which has the advantage of visualization under motion challenge

Frozen Shoulder Syndrome

- Frozen shoulder or adhesive capsulitis is a syndrome characterized by both active and passive limitations in glenohumeral range of motion
- Etiology may include neurological, idiopathic, or post-traumatic

Case Study

Acute Abdominal Pain

Abdominal Pain

- Acute abdominal pain is common presenting complaint in older patients
- Diagnosis may be complicated by coexistent disease, delays in presentation, and physical and social barriers
- Older patients tend to present later in the course of their illness and have more non-specific complaints
- Broader differential diagnosis must be considered in older patients with abdominal pain

Types of Visceral Pain

- Tension pain
- Inflammatory pain
- Ischemic pain

Tension Pain

- Tension pain
  - Commonly referred to as colic and typically results from forcefulness of peristaltic contraction in an effort to eject an irritating substance. Eg. Food, bacteria, and stretching of an organ capsule
  - Characteristics
    - Pain is vague, deep and poorly localized
    - Patients are frequently changing positions in an attempt to get comfortable

Abdominal Aortic Aneurysm

- 15,000 deaths in in US annually due to ruptured AAA
- 9th leading cause of death in men over 55
- 1% of men 55-64 and 4-6% over 75% have a significant AAA
- Published rates for women average about 2%
- Most occur in patients with a hx of hypertension and atherosclerosis

Risk Factors for AAA

- According to the New England Journal of Medicine 90% of patients with AAA are male tobacco users
- Peripheral vascular disease
- Family history of AAA

Routine Screening for AAA

- US Preventable Task Force Recommends routine screening for all males 65-75 with history of tobacco use
- Modality of choice is ultrasonography

Symptoms of AAA

- Most common symptom is a pulsation or throbbing in abdomen
  - Increases with exertion
  - Accompanied by heartbeat sensation when lying down
- Abdominal or low back pain may or may not be present
- Dissecting aneurysms cause excruciating pain described as ripping or tearing pain that often starts in stomach and migrates down the leg
- Often asymptomatic and diagnosed incidentally

Diagnosis of AAA

- Physical exam findings
  - pulsatile epigastric mass greater than 1 inch
  - Auscultation of bruit
  - Poor peripheral pulses
- Classic triad of rupture
  - Hypotension
  - Back pain
  - Pulsatile mass
  - According to Journal of Vascular Surgery & British Medical Journal: triad only present 25-50 % time

Diagnosis of AAA

- Imaging studies
  - Often an incidental finding during other investigations
  - Ultrasound considered preferred study because of its excellent operating characteristics and low cost
  - CT or MRI are definitive imaging studies if rupture is suspected
  - Aneurysms less than 4cm monitored, those over 6cm should usually be repaired

Low Back Pain

- According to the Journal of the American Geriatric society approximately 6 million older adults suffer from recurrent low back pain
- 36% of community-dwelling older adults experience an episode of back pain every year; with 21% qualifying it as moderate to severe
- Third leading cause of chronic health problems in women >65 and fourth for men

Differential Categories for LBP

- Acute mechanical low back pain/strain
- Radiculopathy; Compressive vs. Non-compressive
- Inflammatory spondyloarthropathies
- Rare but serious causes including neoplasm(usually metastases), infections (discitis, TB) and cauda equina syndrome
- Other visceral causes including pelvic infections, nephrolithiasis, pancreatic disease, AAA

Signs & Symptoms of LBP Suggestive of Systemic Pathology

- History
  - Insidious onset and progressive pattern
  - Sacral pain of non-traumatic origin
  - Malignant disease
  - Excessive fatigue
  - Chronic immunosuppressive or corticosteroid therapy
  - Trauma related to physiological changes associated with aging (ie, osteoporosis)

Signs & Symptoms of LBP

- Pain description
  - Nocturnal pain that disrupts sleep
  - Pain that causes constant movement or patient to assume fetal position
  - Pain unrelieved by rest or recumbency
  - Pain that is unaffected by exertion or activity
  - Severe, persistent back pain with full and painless movement of the spine
  - Back pain accompanied by multiple joint pain
  - Pain described as throbbing or pulsating

Signs & Symptoms of LBP

- Other symptoms
  - Constitutional symptoms
    - Fever, sweats, nausea or vomiting
  - Palpable pulsating mass in abdomen
  - Severe and progressive bilateral weakness of lower extremities
  - Neurological findings lasting more than a month
  - Bowel or bladder incontinence, urinary retention, UTI

Common Referral Patterns

- Stomach
- Small intestine
- Large intestine
- Pancreas
- Upper urinary tract (kidneys/ureter)
- Lower urinary tract
- Abdominal Aorta
- Midline low thoracic or right shoulder/neck
- Midline lumber region
- Lumbopelvic region
- Midline thoracolumber region
- Unilateral subcostal and costovertbral region
- Lumbopelvic region
- Lumber region

Common S/S Associated With Malignancy

- Night pain that disrupts sleep
- Pain that is unrelieved by rest
- Unexplained weight loss fever/sweats
- Extreme fatigue
- Altered gastrointestinal or genitourinary function

Chronic Pain Syndromes

- Persistent or chronic pain affects more than 50% of older persons on community settings and over 80% in nursing facilities
- Symptom manifests itself not only as a sensory experience but also by causing psychological distress
- Assessing pain in the aged is even more challenging secondary to the frequent presence of cognitive impairment or communication difficulties

Differentiation of Pain Types

- Acute pain represents pain of recent onset, generally less than a month, which is a warning of actual or potential tissue damage
- Persistent pain is ongoing pain related to tissue damage, it is functional and purposeful
- Chronic pain is ongoing pain which serves no useful purpose, it simply makes the individual miserable

Issues Related to Age

- Age-related changes in the function of nociceptive pathways including alterations in afferent transmission and descending modulation
- Age-related differences in the psychological mediators of pain including altered pain beliefs and attitudes, coping strategy mechanisms, misattribution of symptoms,report bias, and stoicism
- Age-associated psychosocial issues including bereavement, retirement, loss of independence/institutionalization

Key Components Of Assessment Of Pain

- Observation for signs of pain
  - Especially with cognitive/communication impairment
- Description of pain to include
  - Sensory dimension; Nature, location, intensity
  - Affective dimension; Fear, anxiety, depression
  - Impact/disabling effects
    - Functional activities/activities of daily living
    - Participatory activities; Work, socializing, relationships

Key Components con't

- Measurement of pain
  - Standardized scales in a format accessible to patient; numeric graphing rating scale, verbal rating scale, pain thermometer, abbey pain scale,brief pain inventory
- Cause of pain
  - Examination
  - Investigations
  - Identify any treatable causes, but be aware that pain can exist in an absence of findings

Key Observational Changes Associated with Pain

- Autonomic changes; pallor, sweating, tachypnea, altered breathing patterns, tachycardia, hypertension
- Facial expressions; grimacing, wincing, frowning, rapid blinking, lip puckering,squinting
- Body movements; altered gait, pacing, rocking, guarding, bracing, repetitive movements
- Vocalizations; sighing, grunting, groaning, offensive/aggressive speech
- Interpersonal interactions; aggression, withdrawal, resisting

Importance of Diagnosis of Pain Syndromes In Geriatric Patients

- Failure to diagnose by neglecting to ask can lead to errors of omission in management resulting in missing causes of acute pain that demand immediate or urgent action
- Failure to diagnose persistent pain can result in otherwise treatable disease processes progressing beyond the realms of therapeutic intervention
- Failure to diagnose chronic pain can negatively impact quality of life issues on multiple fronts

Therefore, in Conclusion……

- Remember that elderly patients take pain for granted, often assuming that it is a normal aspect of the aging process, and therefore may not chose to or have the capacity to effectively report their pain
- Therefore, it is the responsibility of the health care Practitioner to query the patient, because we can't diagnosis pain if we are unaware it exists

Using the Instruments of Pain Assessment

Fredric Metzger, PhD

Assessing Pain in Older Adults

Fredric A. Metzger, Ph.D.
Assistant Chief of Psychology
St. Louis VA Medical Center
John Cochran Division

Definition of Pain

Pain is more than just a physical sensation, the most common definition comes from the International Association for the Study of Pain:

> "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

Some important concepts

The experience of pain:

Pain is personal. Only the person with pain knows the sensations.

Pain cannot be objectively measured, confirmed, or disconfirmed by another person.

Pain Behavior:

This is the outward, observable expression of pain, including: talking about pain, limping, grimacing, groaning, and laying in bed.

The relationship between pain and pain behavior is not one-to-one.

Pain behavior is influenced by our environment and learning.

Quality of Pain (i.e., what does it feel like?)

Important because different types of pain call for different types of treatment

Importance of assessment

Despite national efforts to improve the assessment of pain, pain remains under identified and under treated.

In Geriatric population:

40% of elders living independently report difficulties with chronic pain

27% to 83% of elders living in institutional settings.

Inadequate Treatment of Pain in the Elderly

Approximately 40% to 80% of community dwelling elderly do not receive any treatment for their pain

In the institutional setting 16% to 27% of older people receive no treatment for their pain.

Challenges to Assessment and Treatment of Pain in the Elderly

Belief that pain is so common in the elderly that it is a normal part of aging.

Residents with cognitive impairment reported less pain than cognitively intact counterparts despite suffering from more physical illness and functional disability.

Perception of drug use: 66% believe that they should only take drugs when in severe pain.

Three quarters believe that people who talk about pain were not taken seriously.

Providers don't trust self report.

Lack of appropriate pain assessment tools.

General Logistics of Assessment

Engaging patient in the assessment process.

- **If the encounter centered around pain complaints allow person to give a brief history.**
- **Know something about the persons pain complaint or history**
- **To keep yourself sane, try to keep person focused on primary pain complaint (use of paper pencil measure help a lot here)**

Special Issues with the Elderly

Allow sufficient time for assessment.

Provide an environment that is quiet, free of distractions, and has adequate lighting.

Have appropriate aids for hearing and vision available

Speak slowly, clearly, and as loudly as needed.

Involve family members or caregivers.

Use enlarged copies of assessment devices.

Explain the use of the pain scale each time it is administered.

Assessment Strategies- Unidimensional

These instruments quantify one aspect of pain, usually pain intensity.

Problems:

Neglect impact of pain on function

Poor content validity- may not adequately assess all aspects associated with pain

In difficult to assess patients (e.g., cognitively impaired) a single domain assessment may result in false negatives.

Assessment Strategies- Unidimensional

Visual Analogue Scale
- Not recommended for use in elderly
- Sensory deficit can affect results
- Self completion required
- Sensitive to even small changes in pain intensity
- Abstract thinking required

Numerical Rating Scale
- Patient needs to be able to perceive pain as numbers
- Useful for illiterate patients
- Difficulties in completion independent of age
- Can be verbally administered.

Assessment Strategies- Unidimensional, continued

Verbal Rating Scale
- Wording requires careful selection
- Not as sensitive as other scales- too many words will cause confusion
- Administered verbally
- Relies on patients vocabulary and interpretation of words.

Numerical Rating Scale
- Visual impairment affects completion
- High Completion rates with older people
- Useful if literacy or fatigue affect assessment.

Assessment Strategies- Multidimensional Assessment

Recommended for initial assessments with unidimensional follow-up.

More complicated assessment and as such are more difficult to complete with individuals with cognitive or sensory impairments.

What can you ask about?
- Intensity
- Duration
- Location
- Meaning of pain
- Fear of movement/re-injury
- Disability
- Mood
- Coping skills….

Assessment Strategies- Multidimensional Assessment

Geriatric Pain Measure
- Designed for ambulatory elderly with multiple medical problems
- Assesses pain intensity and functional problems caused by pain
- Interview assisted device (items can be read to patient for completion)

Geriatric Multidimensional Pain and Illness Inventory
- Designed for elderly patients in an institutional setting
- Frequency and intensity of pain
- Functional impact
- Social Impact
- Emotional Concomitants

Special Issue: Assessing Pain In Dementia

Literally dozens of different observational scales

Most common

Pain Assessment in Non-Verbal Patients Scale (PANPS)- is a non-verbal assessment of pain using behavior observations, e.g., breathing, vocal cues, facial cues, body language, consolability.

The Checklist of Nonverbal Pain Indicators

Designed to differentiate between varying levels of pain in cognitively impaired adults

Special Issue: Identifying Depression in Individuals with Chronic Pain

Depression is common in chronic pain, with estimates ranging between 60-80% of patients with chronic pain also suffering from depression.

However depression within the context of a serious chronic illness is often overlooked because many of the symptoms associated with depression can be attributed to the persons medical condition.

Symptoms of Depression

1. **Depressed mood**
2. **Diminished interest or pleasure in nearly all activities**
3. **Significant change in weight***
4. **Disturbance in sleep***
5. **Psychomotor agitation or retardation.***
6. **Fatigue or loss or energy***
7. **Feelings of worthlessness or guilt**
8. **Diminished ability to think or concentrate***
9. **Recurrent thoughts of death or suicide**

***Can be attributed to the direct physical effects of chronic pain or side effects of treatment**

Special Issues: Addiction

Not all people are at equal risk for developing a psychological dependence on opioids.

Risk of Misuse

- Boston Collaborative Drug Surveillance Project (Porter and Jick, 1980) followed 11,882 patients with no prior history of abuse who received opioids during an inpatient hospitalization.
  - Found only four cases (.03%) of problematic use
  - Problems
    - Excluded people with histories of substance abuse
    - Opioid use was short term

Risk of Misuse, part 2

- Dunbar and Katz (1996): Followed 20 patients with BOTH chronic pain and substance abuse problems for one year. They tracked daily use, relief, side effects, etc., and found:
  - Nine out of 20 abused the medication
  - 11 out of 20 did not abuse medication
    - All non abusers were active in recovery programs and had good family support.

What to do?

- Problem is that patients with substance abuse issues also have a increased risk of suffering from health conditions that produce chronic pain.
- Solution can include grouping patients in high, medium, and low risk categories. These categories can then be used to structure treatment.

Potential Predictors of Misuse

There is very little research concerning the identification of risk factors for opioid misuse. Clinical observations suggest the following:

- History of substance abuse or treatment for substance abuse
- History of physical or sexual abuse
- History of severe depression or anxiety
- Regular contact with high risk people or situations
- Chaotic living environment
- History of criminal behavior
- High number of motor vehicle accidents

Identifying Problems in Ongoing Opioid Use

It is very difficult to identify opioid dependence in patients with chronic pain.

- Traditional diagnostic indicators can lead to false positives.
- Presence of Pseudo-addiction (demanding behavior, anger, depression, occasional over use of medication due to the under treatment of pain).

Determining Dependency in Chronic Pain Patients: Pseudo-Addiction

Pattern of drug seeking behavior of patients receiving inadequate pain control. Behaviors typically include:

- Concerns about availability of drug
- Clock watching
- Unsanctioned dose escalations (1 or 2 times)
- Aggressively complaining
- Drug hoarding during periods of decreased symptoms
- Obtaining medications from other providers*
- Requesting a specific drug

Determining Dependency in Chronic Pain Patients: Signs of Dependency and Misuse

- Selling prescription drugs
- Prescription forgery
- Stealing or borrowing another's medications
- Injection oral formulation
- Concurrent abuse of illicit drugs
- Multiple unsanctioned dose escalations
- Multiple prescription losses
- Escalating drug use in absence of acute changes in medical condition
- Evidence of deterioration of function in social, occupational, or interpersonal function.

Treatment Strategies When There is a Concern Regarding Misuse

- ALWAYS work from a written agreement
  - Document expected frequency of visits and refills
  - Identify one source of opioids
  - Prohibitions
  - Consequence of non-adherence
  - Policy regarding early re-fills or lost prescriptions
  - Risks of use (addiction, side effects, etc.)
- Use random drug screens, medication counts, change refill pattern
- Involve family members or other care providers
- Mandatory involvement in other specialty treatments
  - Psychiatry
  - Substance Abuse
  - Physical Therapy
  - Behavioral Medicine
- Use of longer acting medications, e.g., fentanyl, SR morphine, methadone

Chiropractic Management of Lumbar and Cervical Spine Stenosis

Paul Dougherty, DC

Conservative Care of the patient with Spondylosis and Stenosis

Paul Dougherty, DC
Assistant Professor, New York Chiropractic College
Adjunct Assistant Professor of Orthopedics and Physical Medicine and Rehab. University of Rochester School of Medicine and Dentistry

Aging Population

- Americans are living longer and many must still cope with a host of co-morbidities that directly impact function and quality of life. Epidemiological data suggests that between 2010 and 2030, the over 65 year old population will rise over 70%
- *Economic implications of increased longevity in the United States. Annu Rev Public Health. 2004; 25:457-73. Review*

Aging and Back pain

- The evidence concerning the association of back pain prevalence with age is more sparse than currently believed and this association seems to be modified by the severity of the problem.
- *Age Ageing. 2006 May;35(3):229-34.*

Connection of back pain and degeneration?

- plain spinal radiography is not a valuable tool for non-specific neck or low-back pain.
- There is no firm evidence for the presence or absence of a causal relationship between radiographic findings and nonspecific low back pain.
- *Low back pain investigations and prognosis: a review. Refshauge KM, Maher CG. Br J Sports Med. 2006 Jun;40(6):494-8. Review.*

Modic Type 1 changes (MT1)

- A recent population based study did report that patients with concurrent degenerative disc disease and MT1 changes did have more pronounced clinical symptoms than those with degenerative disc disease alone.
- *Kjaer P et al: Modic changes and their associated clinical findings. Eur. Spine J. 2006 15:1312-19*

So where do we go?

- Although there may not be a correlation between spinal degeneration and pain, there are certainly conditions that the treating physician must be aware of in treating the older adult:
  - Cervical spondylotic myelopathy
  - Neurogenic Claudication

DEFINITION

- Cervical Spondylotic Myelopathy is a neurological disease caused by stenotic encroachment of the cervical spinal cord.
- As a result of the stenosis the cord and/or its blood supply are compressed, resulting in direct mechanical damage and /or neuroischemia .

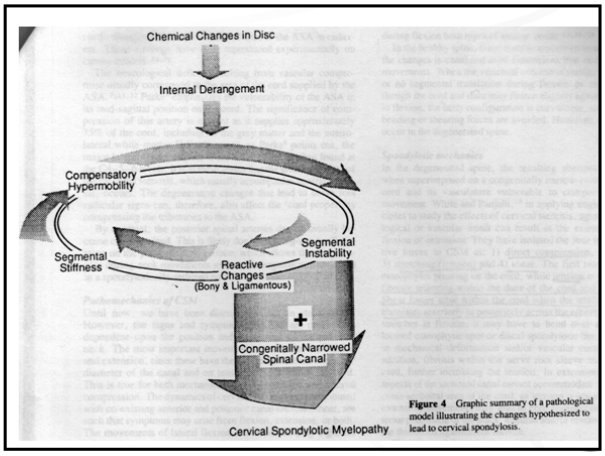


Figure 4 Graphic summary of a pathological model illustrating the changes hypothesized to lead to cervical spondylosis.

RELEVANT ANATOMY

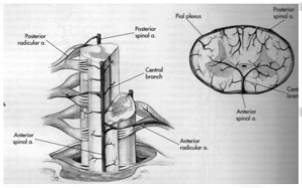
- CENTRAL CANAL:
  - Premorbid shallowness of the central canal represents a predisposing factor to the development of Cervical Myelopathy
  - Body to canal ratio: Pavlov established a 92% accuracy for diagnosis of canal stenosis when the ratios were less than 0.82.

RELEVANT ANATOMY

- SPINAL CORD
  - The spinal cord occupies only about 50% of the central canal at C1, but 75% of the canal at C6.
  - It is primarily due to this dimensional feature that degenerative myelopathy is rare in the cervical spine above C4.
  - This decreasing diameter of the spinal canal also has a direct implication on the cords vascular supply.

RELEVANT ANATOMY

- VASCULAR SUPPLY TO THE SPINAL CORD:
  - Anterior spinal artery: supplies the majority of the cord including the central grey matter and the anterolateral white matter.
  - Posterior Spinal artery: supplies the posterior aspect of the cord including the posterior columns.

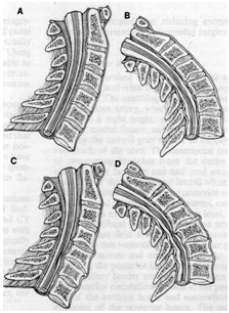


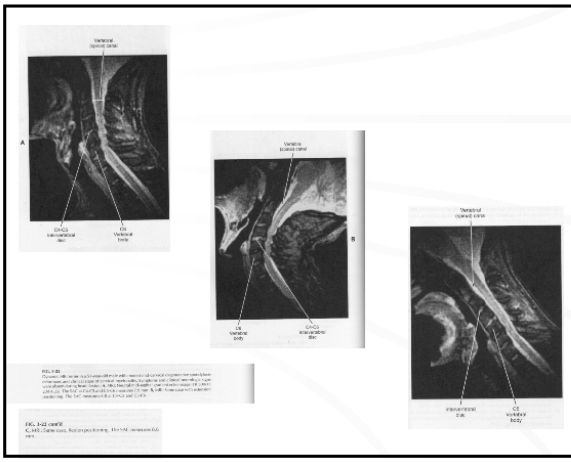
BIOMECHANICS OF THE SPINAL CORD

- Breig et al: "During movement, the cervical cord and its dural covering slide upwards and downwards no more that 2-3 mm. With the vertebral canal. Therefore the cord adopts the length of the spinal canal. J. Biomechanics 1970 3:7-9

BIOMECHANICS OF THE SPINAL CORD

- FLEXION:
  - spinal canal elongates and the cervical cord is stretched and lengthened.
- EXTENSION:
  - causes the spinal cord to relax and shorten.. The flaccid cord deviates according to gravity toward the front or back of the spinal canal, depending on whether the patient is prone or supine

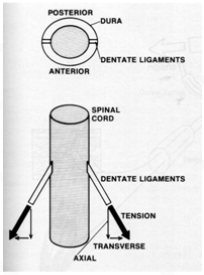




MECHANICS

- Stretching or tension:
  - Is secondary to fibrotic tethering within the dura of the cord and nerve roots.
  - Tensile stresses transmitted to the spinal cord from the dentate ligaments, which attach the lateral pia to the lateral dura. This results in a more lateral stress on the cord.

Tension on the cord



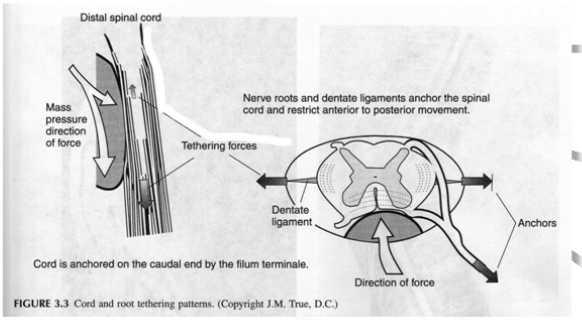
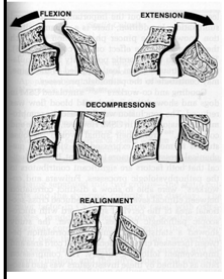


FIGURE 3.3 Cord and root tethering patterns. (Copyright J.M. True, D.C.)

ACTA RADIOLOGICA
1999 40:146-53



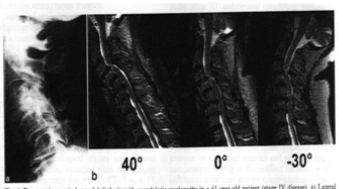


Fig. 4. Degenerative cervical spondylolisthesis with spondylotic myelopathy in a 61-year-old patient (stage IV disease). a) Lateral radiograph reveals anterior spondylolisthesis at C5 with kyphosis and degenerative changes of the lower cervical spine. b) Kinematic MR imaging demonstrates severe spinal stenosis at C5 with signal abnormalities and cord atrophy at neutral position (0°). Due to increased cord impingement and upper cervical cord elongation at extension, hyperextension was avoided intra-operatively.

PATHOPHYSIOLOGY

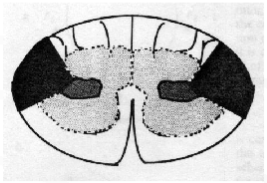
- Bohlman and Emery: Pathophysiology of CSM. Spine 13(7):843-46
- "The major pathologic entities are anterior cord compression and ischemia in conjunction with a congenitally narrow cervical spinal canal.

PATHOPHYSIOLOGY

- Levine DN: Pathogenesis of cervical spondylotic myelopathy. J. Neuro, Neurosurg. And Psych. 62:334-40
- The spinal cord at the level of spondylotic bar is flattened in the anteroposterior dimension but not in the transverse dimension.

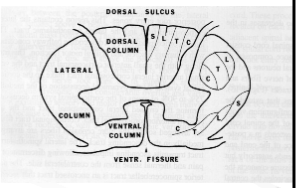
PATHOPHYSIOLOGY

- The damage is most severe in the cross sections at the level of spondylotic bar. There, the lateral columns are the most vulnerable, and in them the involved areas are often wedge shaped with the apex medial and the base lateral.

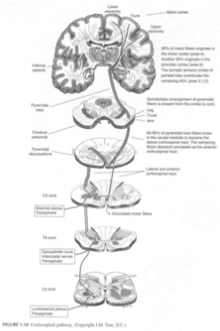


PATHOPHYSIOLOGY

- Because of the area of vulnerability the tract often affected is the Lateral Corticospinal Tract.
- This tract is Somatotopically arranged and therefore this is why we often see lower extremity symptoms first.

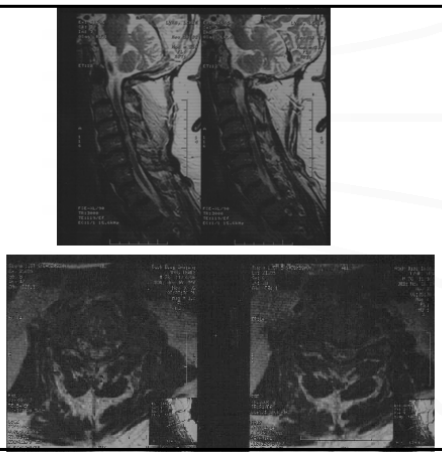


LATERAL CORTICOSPINAL TRACT



CLINICAL PRESENTATION

- Typical patient:
  - Over 50 y/o
  - Painful stiff neck
  - brachialgia and numb hands
  - Spastic leg weakness with unsteadiness of gait
  - Bladder symptoms are rare



IMAGING AND PROGNOSIS

- "Most multisegmental areas of high signal intensity on T2 MR images probably represent irreversible changes in the spinal cord, such as cavitations or cystic necrosis.
- Most focal areas of high signal intensity or areas of low signal intensity on T1 images represent reversible changes, such as edema."
- *Spine 1999 24:455-62*

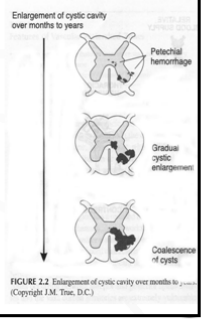


FIGURE 2.2 Enlargement of cystic cavity over months to
(Copyright J.M. True, D.C.)

IMAGING AND PROGNOSIS

- Most significant factors:
  - Transverse area of the spinal cord
  - Duration of symptoms
  - Number of blocks on myelogram

Spine 1999 24:455-62

TRANSCRANIAL MAGNETIC STIMULATION AND CSM

- Uses of MEP's in CSM:
  - Aspecific complaints consistent with myelopathy
  - Radiologic evidence of Cord compression without clinical signs
  - When only see Lower extremity complaints of UMN lesion
  - Identify the symptomatic level
  - Help to classify severity

Muscle and Nerve 1994

CLASSIFICATION OF MYELOPATHY

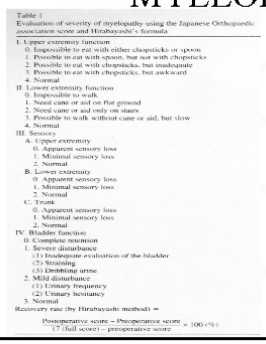


Table 1
Evaluation of severity of myelopathy using the Japanese Orthopaedic Association score and Hirabayashi's formula

I. Upper extremity function
0. Impossible to eat with either chopsticks or spoon
1. Possible to eat with spoon, but not with chopsticks
2. Possible to eat with chopsticks, but inadequate
3. Possible to eat with chopsticks, but awkward
4. Normal
II. Lower extremity function
0. Impossible to walk
1. Need cane or aid on flat ground
2. Need cane or aid only on stairs
3. Possible to walk without cane or aid, but slow
4. Normal
III. Sensory
A. Upper extremity
0. Apparent sensory loss
1. Minimal sensory loss
2. Normal
B. Lower extremity
0. Apparent sensory loss
1. Minimal sensory loss
2. Normal
C. Trunk
0. Apparent sensory loss
1. Minimal sensory loss
2. Normal
IV. Bladder function
0. Complete retention
1. Severe disturbance
(1) Inadequate evaluation of the bladder
(2) Straining
(3) Dribbling urine
2. Mild disturbance
(1) Urinary frequency
(2) Urinary hesitancy
3. Normal
Recovery rate (by Hirabayashi method) =

$$\frac{\text{Postoperative score} - \text{Preoperative score}}{17\ (\text{full score}) - \text{preoperative score}} \times 100\ (\%)$$

- Severe = <7
- Moderate = 7-12
- Mild = > 13

TREATMENT OF CSM

- CSM is slowly progressive with long intervals of partial remission during which the patient may be relatively comfortable and functional. Therefore, non-invasive therapy should is usually the first approach.

CONSERVATIVE TREATMENT OF CSM

- Prospective Randomized Trial:
- N = 48
- Mild to Moderate classification
- Followed at 6,12 and 24 months
- RESULTS:
  - No significant differences in changes over time with the Surgical vs. the Conservative management

Eur. Spine J. 2000 9:538-44

CONSERVATIVE TREATMENT

- Conservative treatment:
  - Continuous cervical traction (3-4 hours/day
  - Immobilization of cervical spine with orthosis
  - drug therapy and exercise therapy
- Conclusion:
  - "Conservative treatment is considered to be effective if it is performed intensively in selected patients"

The Spine Journal 2001 1:269-73

CONSERVATIVE TREATMENT

- N=64
- Treatment methods:
  - Continuous head halter traction: N=2
  - Cervical brace: N=19
  - Plaster bed holding head and trunk: N=15
  - Crutchfield skull traction: N=28

CONSERVATIVE TREATMENT

- RESULTS:
  - A rate of "No Disability" was achieved in 27% of upper extremity and 26% of lower extremity. The achieved function was maintained in most patients and some improved further during the follow-up period (3-19 years).
- *J. Spinal Disorders 1998 11(2):175-9*

TREATMENT OF CSM

- Is there a role for Manipulation in the CSM patient population?
- Murphy: " In a patient with early CSM, with more subtle signs of cord compression, a trial of skilled manipulation by a highly trained practitioner may not only be appropriate, but beneficial."
  Murphy: Cervical Spine Syndromes McGraw-Hill 2000

Complications of Cervical Spine Manipulation Therapy: 5-Year Retrospective Study in a Single-Group Practice

- During a 5-year period, practioners at a single group neurosurgical practice in Tulsa, Oklahoma, treated 22 patients, who were markedly worse during, or immediately after, CSMT.
- Complications in the series included radiculopathy (21 cases), myelopathy (11 cases), Brown-Séquard syndrome (two cases), and vertebral artery (VA) occlusion (one case). Twenty-one patients underwent surgery. Poor outcomes were observed in three, outcome was unchanged in one, and 17 improved.
- *Neurosurg Focus 13(6), 2002. © 2002 American Association of Neurological Surgeons*

Complications of Cervical Spine Manipulation Therapy: 5-Year Retrospective Study in a Single-Group Practice

- CONCLUSIONS:
- "Manipulation of the cervical spine appears to be associated with the possibility of worsening cervical radiculopathy or myelopathy and causing cervical disc herniation; cervical disc herniation can occur in a lateral position, compressing the VA and leading to posterior circulation ischemia"
- *Neurosurg Focus 13(6), 2002. © 2002 American Association of Neurological Surgeons*

TREATMENT OF CSM

- SURGICAL MANAGEMENT:
- Greater than 12 on mJOA scale
- Multiple levels of pathology with imaging findings
- Severe and progressive course of the disease

Cochrane Review on the Role of Surgery in Cervical Spondylotic Radiculomyelopathy

- **Results.** The short-term effects of surgery, in terms of pain, weakness, or sensory loss were superior. However, at 1 year no significant differences between the groups were observed. Another trial with 49 patients compared the effects of surgery with those of conservative treatment in patients who had a mild functional deficit associated with cervical myelopathy. No significant differences were observed between the groups up to 2 years after treatment.
- **Conclusions.** The data from the reviewed trials were inadequate to provide reliable conclusions on the balance of risk and benefit from cervical spine surgery for spondylotic radiculopathy or myelopathy.
- *Spine 2002;27:736–747*

LUMBAR SPINAL STENOSIS

- Spinal stenosis: A narrowing of the central canal, the lateral recess or the intervertebral foramen.
- Incidence: 1.7 to 8% of the general population.

Neurosurg. Focus 2003

Spinal Stenosis

- Lumbar spinal stenosis is a common cause of low back pain and the leading indication for lumbar surgery in the United States for persons over 65 years of age.
- *Clinics in Geriatric Medicine 2008*

NEUROGENIC CLAUDICATION

- Is characterized by intermittent development of pain in the lower back and legs in combination with signs of lumbosacral root dysfunction (dysesthesias, numbness, or motor weakness).
- ***Spine 2002 27(20):2284-90***

ETIOLOGY OF STENOSIS

- Degenerative soft tissue (ligamentum flavum)
- Bony Pathology: DISH, Paget's
- Vertebral displacement with an intact neural arch (Degenerative Spondylolisthesis)

Clin. Biomech. 1992 7:3-17

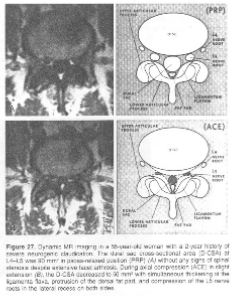
PROBLEMS?

- Spinal stenosis alone does not explain all of the symptoms. Spinal stenosis is sometimes entirely asymptomatic.
- The small canal therefore is only one factor in the pathology.

PROBLEMS?

- Central stenosis at one level does not account for the symptoms.
- Root canal stenosis cannot fully explain the symptoms
- One of the radiologic features of neurogenic claudication is the high frequency of multiple level stenosis in the central or root canals.

PATHOLOGY: Dynamic changes in canal diameter



PATHOPHYSIOLOGY

- NEUROPATHOLOGY:
  - Probably the result of inadequate oxygenation or accumulation of metabolites in the cauda equina.
  - Nerve function is adequate at rest but inadequate during exercise, therefore the changes have been shown to be reversible.

  Spine 2002 27(20):2284-90

PATHOPHYSIOLOGY

- MULTIPLE LEVEL PATHOLOGY:
  - The venous anatomy of the the roots of the cauda equina make the vulnerable to congestion at multiple levels.

  - *Porter and Ward: Cauda Equina Dysfunction: The significance of two-level pathology. Spine 1992 17(1):9-15*

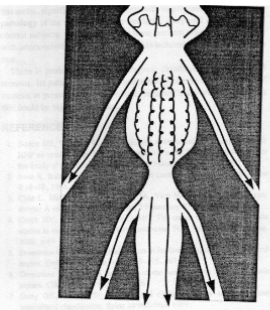


Fig 4. A two-level central canal stenosis near the venous pressure causes venous congestion and pooling in the nerve roots of the cauda equina, between the levels of stenosis.

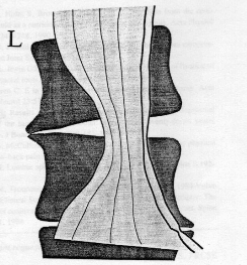


Fig 6. Diagram shows that a lumbar scoliosis concave to the left can cause central canal stenosis at the apex of the curve. One might initially expect left root claudication if the significant lesion were at the apex of the curve, but right L5 root canal stenosis can be part of a two-level lesion, with congestion of the L5 root and right-sided claudication.

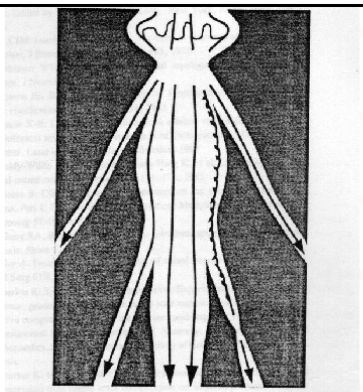


Fig 5. A one-level central canal stenosis combined with a one-level root canal stenosis near the venous pressure will produce venous congestion in one nerve root as well as pooling of venous blood.

PATHOPHYSIOLOGY

- If it is venous pooling, then why not constant symptoms?
  - Pressure of stenosis increases with walking
  - Increased venous return from the exercised extremities

Takahashi et al: Changes in Epidural pressure during walking in patients with LSS
Spine 1995 20(24):2746-49

SURGICAL TREATMENT

- Total Laminectomy at one or various levels, with a partial or total facetectomy, has been the classic approach used to achieve a thorough decompression of the spinal canal.

Lumbar Spinal Stenosis: Lippincott Williams and Wilkins, Philadelphia 2000

SURGICAL TREATMENT

- "There is no scientific evidence on the effectiveness of any form of surgical decompression or fusion for degenerative spondylosis compared with natural history, placebo, or conservative care"
- *Cochrane Review for Lumbar Disc Prolapse and Degenerative Lumbar Spondylosis. Spine 1999 24(17):1820-32*

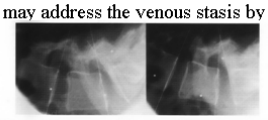
CONSERVATIVE TREATMENT

- EXERCISES: need to avoid extension
- SUPPORTS: Flexion bracing
- MEDICATION: NSAID's, Calcitonin, Calcium supplements and HRT
- EPIDURAL STEROIDS

Neurosurg. Focus 2003 14:1-9

MANIPULATIVE TREATMENT

- MANIPULATION:
  - Flexion/ Distraction: may address the central stenosis and may address the venous stasis by increasing the



DuPreist: JMPT 16(6):411-14
Snow: JMPT 2001 24(4):300-4

Flexion Distraction

- A treatment approach focusing on DM and NM may be useful in bringing about clinically meaningful improvement in disability in patients with LSS.

A non-surgical approach to the management of lumbar spinal stenosis: a prospective observational cohort study. Murphy DR, Hurwitz EL, Gregory AA, Clary R. BMC Musculoskelet Disord. 2006 Feb 23;7:16.

MANIPULATIVE TREATMENT

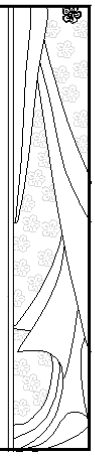
- HVLA:
  - Are central stenosis and Neurogenic Claudication contraindications to HVLA manipulation?
  - Does HVLA manipulation address the underlying pathology?

Interrupting the Cycle of Musculoskeletal Pain: Acupuncture for Older Adults

Linda Smith, DC

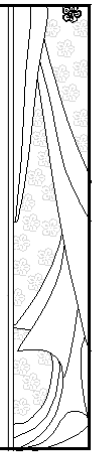
Interrupting the Cycle of Musculoskeletal Pain: Acupuncture for the Elderly

Linda Wheatland Smith, D.C.
Doctor of Chiropractic
Certified in Acupuncture

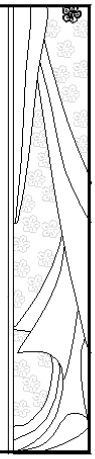


Musculoskeletal Pain and the Elderly

- The impact of musculoskeletal conditions on functional impairment outstrips that resulting from cardiovascular, respiratory, renal, gastrointestinal, psychiatric, and neurologic conditions in the United States [Sprangers *et al*. 2000].
- With the aging of the population and looming baby-boomer generation retirements, the burden of musculoskeletal disorders is only likely to increase.

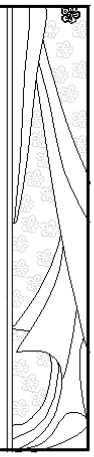


- Back and spine impairments are more common in women than men (73.3 versus 57.7 per 1000 population) and are most common between the ages of 45 and 64
- Lifetime prevalence of back pain exceeds 70%,with an annual cost in the United States estimated to be from $38 billion to more than $50 billion.

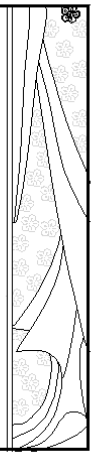


Osteoarthritis

- Osteoarthritis (OA) is a degenerative process involving all of the major joint tissues. It ultimately affects 8 of 10 elderly individuals of both sexes.
- Over the past 30 years, NSAIDs have been used for OA pain relief with only modest improvement over placebos and about as effective as acetaminophen.

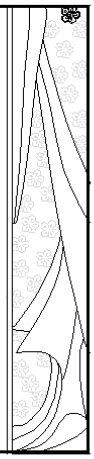


- It is apparent that **all** non-steroidal antiinflammatory drugs (NSAIDS), which include NSAIDs and COX-2 inhibitors, lead to variable degrees of fluid retention and blood pressure effects.
- These agents lead to increased blood pressure, an excessive risk of congestive heart failure and pro-thrombotic effects, especially in high risk populations.

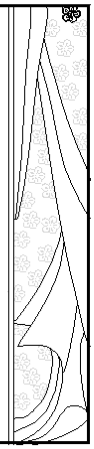


Acupuncture

- Acupuncture is commonly used for the treatment of pain. In traditional Chinese medicine the concepts of "meridian" and the vital energy "Qi" form part of the theoretical basis for needling at specific acupuncture points.

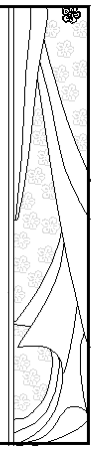


- Studies indicate that penetration of a needle through the skin, whether at an acupuncture point or not, has physiological effects. The "gate control theory" and the release of endogenous opiods have been suggested as explanations for the apparent analgesic effect of acupuncture.

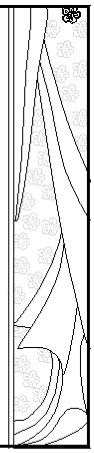


History of Acupuncture in the West

- Acupuncture was virtually unknown in the west until President Richard Nixon made his famous trip to China in 1972. James Reston of the *New York Times* had an emergency appendectomy on that trip and apparently developed paralytic ileus.
- Instead of passing a nasogastric tube, the Chinese physician inserted a needle (probably in his leg); Reston passed his gas, and the rest is history. Soon photographs and films were seen around the world of awake individuals undergoing surgery in apparent comfort with only acupuncture needles to prevent pain



- I spoke with Mr. Reston after this trip. He said that based on his experience, if he could study one more subject in his life, it would be acupuncture. His experience was transformative.

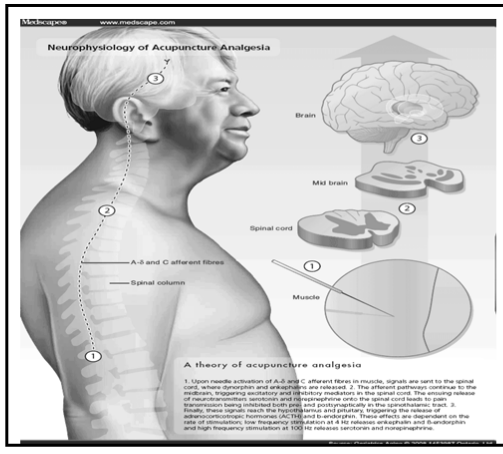


Efficacy of Acupuncture

- Research on the neurophysiology of acupuncture analgesia supports the theory that it is mediated primarily via the **selective release in the central nervous system of neuropeptides.**
- Evidence of its anti-inflammatory effects is emerging. Meta-analyses of randomized controlled trials provide evidence for acupuncture's effectiveness in treating back pain, neck pain, and osteoarthritis.

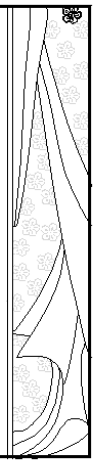
Mechanisms of Acupuncture

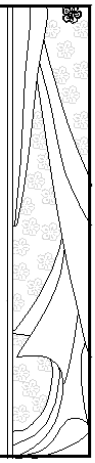
- There is evidence that the **limbic system** plays a significant role in acupuncture-induced analgesia.
- Research with animal models of acupuncture indicates that many of the beneficial effects may be mediated at the **subcortical level in the brain.**



Safety and Contraindications of Acupuncture

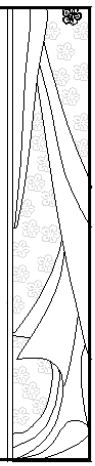
- When considering acupuncture as a potential treatment, there is no contraindication based on risk if the therapist knows the anatomy and a clean needle technique is used.





- Local skin infection or breakdown dictates that points in the area of skin involvement not be used.
- The most problematic contraindication is the presence of a cardiac pacemaker when electrical stimulation on needles is indicated.

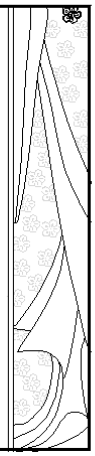
Vitamin D Screening and PAin



- Before using acupuncture to treat musculoskeletal aches and pains, screening for hypovitaminosis D should be considered.
- Chronic nonspecific musculoskeletal pain is linked to low levels of 25-OH-vitamin D3.[12,13] The level that reduces fracture risk is now generally accepted as 75 nmol/L (30 ng/mL),[8,14] and the optimal range is considered by some experts to be 130-170 nmol/L (52–68 ng/mL), the level that the body maintains when most vitamin D comes from sun exposure.[15]

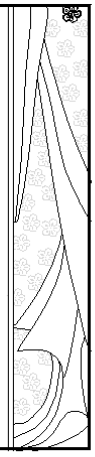
Myofascial Pain

- This type of pain can be treated with acupuncture aimed at releasing tightness and pain by dry-needling trigger points directly with an acupuncture needle, usually giving quick relief that is cumulative with several treatments.



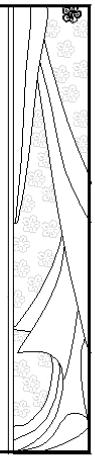
Myofascial Pain and Acupuncture

- Whether there is complete resolution of symptoms depends on the underlying cause, whether there is the opportunity to treat the person enough times, and the extent to which one integrates acupuncture treatment with nutritional and lifestyle changes, exercise, good chiropractic and physiotherapy, attention to perpetuating factors, and ergonomic adjustments.



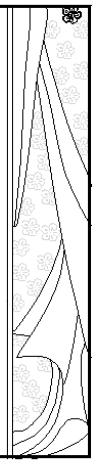
Anti-inflammatory Effects

- Acupuncture has anti-inflammatory effects in addition to analgesic effects; the **autonomic nervous system** may be involved.[26,27] Treating a swollen arthritic knee joint usually results in decreased swelling and increased range of motion, not just pain relief, providing objective evidence that inflammation has been reduced.[28]

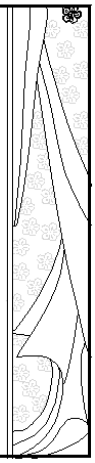


A Clinician's Approach

- Methodical medical history, examination, and imaging must exclude diagnoses that require alternate medications, interventions and treatments.

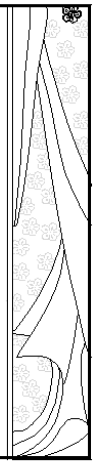


- Diagnoses that have proved responsive to acupuncture include **myofascial damage throughout the body, osteoarthritis, spinal degeneration including spinal stenosis, sciatica, disc bulging and degeneration, tendinopathy, bursitis, and tension headaches.**



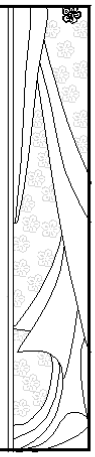
Can you reproduce the patient's pain with palpation of the musculature of the area?

- Examination of the patient should include careful palpation of the involved area.

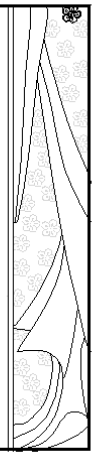


Acupuncture Needle Technique

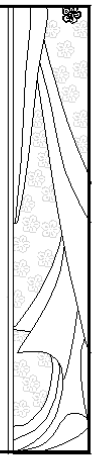
- Needle technique includes choices of general points shown to stimulate endorphins: ie LI4 on the hand, BL 40 on the back of the knee.
- Choice of needle placement in the area of pain is based upon palpation and reproduction of symptoms.
- **Surround The Dragon**



- Location of area Trigger Points is a key to success.
- Needles are placed deep into the injury, until an aching sensation is felt by the patient.



- Electric stimulation is connected to enhance the effect of the needles. This may make the difference between a treatment that helps and one that has no effect.
- The needles with the electric stim are left in place for 20 minutes. This is the optimum time for endorphin stimulation. The room is quiet with nice music and a pleasant temperature.



Needles in Place with Electric Stim

Signs of Success with Acupuncture

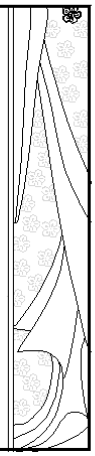
- The patient may experience pain relief and improved mobility immediately.
- The patient may experience increased pain and soreness for 24-48 hours.
- After 5-7 days it should be very clear what the acupuncture has accomplished.
- Within four to six treatments pain levels should decrease and function should improve significantly.

Case Presentation
Bilateral Sciatica and Low Back Pain

- 72 yo male HT 6'1", 240
- Meds include Cozzar for HBP, Celebrex for pain, Fexofenidene for allergies
- Pt in this office since 1998
- Previous treatment here for HA, neck pain, LBP. Pt was responsive to manipulation, massage, and exercise.

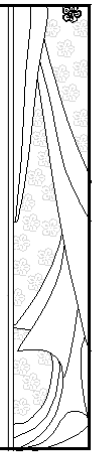
Current Presentation

- Pt. presents 6 weeks ago with LBP, deep buttock pain and sciatic pain down both legs. Pain intensifies with walking and lessens with sitting.
- MRI of lumbar spine indicates degenerative disc disease with mild diffuse disc bulging from L1 through sacrum.



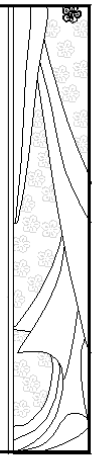
Treatment Plan

- Tx plan includes acupuncture, deep tissue massage and Cox distraction technique.
- 1x week treatment plan
- Tx also includes functional activities with a focus on the function and strength of the lower abdominal muscles

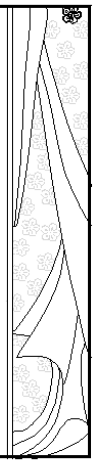


Acupuncture Methodology

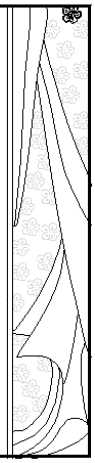
- Position patient on the flat table prone with a flat pillow under pelvis and fatter pillow under lower legs. This is very important so the lumbar spine and musculature can relax.
- Attach electro-acupuncture to LI4 and BL40. Stimulation of LI4 has shown high production of endorphins. BL 40 is traditionally chosen for LBP and sciatica.



- Using 2 inch needles, search for the tender/trigger point areas of pain in the low back and buttocks.The goal is to reproduce the patient's ache of injury with palpation and needle placement.
- Attach electric stim to these needles and allow the patient to rest for 20 minutes.

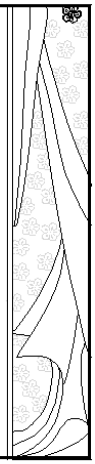


- Remove the needles and use deep trigger point massage and stripping massage technique to release the tightness and congestion in the musculature of the low back and buttocks.
- Instruct the patient in exercise and body mechanics



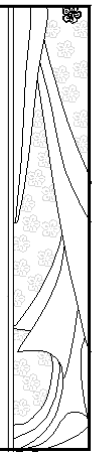
Results

- Patient has been treated here for four visits. Two acupuncture and two traction sessions.
- The patient has improved by at least 60%. He can walk with less pain and sleep more comfortably.
- He is now able to pursue his exercise goals which will continue to help reduce his pain.



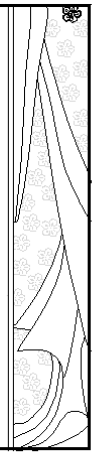
Severe Spinal Stenosis and Sciatica

- 81 year old female,5'3", 145lbs
- Normal vital signs
- Ultracet
- Complaint is right hip and buttock pain with significant sciatica
- MRI demonstrates severe spinal stenosis with multilevel disc degeneration



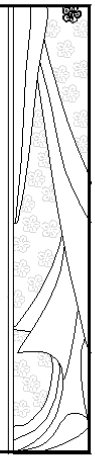
History

- Duration of buttock and leg pain is 11 months
- Previous tx includes medication, physical therapy and 2 epidural steroid shots, all of which was not helpful
- The patient had polio and now wears a brace on her right foot. This affects her body mechanics while walking.

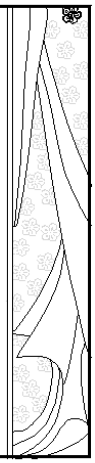


Acupuncture Methodology

- Pt lay on side with pillow between knees.
- Electro-acupuncture attached to LI4 and ST36
- Needles were placed in the hip and buttocks, reproducing the pain syndrome. The piriformis muscle was contracted and very involved in the pain syndrome. SIx needles were placed there. The needles were connected to electric stim and left in place for 20 minutes. The room was pleasant and nice music was played.

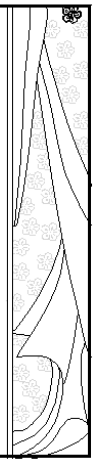


- Deep tissue massage was performed following the acupuncture treatment.
- The patient was given very simple low abdominal exercises and gluteus medius exercises to stabilize her core and pelvis.



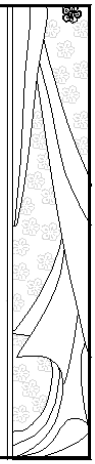
Outcome

- Very successful case. The patient's pain resolved 100%.
- She was able to resume walking, travel, and volunteering.
- She worked on her exercises after she was out of pain.



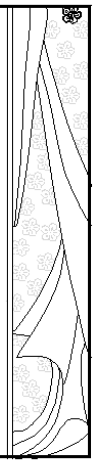
Follow Up

- I saw her again this year for a flair up of pain. This was three and one half years after her care here.
- This time it was only local back pain. I saw her 4 times and the pain again resolved. She is now 85.



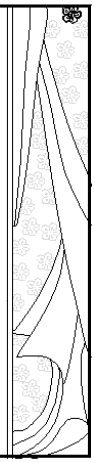
Hip Bursitis

- 55 year old female with hip pain
- Dx with hip bursitis by orthopedist
- Went to PT 3 times/week for three weeks and received exercises such as wall sits.
- She had no relief form this treatment



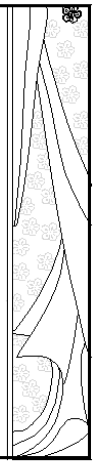
Diagnosis and Treatment

- MRI revealed no bursitis
- Dx Myofascial Pain Syndrome
- Acupuncture to right hip
- Two visits
- Pain resolved completely



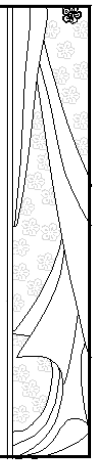
Outcome and Follow Up

- Follow Up two months later. Patient can now walk five miles with only a little tenderness.
- She is working with a trainer to strengthen her core and hip musculature



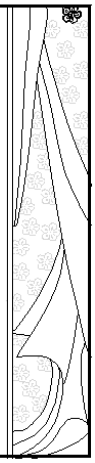
Recommendations for Referral for Acupuncture

- Chiropractors have good backgrounds in body mechanics and diagnosis of pain syndromes. Find a chiropractor with training in acupuncture for referrals.
- Moderate chronic pain syndromes are most responsive to acupuncture
- Severe acute pain needs a different approach, ie severe herniated discs with attendant disabling pain, pinched cervical nerves with acute arm pain.

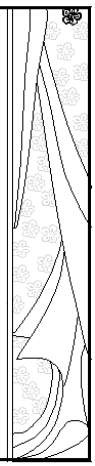


Recommendations continued

- Back, Hip, Elbow, Shoulder, Neck are most responsive. Areas with muscular tissue available for needling. Bursitis, Tendinitis, Plantar Fascitis, Lumbar Disc Syndrome, Sacroiliac Syndrome, Piriformis Syndrome, Rotator Cuff injuries.

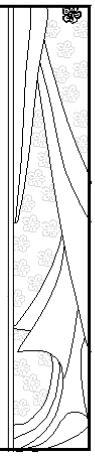


- Electric Stim is KEY to success. 20 minutes is optimal time frame for treatment. Endorphin/Enkephalin production peaks at 20 minutes. Alternating Hz from low (4hz) to high (100hz) helps produce range of neurotransmitters from short acting to longer acting for pain relief.



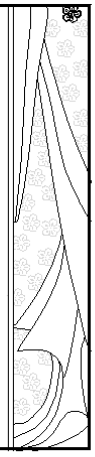
Recommendations continued

- Deep trigger point massage, Active Release Technique VERY helpful adjunct to the acupuncture.
- Helpful to include body mechanics, posture in education of patient

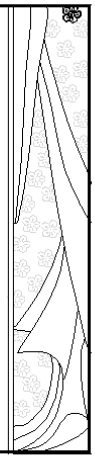


WHAT is Acupuncture doing for the patient in this protocol?

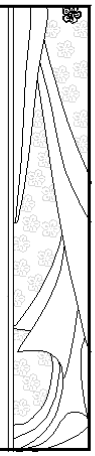
- It is interrupting the myofascial pain pattern at the local level of the musculature and at the level of the brain where the pain syndrome becomes a recalcitrant pattern.
- The needling deep into the musculature helps break up the tight, stiff, painful tissue that hands-on work and physical agents cannot penetrate.



- Peripheral acupuncture points stimulate endorphin production in the brain which helps promote homeostasis in the body and decreases pain signals from the brain to the area of damage.



Questions



Guided Imagery for Pain Management

Jane Hart, MD

Guided Imagery

Jane Hart, MD
Chair, Integrative , Complementary and Alternative Medicine Committee
Case Western Reserve University School of Medicine

Objectives

- Definitions
- Theory
- Research
- Pain Research

Things to Consider

- Reducing emotional stress and physical tension is key in the management of chronic pain
- Complementary therapies may be particularly useful for this aspect of pain management
- Therapies must be tailored for the individual to be successful

Things to Consider

- There is no single remedy in the management of chronic pain
- An integrative approach will consider:
  - Conventional methods
  - Lifestyle behavior change
  - Complementary therapies
  - Specialists
  - Regular patient-physician communication and follow-up

What is Guided Imagery?

- Complementary therapy
- Considered a mind-body therapy by National Center for Complementary and Alternative Medicine
- Increasingly popular in clinical settings
- Blue Shield of California
- Cleveland Clinic Foundation

Definitions

- Use of story or narrative to guide images the mind creates to bring about beneficial emotional and physical effects
- "Any of various techniques (as a series of verbal suggestions) used to guide another person or oneself in imagining sensations and especially in visualizing an image in the mind to bring about a desired physical response (as a reduction in stress, anxiety, or pain)" (Merriam Webster's Dictionary)

Theory

- Thoughts are powerful
- Habitual negative or frightening thoughts and images may increase pain or anxiety
- A person may be trained to focus on positive or calming thoughts and images that reduce pain and anxiety
- Guided imagery may include positive thinking but is not limited to that construct – example

Typical Session

- Guided imagery may be delivered by a live practitioner, through audio or video or a person may guide his or herself through an imagery session
- Group or individual setting
- Session begins with relaxation – deep breathing and/or progressive muscle relaxation, music may be included
- Then the person begins to visualize imagery through other or self-direction created to promote healing

Types of Imagery

- Different types of guided imagery have been described:
  - Pleasant imagery (imagining a calm place)
  - Physiologic focused imagery (focusing on a physiologic function that needs healing)
  - Mental rehearsing or reframing (imagining a specific task or performance before the event occurs or reframing a prior event)

Van Kuiken D. J Holist Nurs 2004;22:164–179.

Mechanism of Action

- Exact mechanism of action not well-known
- Attenuation of the stress response through psychoneuroimmunologic pathways
- Gate Control Theory
- Endorphin release

Research

- Guided imagery may be particularly helpful with:
  - Stress-reduction
  - Reducing anxiety
  - Reducing pain
  - Preparation for and recovery from surgical procedures

Research

- Limitations of guided imagery research include:
  - Heterogeneous populations, interventions and outcomes across studies
  - Lack of research
  - Small study size
  - Optimal timing and "dose" of sessions
  - Who best benefits from this complementary therapy – unique characteristics and specific medical conditions and comparison with other complementary therapies

Pain Research

- Guided Imagery and Pain

Outcomes

- Success of imagery may be affected by:
  - Type of pain
  - Intensity of pain
  - Prior use of imagery
  - Pacing of imagery
  - Type of imagery

Things to Consider

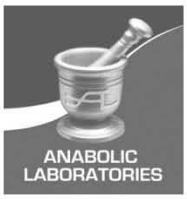
- Clinicians should think about guided imagery as an inexpensive adjunctive therapy in the treatment of some pain conditions
- Network with colleagues to find credible practitioners
- Work with practitioners that are familiar with your patients' conditions

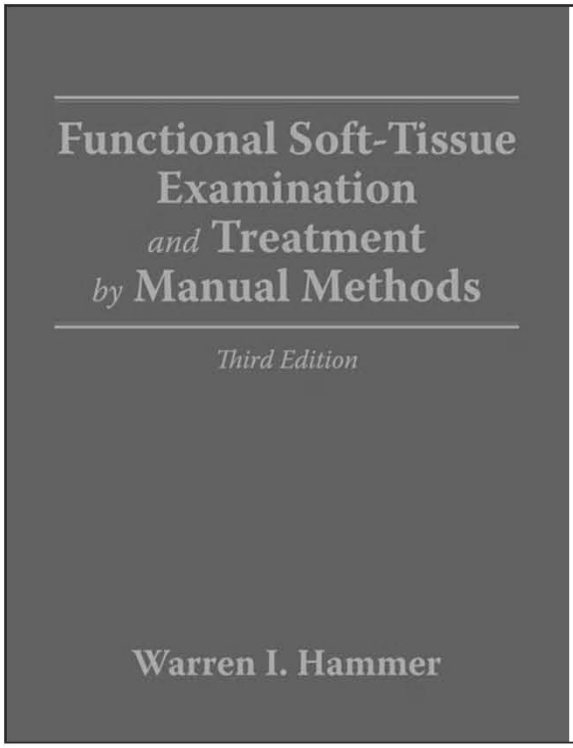
The Chemistry of Inflammation and Nociception: Insights into Nutritional Modulation

David Seaman, DC

Chronic pain in the aging population: Nutritional considerations

David R. Seaman, DC, MS, DACBN

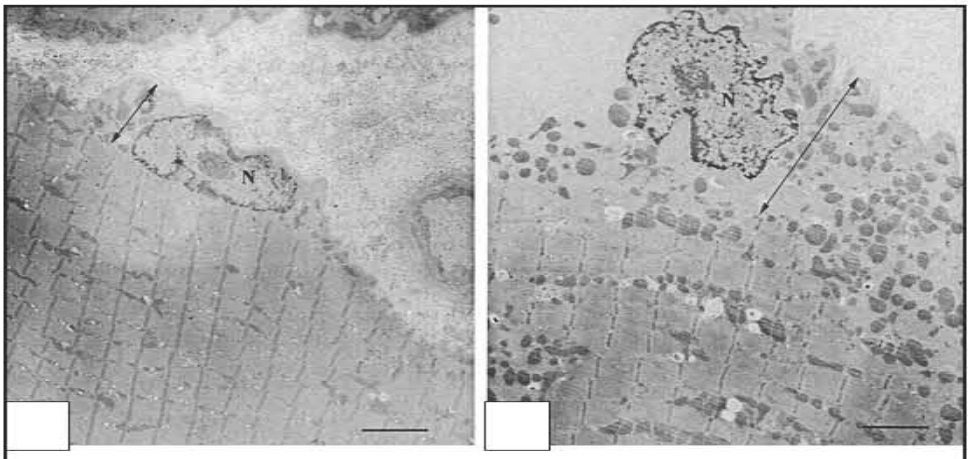
Dir Clin Ed	Adj Assoc Prof PCCF	Private Practice
		



Seaman DR.

Nutritional considerations in the treatment of soft tissue injuries.

In Hammer WI. Editor. Functional soft-tissue examination and treatment by manual methods. Boston: Jones & Bartlett; 2007: p.717-734



Electron micrograph of skeletal muscle.

Which one is normal??

Conley KE, Marcinek DJ, Villarin J.

Mitochondrial dysfunction and age.

Curr Opin Clin Nutr Metab Care. 2007; 10:688–692.

Rejuvenating mitochondria as we age:

- Calorie restriction***
- Endurance training
- Strength training

Arth Rheum. 2009; 60(2):470-81

ARTHRITIS & RHEUMATISM
Vol. 60, No. 2, February 2009, pp 470–481
DOI 10.1002/art.24268

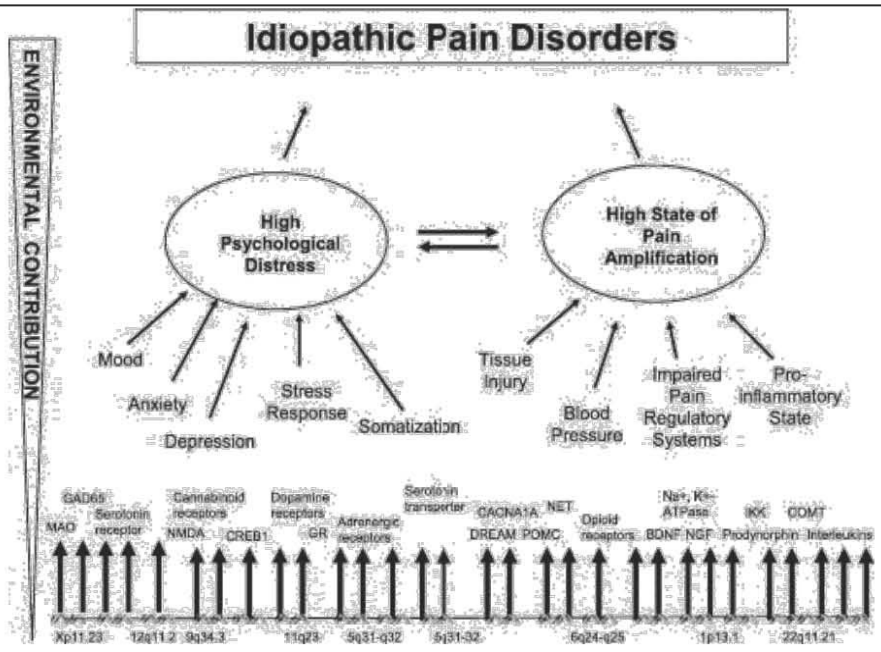
Associations of 25 Structural, Degradative, and Inflammatory Candidate Genes With Lumbar Disc Desiccation, Bulging, and Height Narrowing

Tapio Videman,[1] Janna Saarela,[2] Jaakko Kaprio,[3] Annu Näkki,[3] Esko Levälahti,[4] Kevin Gill,[5] Leena Peltonen,[2] and Michele C. Battié[1]

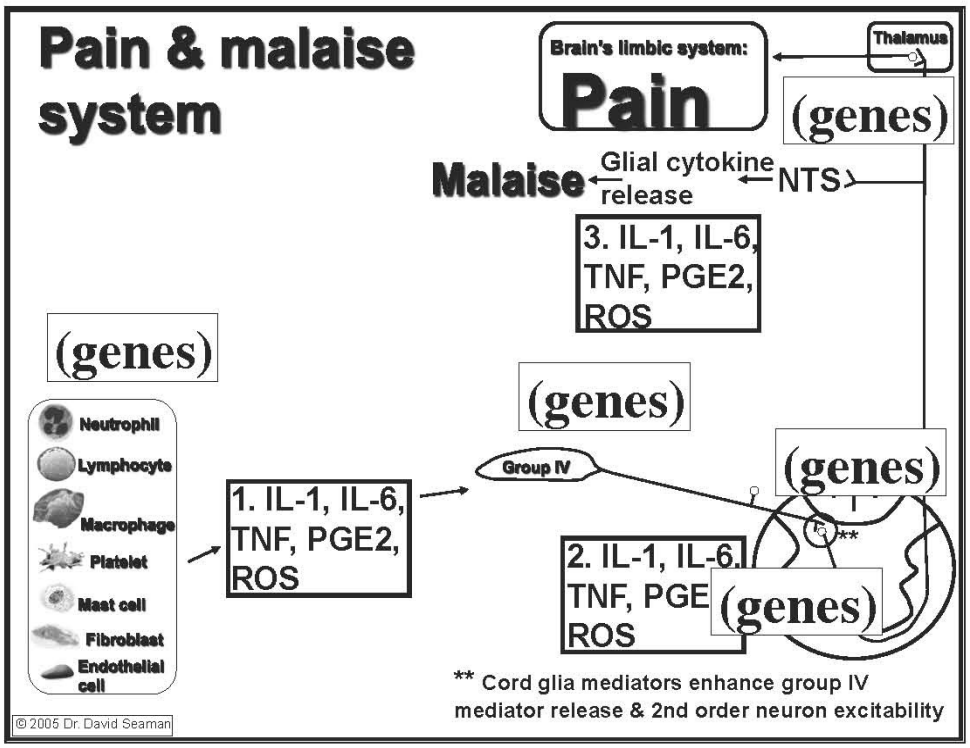
Objective. **To examine the allelic diversity of structural, inflammatory, and matrix-modifying gene candidates and their association with disc degeneration.**

Methods. **Subjects were 588 men ages 35–70 years. We investigated associations of single-nucleotide polymorphisms in AGC1 and in 12 collagen, 8 interleukin, and 4 matrix metalloproteinase genes with quantitative magnetic resonance imaging measurements of disc desiccation and disc bulging and height narrowing scores, after controlling for age and suspected risk factors. Analyses were performed using QTDT software. *P* values were derived from 1,000 permutations, and empirical *P* values for global significance also were applied.**

Results. **Twelve of the 99 variants in 25 selected candidate genes provided evidence of association ($P < 0.05$) with disc signal intensity in the upper and/or lower lumbar regions. Allelic variants of AGC1 (rs1042631; $P = 0.001$), COL1A1 (rs2075555; $P = 0.005$), COL9A1 (rs696990; $P = 0.00008$), and COL11A2 (rs2076311; $P = 0.018$) genes provided the most significant evidence of association with disc signal intensity. The same variants of AGC1 ($P = 0.010$) and COL9A1 ($P = 0.014$), as well as variants in the COL11A1 gene (rs1463035 [$P = 0.004$]; rs1337185 [$P = 0.015$]) were also associated with disc bulging, as was AGC1 with disc height narrowing (rs1516797; $P = 0.005$). In addition, 4 allelic variants in the immunologic candidate genes (rs2071375**



Diatchenko L, Nackley AG, Slade GD, Fillingim RB, Maixner W. Idiopathic pain disorders - pathways of vulnerability. Pain 2006; 123:226-30



ELSEVIER

Available online at www.sciencedirect.com

SCIENCE DIRECT®

European Journal of Pharmacology 469 (2003) 65–69

ejp

www.elsevier.com/locate/ejphar

Does Mg^{2+} deficiency induce a long-term sensitization of the central nociceptive pathways?

Abdelkrim Alloui[a,*], Sophie Begon[a], Claude Chassaing[a], Alain Eschalier[a], Eliette Gueux[b], Yves Rayssiguier[b], Claude Dubray[a]

[a] *INSERM EMI 9904/UdA Laboratoire Pharmacologie Fondamentale et Clinique de la Douleur, Faculté de Médecine, B.P. 38, 63001 Clermont-Ferrand, Cedex 1, France*

[b] *Unité Maladies Métaboliques et Micronutriments, INRA, 63122 St-Genes-Champanelle, France*

Received 21 October 2002; received in revised form 31 March 2003; accepted 4 April 2003

Abstract

In rats, a Mg^{2+}-deficient diet, which in a few days dramatically decreased the Mg^{2+} concentration in plasma, cerebrospinal fluid (CSF) and spinal cord, was accompanied by a significant lowering of the nociceptive threshold. After reloading, the Mg^{2+} concentration was rapidly normalized in both spinal cord and CSF. In parallel, the neurological disturbances induced by Mg^{2+} deficiency vanished in less that 24 h, but the reversal of the hyperalgesia was delayed for up to 11 to 20 days. In this model, repeated doses of dizocilpine (MK-801), a non-competitive NMDA receptor antagonist, given at start of the Mg^{2+}-depleted diet, prevented hyperalgesia, suggesting the involvement of NMDA receptor channels. The delayed recovery of a normal pain threshold argues for long-term sensitization of the nociceptive pathways.

Eur J Pharmacol. 3002; 469:65-69

Pain. 2005; 114:455-61

PAIN

Pain 114 (2005) 455–461

www.elsevier.com/locate/pain

Analgesic effects of dietary caloric restriction in adult mice

Walter A. Hargraves, Ian D. Hentall*

College of Medicine, University of Illinois, Rockford, IL 61106, USA

Received 2 July 2004; received in revised form 6 December 2004; accepted 18 January 2005

**** Never studied in humans**

Abstract

Nociception was studied in male mice, mostly of the C57BL/6 strain, during continuous or prolonged restriction of caloric intake (60% of ad-libitum) from midlife to senescence (up to 105 weeks). Restricted mice showed fewer licking or biting responses 20–60 min after hind paw injection of 5% formalin at 46 and 70 weeks, but not at 93 weeks. Also, they showed longer response latencies around 46 weeks of age in the 52 °C hot-plate test, which partial tail amputation failed to affect, although it did produce at least 2 weeks of chronic neuropathic hypersensitivity in ad libitum controls. Injection of collagen subcutaneously at 36–42 weeks led to chronic hyperalgesia in the DBA/1 but not the C57BL/6 strain, measured weekly by the barely nociceptive 50 °C hot-plate test to minimize damage. This collagen-induced arthritic hyperalgesia was then gradually and reversibly blocked during 9–15 weeks of caloric restriction starting at 53–58 weeks. In longitudinal trials on normal mice, performed every 2–4 weeks between 42 and 105 weeks with the 50 °C hot-plate, caloric restriction led to altered latencies (higher relative to controls) only in the last 10–20 weeks, perhaps because it delayed the onset of age-related peripheral neuropathies. In conclusion, long-term caloric restriction leads to significant hypoalgesia in pre-senescent mice subjected to above-threshold pain of widely different durations, the effect disappearing at later ages unless spontaneous neuropathies become influential. A reduction in cumulative food intake thus appears to generate antinociceptive signals in adult male mice, perhaps serving specifically to promote riskier behavior during prolonged food shortages.

Pain. 2007; 129:5-7

PAIN

Pain 129 (2007) 5–7

www.elsevier.com/locate/pain

Editorial

Food and pain: Should we be more interested in what our patients eat?

Hippocrates wrote "Let food be thy medicine…". In this issue of Pain, Goldberg and Katz present an interesting meta-analysis of studies investigating the relief of chronic inflammatory pain using omega-3 polyunsaturated fatty acid supplementation.

That diet may have relevance for pain and pain treatment should not come as a surprise. At the most basic level, the nervous system requires nutrients in order to function optimally. For example, endogenous pain-relieving systems require essential amino acids such as tryptophan, which is the precursor of serotonin and abundant in turkey, chicken, avocados and bananas. Vitamin deficiency can result in painful neuropathies.

Links between diet and pain abound. Particular food types have been associated with analgesia. It is well

The concept of *functional food* was developed in the 1990s (Palou et al., 2003). A functional foodstuff is more than a simple nutrient, having in addition an effect which promotes health or combats disease. Phytosterol-enriched foods which decrease cholesterol levels are an example of manufactured functional food. Herbs and spices are rich in bioactive compounds and there is ongoing research into their possible health-promoting effects (Tapsell et al., 2006). Dietary polyphenol antioxidants and flavonoids in plant foods may also provide health benefits, chronic disease being linked to oxidative stress (Urquiaga and Leighton, 2000). One example is resveratrol, a polyphenol compound found in grapes, berries and peanuts, which has both anti-inflammatory and antioxidant activity (de la Lastra and Villegas,

Modern diet - source of calories

10% dairy products

1-2% alcohol

20% refined grains/pasta/bread/cereal

20% refined sugars

20% refined vegetable oils

15-20% obese meat

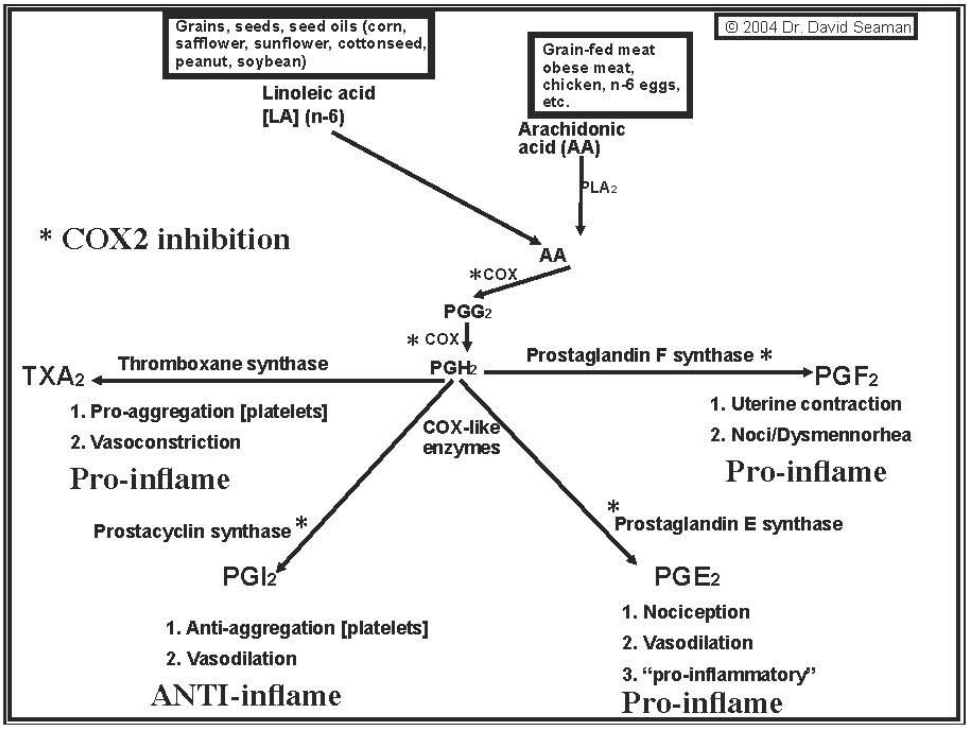
<10% vegetables, fruit (potatoes, **legumes, whole grains**)

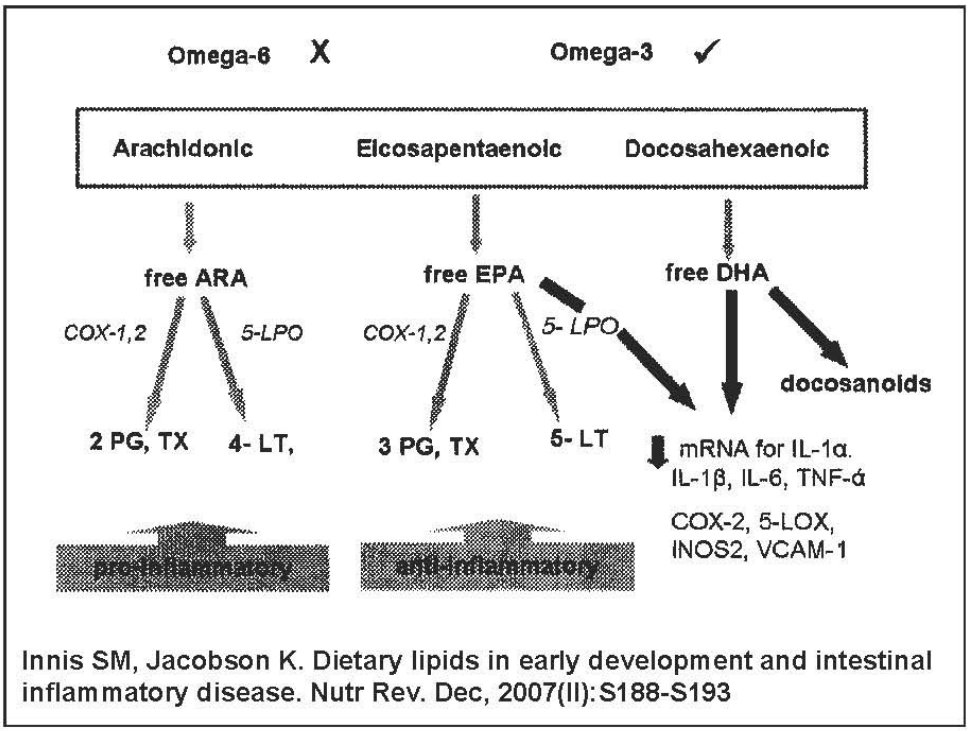
Cordain L et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr. 2005; 81(2):341-54.

COX-2 Dangers

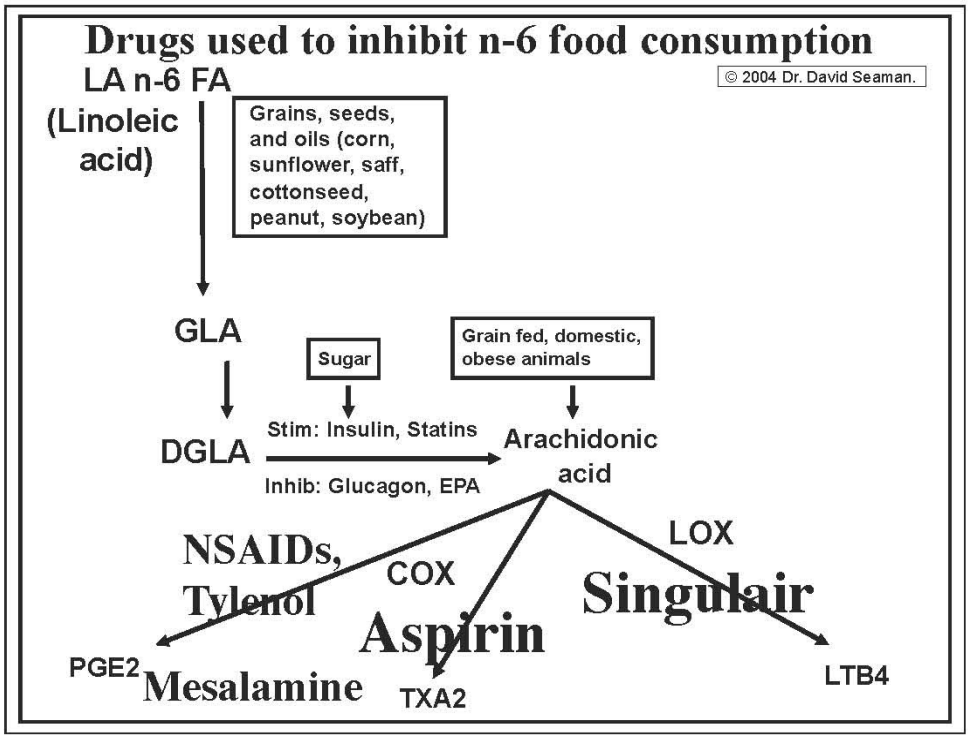
Low dose aspirin	COX-2 inhibitors
↓Thromboxane synthesis	-- Thromboxane synthesis
-- Prostacyclin synthesis	↓ Prostacyclin synthesis
therefore,	*therefore,*
Anti-thrombobtic	**Pro-thrombobtic**

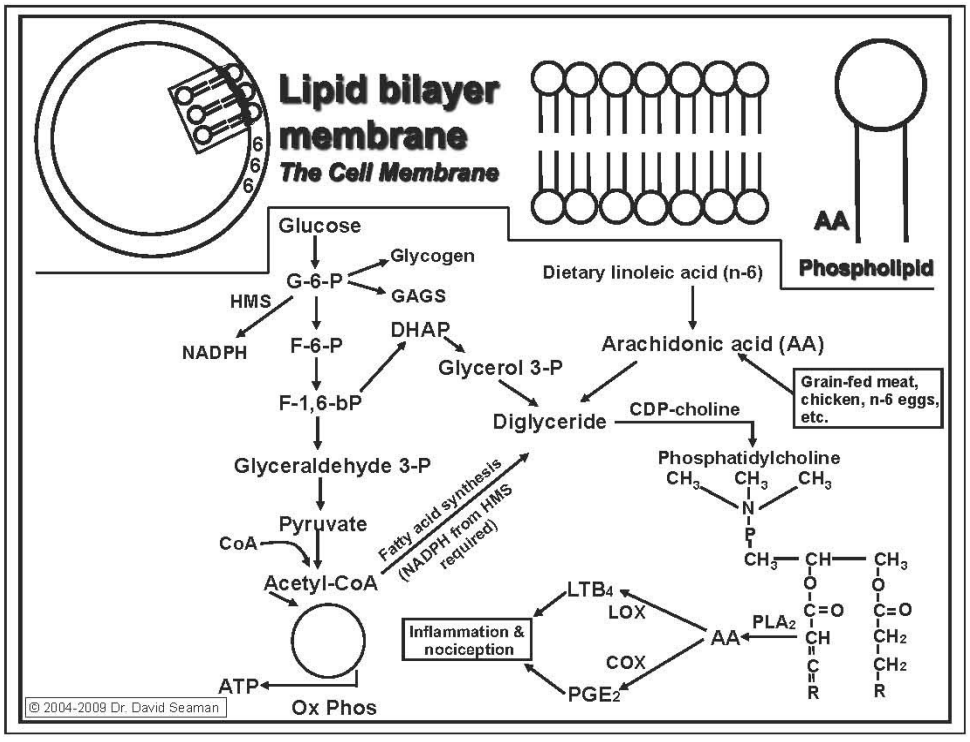
Wallace JL, Muscara MN. Selective cyclo-oxygenase-2 inhibitors: cardiovascular and gastrointestinal toxicity. Digest Liver Dis 2001: 33(suppl 2): S21-S28

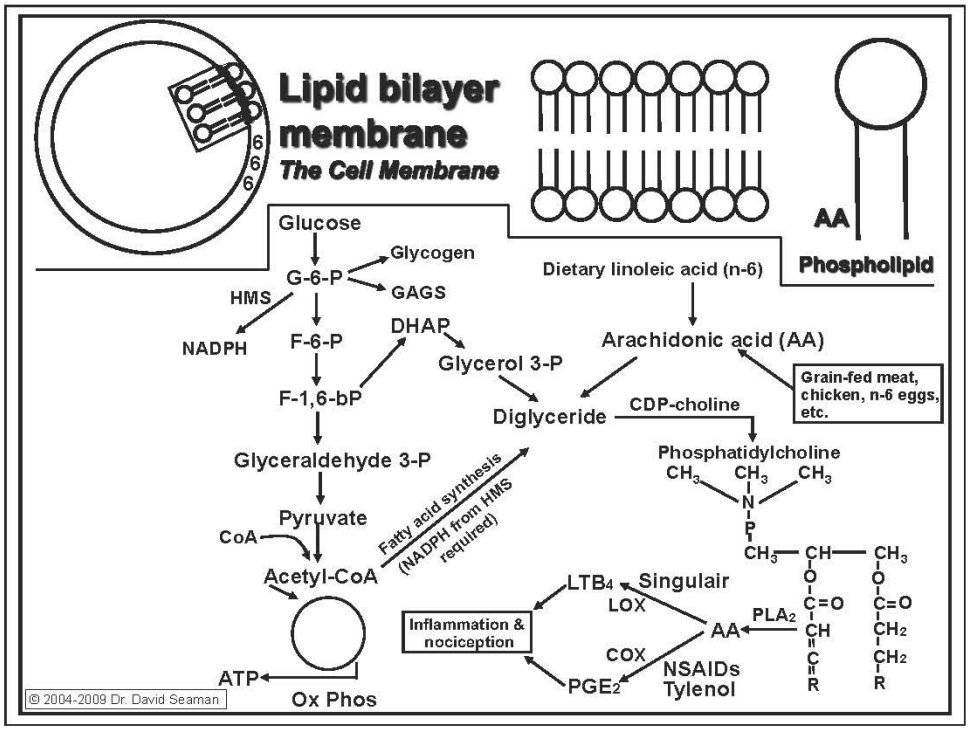


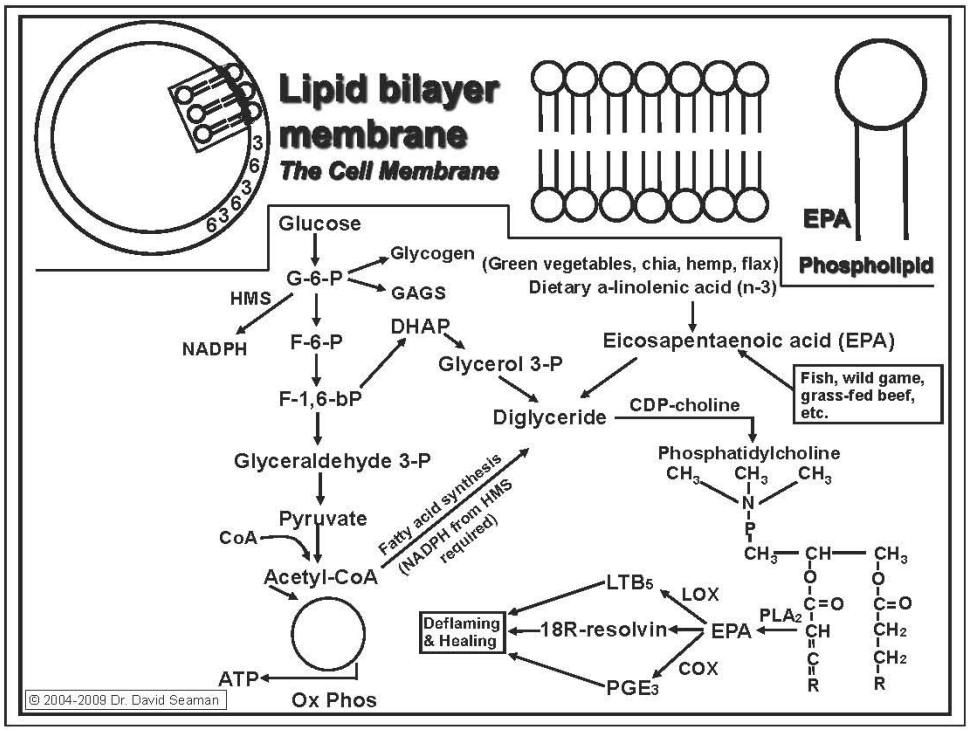


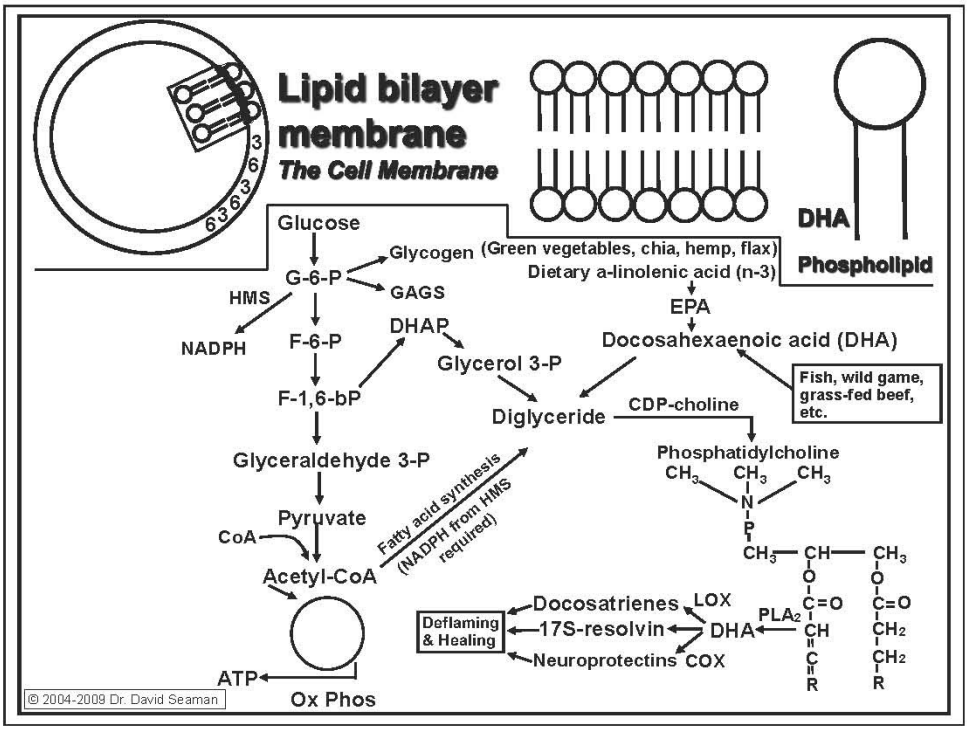
Innis SM, Jacobson K. Dietary lipids in early development and intestinal inflammatory disease. Nutr Rev. Dec, 2007(II):S188-S193

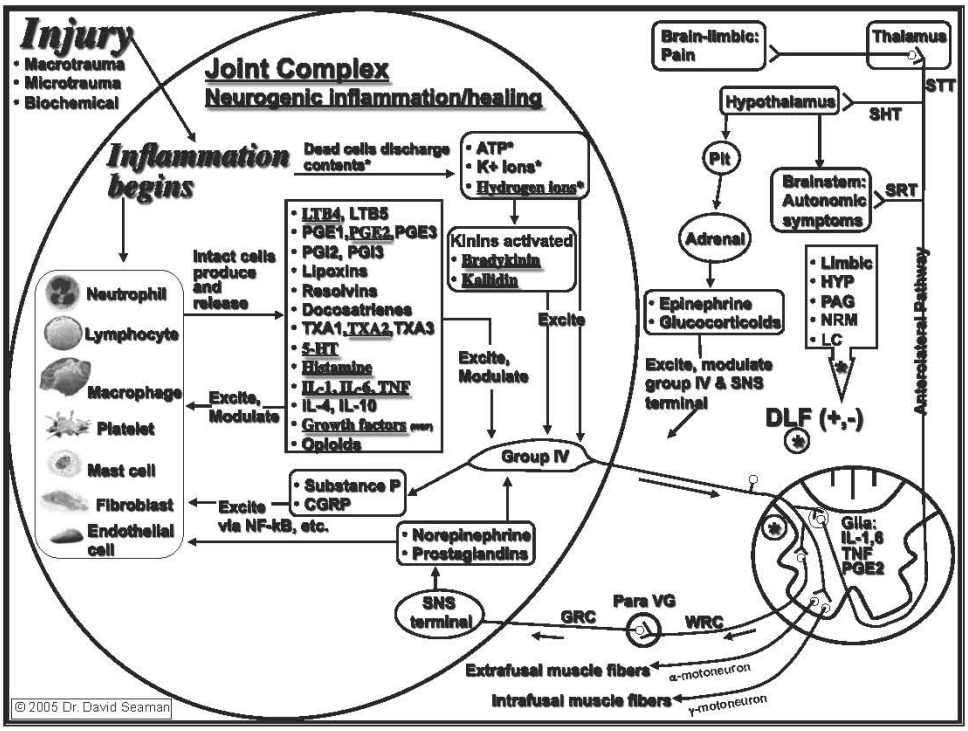

Drugs used to inhibit n-6 food consumption
© 2004 Dr. David Seaman.
LA n-6 FA
(Linoleic acid)
Grains, seeds, and oils (corn, sunflower, saff, cottonseed, peanut, soybean)
GLA
Sugar
Grain fed, domestic, obese animals
DGLA
Stim: Insulin, Statins
Inhib: Glucagon, EPA
Arachidonic acid
NSAIDs, Tylenol
COX
LOX
Singulair
Aspirin
PGE2
Mesalamine
TXA2
LTB4


Lipid bilayer membrane
The Cell Membrane
AA
Phospholipid
Glucose
Glycogen
G-6-P
GAGS
HMS
NADPH
F-6-P
DHAP
F-1,6-bP
Glycerol 3-P
Dietary linoleic acid (n-6)
Arachidonic acid (AA)
Grain-fed meat, chicken, n-6 eggs, etc.
Diglyceride
CDP-choline
Phosphatidylcholine
Glyceraldehyde 3-P
Pyruvate
CoA
Fatty acid synthesis (NADPH from HMS required)
Acetyl-CoA
ATP
Ox Phos
LTB4
LOX
Inflammation & nociception
COX
PGE2
AA
PLA2
© 2004-2009 Dr. David Seaman


Lipid bilayer membrane
The Cell Membrane
6
6
6
AA
Phospholipid
Glucose
Glycogen
G-6-P
GAGS
HMS
NADPH
F-6-P
DHAP
Glycerol 3-P
F-1,6-bP
Dietary linoleic acid (n-6)
Arachidonic acid (AA)
Grain-fed meat, chicken, n-6 eggs, etc.
Diglyceride
CDP-choline
Phosphatidylcholine
Glyceraldehyde 3-P
Pyruvate
CoA
Fatty acid synthesis (NADPH from HMS required)
Acetyl-CoA
LTB4
Singulair
LOX
Inflammation & nociception
PLA2
AA
COX
PGE2
NSAIDs
Tylenol
ATP
Ox Phos
© 2004-2009 Dr. David Seaman


Lipid bilayer membrane
The Cell Membrane
3
6
3
6
3
6
EPA
Phospholipid
Glucose
Glycogen
G-6-P
GAGS
HMS
NADPH
F-6-P
DHAP
Glycerol 3-P
F-1,6-bP
(Green vegetables, chia, hemp, flax)
Dietary a-linolenic acid (n-3)
Eicosapentaenoic acid (EPA)
Fish, wild game, grass-fed beef, etc.
Diglyceride
CDP-choline
Phosphatidylcholine
Glyceraldehyde 3-P
Pyruvate
CoA
Fatty acid synthesis (NADPH from HMS required)
Acetyl-CoA
LTB5
LOX
Deflaming & Healing
18R-resolvin
PLA2
EPA
COX
PGE3
ATP
Ox Phos
© 2004-2009 Dr. David Seaman


Lipid bilayer membrane
The Cell Membrane
DHA
Phospholipid
Glucose
Glycogen
G-6-P
GAGS
HMS
NADPH
F-6-P
DHAP
Glycerol 3-P
F-1,6-bP
Glyceraldehyde 3-P
Pyruvate
CoA
Acetyl-CoA
Fatty acid synthesis (NADPH from HMS required)
ATP
Ox Phos
(Green vegetables, chia, hemp, flax)
Dietary a-linolenic acid (n-3)
EPA
Docosahexaenoic acid (DHA)
Fish, wild game, grass-fed beef, etc.
Diglyceride
CDP-choline
Phosphatidylcholine
Docosatrienes
17S-resolvin
Neuroprotectins
LOX
COX
DHA
PLA2
Deflaming & Healing
© 2004-2009 Dr. David Seaman


Injury
• Macrotrauma
• Microtrauma
• Biochemical
Joint Complex
Neurogenic inflammation/healing
Inflammation begins
Dead cells discharge contents*
• ATP*
• K+ ions*
• Hydrogen ions*
Kinins activated
• Bradykinin
• Kallidin
Intact cells produce and release
• LTB4, LTB5
• PGE1, PGE2, PGE3
• PGI2, PGI3
• Lipoxins
• Resolvins
• Docosatrienes
• TXA1, TXA2, TXA3
• 5-HT
• Histamine
• IL-1, IL-6, TNF
• IL-4, IL-10
• Growth factors (NGF)
• Opioids
Excite
Excite, Modulate
Excite, Modulate
Neutrophil
Lymphocyte
Macrophage
Platelet
Mast cell
Fibroblast
Endothelial cell
Group IV
• Substance P
• CGRP
Excite via NF-kB, etc.
• Norepinephrine
• Prostaglandins
SNS terminal
Para VG
GRC
WRC
Extrafusal muscle fibers
α-motoneuron
Intrafusal muscle fibers
γ-motoneuron
Brain-limbic: Pain
Thalamus
STT
Hypothalamus
SHT
Plt
Brainstem: Autonomic symptoms
SRT
Adrenal
• Epinephrine
• Glucocorticoids
• Limbic
• HYP
• PAG
• NRM
• LC
Excite, modulate group IV & SNS terminal
DLF (+,-)
Anterolateral Pathway
Glia: IL-1,6 TNF PGE2
© 2005 Dr. David Seaman

- LTB4, LTB5
- PGE1, PGE2, PGE3
- PGI2, PGI3
- Lipoxins
- Resolvins
- Docosatrienes
- TXA1, TXA2, TXA3

Fatty acid derived mediators

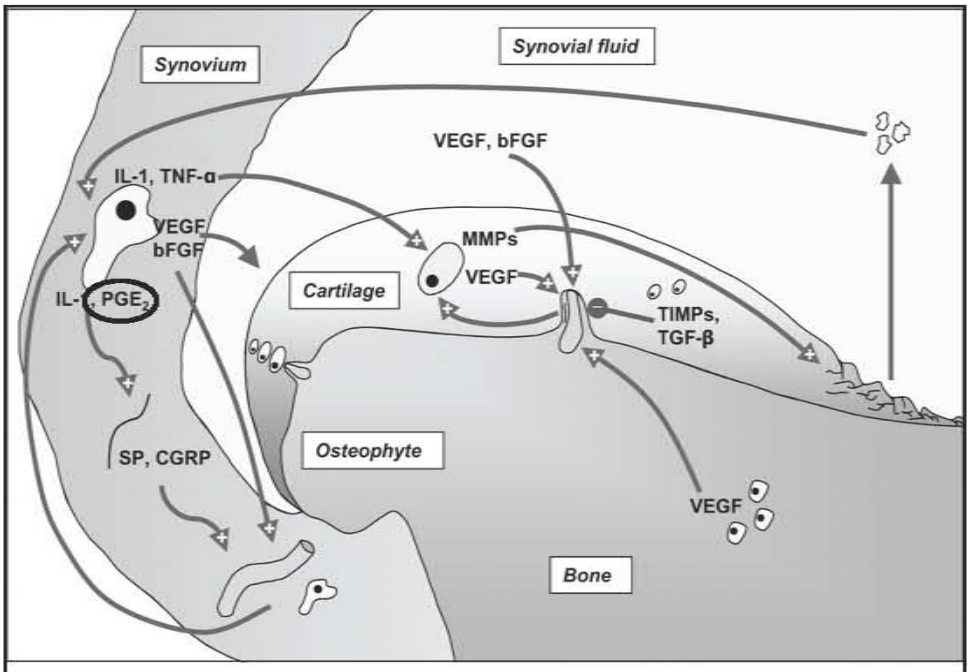
- 5-HT
- Histamine
- IL-1, IL-6, TNF
- IL-4, IL-10
- Growth factors
- Opioids

Amino acid/protein derived mediators

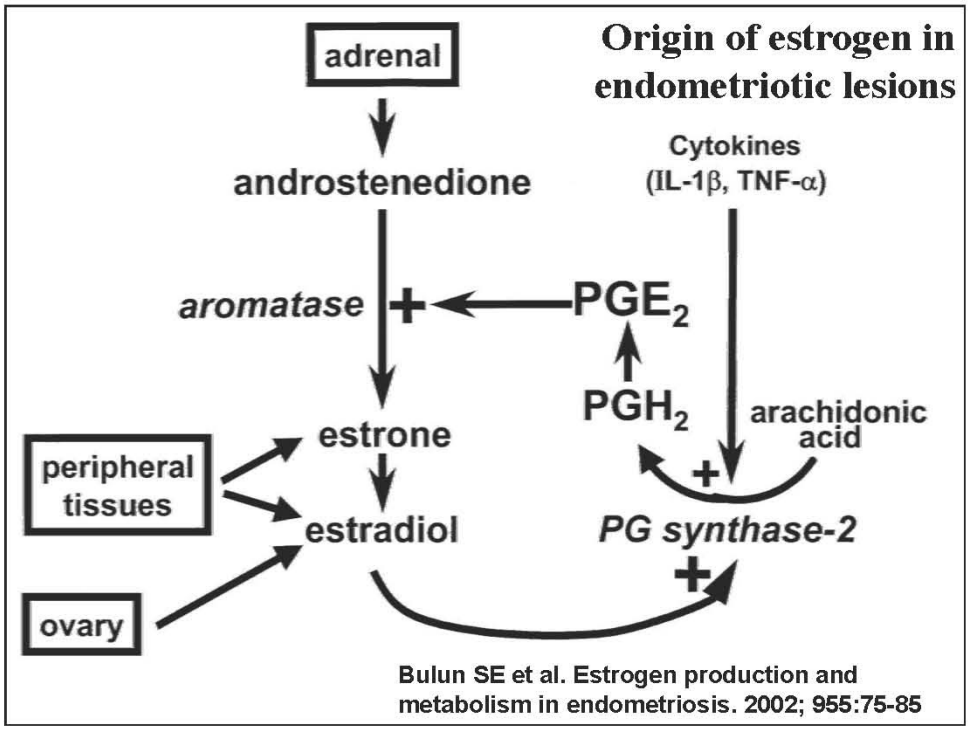
Underlined mediators are pro-inflammatory - not underlined are anti-inflammatory

Pro-inflammatory mediators - increased by:

1. Reduced micronutrient intake (vits & mins)
2. Lack of NF-kB modulation
3. Increased n-6 fatty acids, reduced n-3
4. Reduced magnesium intake
5. Reduced potassium intake
6. Reduced phytonutrient/antiox intake
7. Reduced vitamin D
8. Syndrome X/diabetes

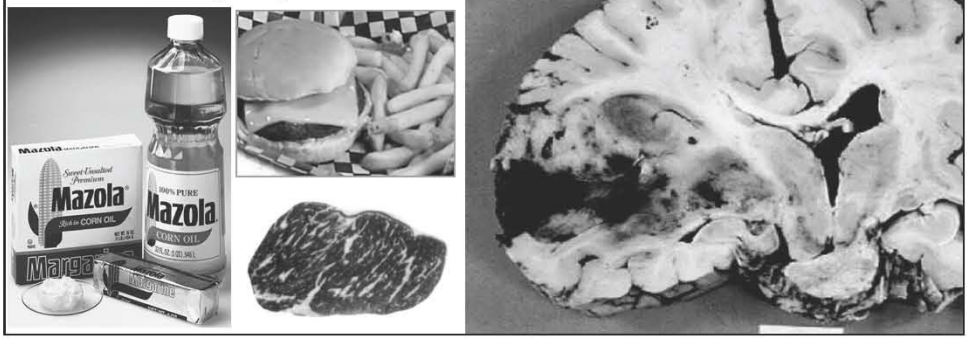


Bonnet CS, Walsh DA. Osteoarthritis, angiogenesis and inflammation. Rheumatology (Oxford). 2005 Jan;44(1):7-16



Nathoo N, Barnett GH, Golubic M. The eicosanoid cascade: possible role in gliomas and meningiomas. J Clin Pathol 2004; 57(1):6-13

- **The importance of AA metabolism in human gliomas and meningiomas has been emphasised by reports demonstrating raised concentrations of linoleic and arachidonic acid compared with normal white or grey matter.**

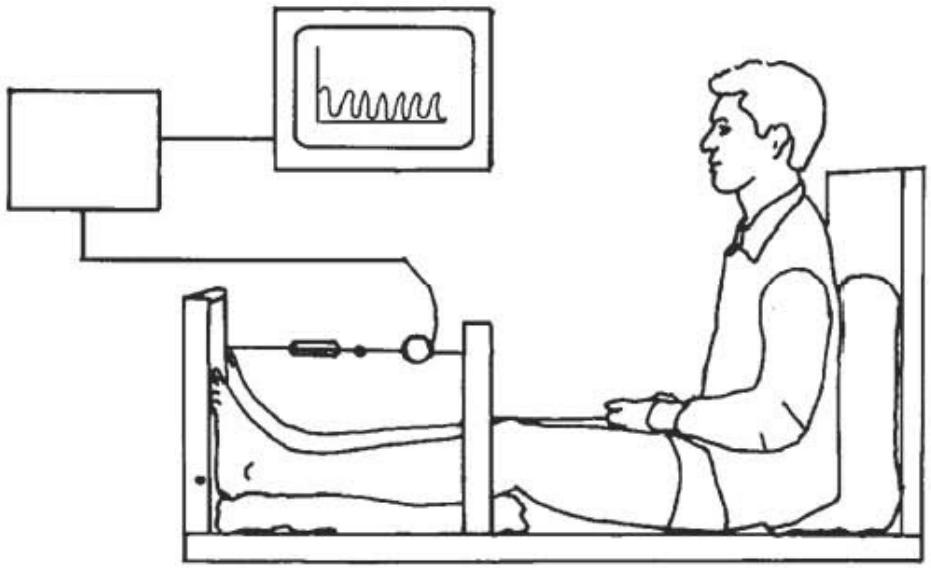


COX2 & normal tendon func

- Mechanical loading is known to increase connective tissue blood flow of human tendons and to cause local release of vasodilatory substances. The present study investigated the importance of prostaglandins (PG) formed by cyclo-oxygenase isoforms (COX-1 and 2) for the exercise-related increase in blood flow in connective tissue.

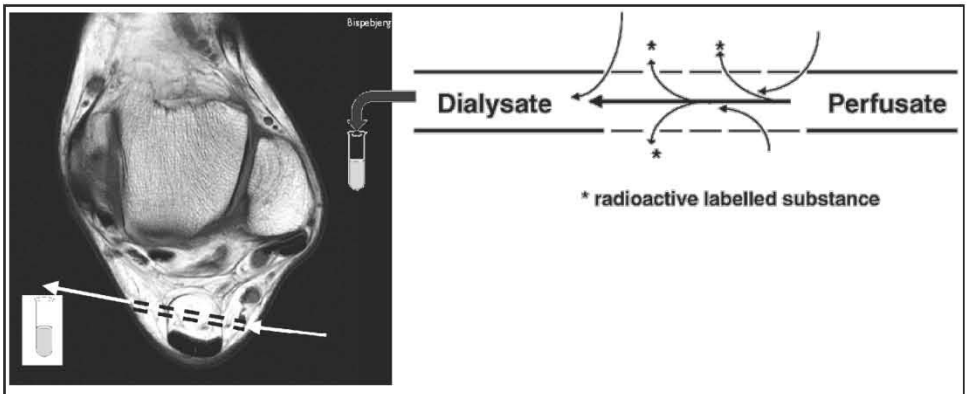
- The findings indicate that COX-2 specific mechanisms are responsible for the exercise-induced increase in prostaglandin synthesis, and that increase in tissue prostaglandin plays an important role for blood flow in peritendinous connective tissue during physical loading in vivo.

Langberg H et al. Cyclo-oxygenase-2 mediated prostaglandin release regulates blood flow in connective tissue during mechanical loading in humans.J Physiol. 2003;551(Pt 2):683-9

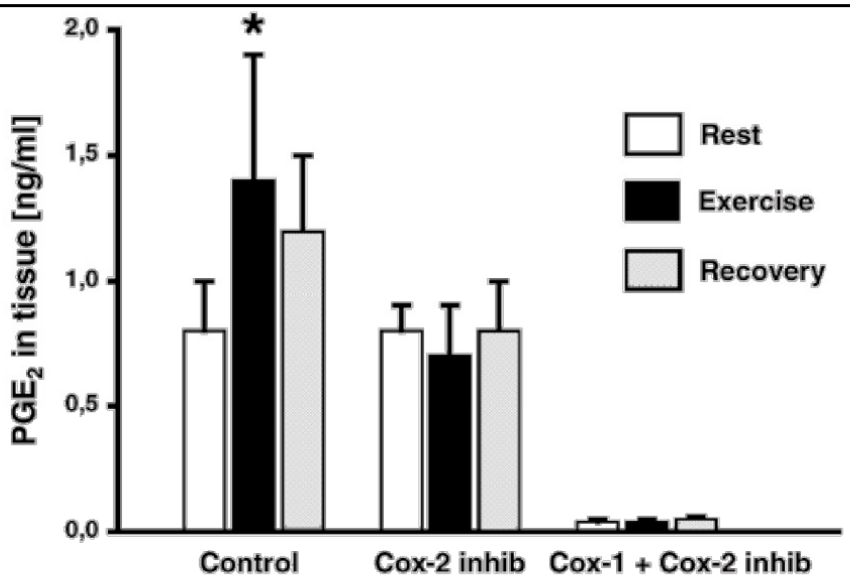


Langberg H et al. Cyclo-oxygenase-2 mediated prostaglandin release regulates blood flow in connective tissue during mechanical loading in humans.J Physiol. 2003;551(Pt 2):683-9

mined
flow and
2 levels.



Interstitial tissue concentrations of prostaglandin E2 (PGE2) in human connective tissue around the Achilles tendon was determined using microdialysis *in vivo*. Intermittent, isometric plantar flexion was performed for 30 min by healthy males, either without (Control) or with blockade of cyclo-oxygenase 1 and 2 (indomethacin and acetyl salicylic acid) (COX-1and COX-2) or cyclo-oxygenase-2 (Celecoxib) (COX-2).



Tissue prostaglandin concentrations around the human Achilles tendon, and the effect of cyclo-oxygenase blockade at rest and during physical activity

n6 fatty acids drive OA

- **Normal cartilage has low levels of pro-inflammatory n6 fatty acids, but as we age, concentrations steadily increase; a trend which is especially pronounced in osteoarthritic cartilage.**
- **Lipid accumulation in chondrocytes generally precedes local tissue degeneration in several models of degenerative arthritis.**
- **Histological severity of osteoarthritis has been related to accumulation of arachidonic acid, an omega-6 fatty and the precursor of pro-inflammatory eicosanoids (PGE2, LTB4, TXA2).**

Tiku ML, Shah R, Allison GT. Evidence link chondrocyte lipid peroxidation to cartilage matrix protein degradation: possible role in cartilage aging and the pathogenesis of osteoarthritis. J Biol Chem 2000; 275: 20069-76

Normal Cartilage: no n-6 fatty acids

Normal, young cartilages, in distinction from all other tissues examined, have unusually high levels of n-9 (20:3) PUFA (Mead acid) and low levels of n-6 PUFA.

This apparent deficiency is consistently observed in cartilage of all species so far studied (young chicken,fetal calf,new born pig, rabbit, and human), even though levels of n-6 PUFA in blood and all other tissues is normal.

Because eicosanoids, which are derived from EFA, have been implicated in the inflammatory responses associated with arthritic disease, reduction of n-6 PUFA and accumulation of the n-9 20:3 acid in cartilage **may be important for maintaining normal cartilage structure**.

Adkisson HD et al. Unique fatty acid composition of normal cartilage: discovery of high levels of n-9 eicosatrienoic acid and low levels of n-6 polyunsaturated fatty acids. FASEB J. 1991; 5(3): 344-53.

Plumb MS, Aspden RM. High levels of fat and (n-6) fatty acids in cancellous bone in osteoarthritis. Lipids Health Dis. 2004, 3:12

Objectives: To test the hypothesis that OA bone contains more fat than OP bone.

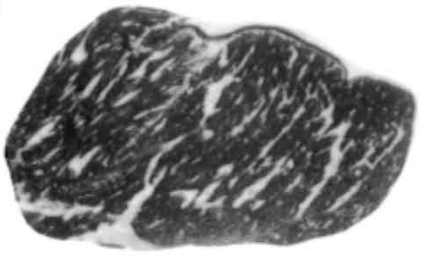
Methods: Cores of cancellous bone were obtained from femoral heads of patients undergoing surgery for either OA or OP. Lipids were extracted using chloroform-methanol, weighed and expressed as a fraction of core mass and volume. A fatty acid analysis was performed using gas chromatography.

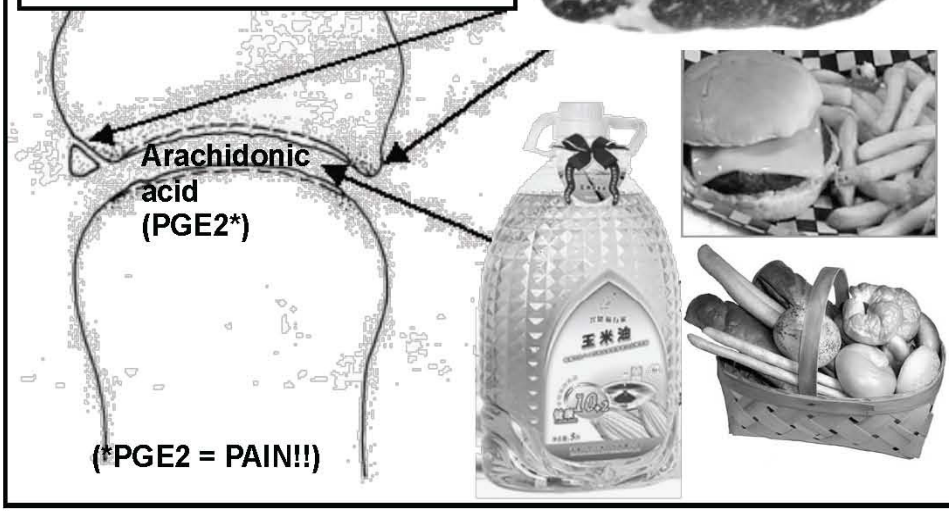
Plumb MS, Aspden RM. High levels of fat and (n-6) fatty acids in cancellous bone in osteoarthritis. Lipids Health Dis. 2004, 3:12

Results: OA bone contained twice as much fat per unit volume of tissue as OP. Levels of n-6 fatty acids were elevated in OA, especially arachidonic acid (C20:4 n-6) which was almost double that found in OP.

Conclusions: These data support the hypothesis that lipids may play a significant role in the pathogenesis of OA and may provide part of the key to understanding why OA and OP lie at opposite ends of the spectrum of bone masses.

Why monotherapies (pharm or nutr supp) fail in the treatment of osteoarthritis.





Modern diet - source of calories

10% dairy products

1-2% alcohol

20% refined grains/pasta/bread/cereal

20% refined sugars

20% refined vegetable oils

15-20% obese meat

<10% vegetables, fruit (potatoes, **legumes, whole grains**)

Cordain L et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr. 2005; 81(2):341-54.

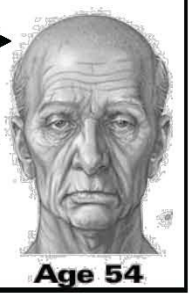
Inflamed foods = accelerated aging & chronic disease

Farmed-raised catfish & tilapia

J Am Diet Assoc. 2008;108:1178-1185.

Age 24

80% of the calories consumed by Americans come from refined sugar, grains, n-6 oils, and obese meat. These inflamed foods accelerate aging and cause chronic disease.



Age 54

Polymeal ingredients

Wine (red wine)	Food choices for disease prevention and health promotion.
Fish (n-3 meat, chicken, eggs)	
Dark chocolate	
Vegetables & Fruit (potatoes)	
Garlic (all spices)	
Almonds (all raw nuts)	
Combine effect	

Franco OH et al. The Polymeal: a more natural, safer, and probably tastier (than the Polypill) strategy to reduce cardiovascular disease by more than 75%. BMJ. 2004; 329:1447-50

Ames BN. Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage. PNAS. 2006;103(47):17589-94.

Ames presents argument for eating more fruits/ vegetables and taking key supplements:

- Multivitamin/mineral
- Magnesium
- Fish oil (EPA/DHA)
- Vitamin D
- a-Lipoic acid & acetyl-L-carnitine (ALCAR)
- Fiber (CoQ10 , glucosamine/chondroitin sulfate, anti-inflammatory botantical)

Identifying and Treating Pain Among Older Patients

Joseph Flaherty, MD

Objectives

1. Know the prevalence of the problem, and don't be afraid talk about it.
2. Know your options for assessment tools, and know they work, even for patients with dementia.
3. Know your pharmacological options
4. Remember, function as well as pain control is the goal.

1. Know the prevalence of the problem, and don't be afraid talk about it.

PERSISTENT PAIN

Among community dwelling elderly

- Common
- Commonly not discussed….

40%–80%

The prevalence of pain in elderly nursing home residents

- Marzinski LR: **The tragedy of dementia: clinically assessing pain in the confused non-verbal elderly.** *Journal of Gerontological Nursing* 1991, **17**(6):25-28.
- Sentagen EA, King SA: **The problems of pain and its detection among geriatric nursing home residents.** *Journal of the American Geriatrics Society* 1993, **41**(5):541-544.
- Ferrell BA, Ferrell BR, Rivera L: **Pain in cognitively impaired nursing home patients.** *Journal of Pain and Symptom Management* 1995, **10**(8):591-598.
- Wagner AM, Goodwin M, Campbell B, Eskro S, French SA, Shepherd PA, Wade M: **Pain prevalence and pain treatments for residents in Oregon nursing homes.** *Geriatric Nursing* 1997, **18**(6):268-272.
- Proctor WR, Hirdes JP: **Pain and cognitive status among nursing home residents in Canada.** *Pain Research and Management. The Journal of the Canadian Pain Society* 2001, **6**(3):119-125.
- Blomqvist K, Hallberg IR: **Recognizing pain in older adults living in sheltered accommodation: the views of nurses and older adults.** *International Journal of Nursing Studies* 2001, **38**:305-318.

As high as 80%

The prevalence of pain in elderly with cancer

- Rao A. Cohen HJ. J Natl Cancer Inst Monogr 2004
- Potter J, Higginson IJ. Lung Cancer 2004

Assessment Inadequate Undertreated

There is evidence that pain assessment is currently inadequate and that elderly people with dementia are being undertreated

- Horgas AL, Tsai PF: **Analgesic drug prescription and use in cognitively impaired nursing home residents.** *Nursing Research* 1998, **47**(4):235-242.
- Loeb JL: **Pain Management in long-term care.** *American Journal of Nursing* 1999, **99**(2):48-52
- Morrison RS, Siu AL: **A comparison of pain and its treatment in advanced dementia and cognitively intact patients with hip fracture.** *Journal of Pain and Symptom Management* 2000, **19**(4):240-248.
- Scherder E, Oosterman J, Swaab D, Herr K, Ooms M, Ribbe M, Segeant J, Pickering G, Benedetti F: **Recent developments in pain in dementia.** *British Medical Journal* 2005, **26:330**(7489):461-464
- Sentagen EA, King SA: **The problems of pain and its detection among geriatric nursing home residents.** *Journal of the American Geriatrics Society* 1993, **41**(5):541-544.
- Ferrell BA, Ferrell BR, Rivera L: **Pain in cognitively impaired nursing home patients.** *Journal of Pain and Symptom Management* 1995, **10**(8):591-598.

Definition of Pain

- An individual's unpleasant sensory or emotional experience

Subjective

Pain

- Physiological responses are often not specific enough to serve as pa
- Physiological
to d

Subjective

Persistent Pain

- **Pain that persists beyond the expected time of healing, or more than 3 to 6 months.**
- **Several disorders may cause persistent pain**

Weiner DK, Am J Med 2007

Pain among Older Persons in the Nursing Home

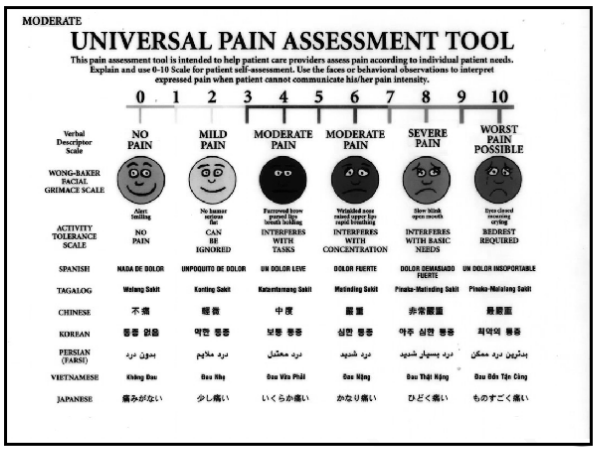
Source: Stein et al. Clinics in Geriatric Medicine: 1996

Condition causing pain	Frequency (%)
Low back pain	40
Arthritis	37
Previous fractures	14
Neuropathies	11
Leg cramps	9
Claudication	8
Headache	6
Generalized pain	3
Neoplasm	3

http://www.amda.com/tools/clinical/chronicpain/slides.cfm

Assessment of Pain

- The **PQRST** mnemonic (**P**rovocation/Palliative factors, **Q**uality, **R**egion, **S**everity, and **T**emporal features)



Scales

- Sensory-discriminative (presence and intensity)
  - Verbal rating scale
  - Visual analog scale
  - Numerical rating scale
  - Faces pain scale
- Motivational-affective (affect and intensity)
  - PAINAD
  - PACSLAC
  - NOPPAIN
  - DOLOPLUS-2
  - PADE
  - Abbey

Definition of Dementia

- Development of multiple cognitive deficits (including memory impairment)
- With at least one of the following cognitive disturbances: **aphasia**, apraxia, agnosia, or a disturbance in executive functioning

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. 1994:133-134.

Usefulness of "traditional" scales?

- DSM-IV criteria Dementia, MMSE <11
- 3 self-assessment tools--the verbal, horizontal visual, and faces pain scales--were administered in randomized order.
- A nursing team independently completed an observational pain rating scale. Main outcomes were comprehension (ability to explain scale use and correctly indicate positions for no pain and extreme pain, on two separate occasions), inter- and intrarater reliability, and comparison of pain intensities measured by the different scales.

•Pautex, S Pain in severe dementia: self-assessment or observational scales?. Source Journal of the American Geriatrics Society. 54(7):1040-5, 2006 Jul

Usefulness of "traditional" scales?

- 61% of 129 severely demented patients (mean age 83.7, 69% women) demonstrated comprehension of at least one scale.
- Comprehension rates were significantly better for the verbal and the faces pain scales.
- Inter- and intrarater reliability of the three self-assessment scales was high (intraclass correlation coefficient=0.88-0.98), (for the 61%)

•Pautex, S Pain in severe dementia: self-assessment or observational scales?. Source Journal of the American Geriatrics Society. 54(7):1040-5, 2006 Jul

Loss of Placebo effect in AD?

- A local anesthetic was applied, either overtly or covertly, to the skin of AD patients to reduce burning pain after venipuncture.
- AD patients with reduced Frontal Assessment Battery scores showed reduced placebo component of the analgesic treatment.
- Loss of these placebo-related mechanisms reduced treatment efficacy, such that a dose increase was necessary to produce adequate analgesia

Benedetti, F Loss of expectation-related mechanisms in Alzheimer's disease makes analgesic therapies less effective. Pain. 121(1-2):133-44, 2006

Pain in a person with Dementia

- **Facial expressions**
  - Sad or frightened face, grimacing, wrinkled forehead, closed or tightened eyes, distorted expression, rapid blinking
- **Verbalizations, vocalizations**
  - Sighing, moaning, groaning, grunting, chanting, calling out, noisy breathing, asking for help, verbally abusive
- **Body movements**
  - Rigid/tense body posture, guarding, fidgeting, increased pacing, rocking, restricted movement, gait or mobility changes

AGS Panel on Persistent Pain in OlderPersons
J AmGeriatrSoc 2002; 50 (suppl 1): S205-S224

Pain in a person with Dementia

- **Changes in interpersonal interactions**
  - Aggressive, combative, resisting care, decreased social interactions, socially inappropriate, disruptive, withdrawn
- **Changes in activity patterns or routines**
  - Refusing food, appetite change, increase in rest periods, sleep/rest pattern changes, sudden cessation of common routines, increased wandering
- **Mental status changes**
  - Crying or tears, increased confusion, irritability or distress

AGS Panel on Persistent Pain in OlderPersons
J AmGeriatrSoc 2002; 50 (suppl 1): S205-S224

Residents with Dementia

Can verbally Communicate “with accurate words”	Cannot verbally communicate “with accurate words”

Scales

1. Non-Communicative Patient's Pain Assessment (NOPPAIN)[1]
2. Pain Assessment for the Dementing Elderly (PADE)[2]
3. Pain Assessment in Advanced Dementia (PAINAD)[3]
4. Pain Assessment Checklist for Seniors With Limited Ability to Communicate (PACSLAC)[4]
5. DOLOPLUS-2[5]
6. Pain Assessment in the Communicatively Impaired (PACI)[6]
7. Checklist of Nonverbal Pain Indicators (CNPI)[7]

1. Snow et al 2004
2. Villaneuva et al. 2003
3. Warden et al. 2003
4. Fuchs-Lacelle et al. 2004
5. Wary and Doloplus 1999
6. Kaasalainen & Crook, 2003
7. Feldt 2000

Review article of above: Kaasalainen, S. McMaster University, Hamilton, Ontario, Canada. J Gerontological Nursing. 33(6):6-10, 2007 Jun.

Pain Assessment Checklist for Seniors with Limited Ability to Communicate (PACSLAC)

Facial Expressions	Present	Activity/Body Movement	Present	Social/Personality/Mood	Present
Grimacing		Decreased activity		Upset	
Sad Look		Refusing medications		Agitated	
Tighter face		Moving slow		Cranky/Irritable	
Dirty look		Impulsive Behaviour (e.g.		Frustrated	
Change in eyes (squinting, dull,		repetitive movements)		Other*	
bright, increased movement)		Uncooperative/Resistant to care		Pale Face	
Frowning		Guarding sore area		Flushed, red face	
Pain expression		Touching/holding sore area		Teary eyed	
Grim face		Limping		Sweating	
Clenching teeth		Clenched fist		Shaking/Trembling	
Wincing		Going into foetal position		Cold & clammy	
Opening mouth		Stiff/Rigid		Changes in sleep (please circle):	
Creasing forehead		**Social/Personality/Mood**		Decreased sleep or	
Screwing up nose		Physical aggression (e.g., pushing		Increased sleep during day	
Activity/Body Movement		people and/or objects, scratching		Changes in Appetite (please	
Fidgeting		others, hitting others, striking,		Decreased appetite or	
Pulling Away		kicking)		Increased appetite	
Flinching		Verbal aggression		Screaming/Yelling	
Restless		Not wanting to be touched		Calling out (i.e. for help)	
Pacing		Not allowing people near		Crying	
Wandering		Angry/Mad		A specific sound or vocalization	
Trying to leave		Throwing things		For pain 'ow', ouch'	
Refusing to move		Increased confusion		Moaning and groaning	
Thrashing		Anxious		Mumbling	
				Grunting	

DOLOPLUS-2 SCALE BEHAVIOURAL PAIN ASSESSMENT IN THE ELDERLY

NAME : Christian Name : Unit :

Behavioural Records

		DATES			
SOMATIC REACTIONS					
1• Somatic complaints	• no complaints	0	0	0	0
	• complaints expressed upon inquiry only	1	1	1	1
	• occasional involuntary complaints	2	2	2	2
	• continuous involuntary complaints	3	3	3	3
2• Protective body postures adopted at rest	• no protective body posture	0	0	0	0
	• the patient occasionally avoids certain positions	1	1	1	1
	• protective postures continuously and effectively sought	2	2	2	2
	• protective postures continuously sought, without success	3	3	3	3
3• Protection of sore areas	• no protective action taken	0	0	0	0
	• protective actions attempted without interfering against any investigation or nursing	1	1	1	1
	• protective actions against any investigation or nursing	2	2	2	2
	• protective actions taken at rest, even when not approached	3	3	3	3
4• Expression	• usual expression	0	0	0	0
	• expression showing pain when approached	1	1	1	1
	• expression showing pain even without being approached	2	2	2	2
	• permanent and unusually blank look (voiceless, staring, looking blank)	3	3	3	3
5• Sleep pattern	• normal sleep	0	0	0	0
	• difficult to go to sleep	1	1	1	1
	• frequent waking (restlessness)	2	2	2	2
	• insomnia affecting waking times	3	3	3	3
PSYCHOMOTOR REACTIONS					
6• washing &/or dressing	• usual abilities unaffected	0	0	0	0
	• usual abilities slightly affected (careful but thorough)	1	1	1	1
	• usual abilities highly impaired, washing &/or dressing is laborious and incomplete	2	2	2	2
	• washing &/or dressing rendered impossible as the patient resists any attempt	3	3	3	3
7• Mobility	• usual abilities & activities remain unaffected	0	0	0	0
	• usual activities are reduced (the patient avoids certain movements and reduces his/her walking distance)	1	1	1	1
	• usual activities and abilities reduced (even with help, the person cuts down on his/her movements)	2	2	2	2
	• any movement is impossible, the person resists all persuasion	3	3	3	3
PSYCHOSOCIAL REACTIONS					
8• Communication	• unchanged	0	0	0	0
	• heightened (the patient demands attention in an unusual manner)	1	1	1	1
	• lessened (the patient cuts him/herself off)	2	2	2	2
	• absence or refusal of any form of communication	3	3	3	3
9• Social life	• participates normally in every activity (meals, entertainment, therapy workshop)	0	0	0	0
	• participates in activities when asked to do so only	1	1	1	1
	• sometimes refuses to participate in any activity	2	2	2	2
	• refuses to participate in anything	3	3	3	3
10• Problems of behaviour	• normal behaviour	0	0	0	0
	• problems of repetitive reactive behaviour	1	1	1	1
	• problems of permanent reactive behaviour	2	2	2	2
	• permanent behaviour problems (without any external stimulus)	3	3	3	3

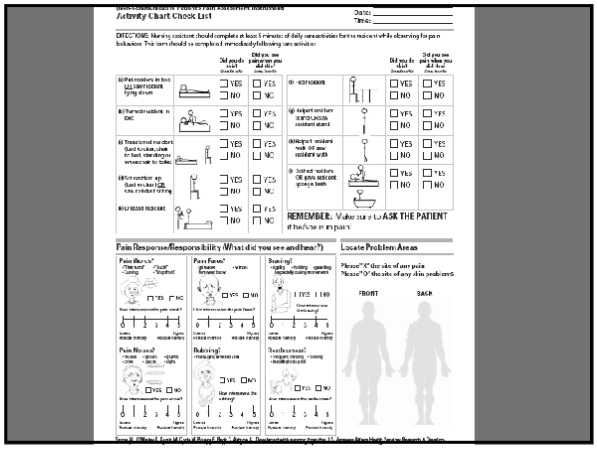
Pain Assessment in Advanced Dementia (PAINAD) Scale Page 1 of 2

Pain Assessment in Advanced Dementia (PAINAD) Scale

Items*	0	1	2	Score
Breathing independent of vocalization	Normal	Occasional labored breathing. Short period of hyperventilation.	Noisy labored breathing. Long period of hyperventilation. Cheyne Stokes respirations.	
Negative vocalization	None	Occasional moan or groan. Low level speech with a negative or disapproving quality.	Repeated troubled calling out. Loud moaning or groaning. Crying.	
Facial expression	Smiling or inexpressive	Sad. Frightened. Frown.	Facial grimacing.	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting.	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out.	
Consolability	No need to console	Distracted or reassured by voice or touch.	Unable to console, distract or reassure.	
			Total**	

*Five-item observational tool (see the description of each item below).

**Total scores range from 0 to 10 (based on a scale of 0 to 2 for five items), with a higher score indicating more severe pain (0="no pain" to 10="severe pain").



Best scoring scales

	Content validity	Construct validity	Reliability	Clinical Use	Global score
	(%)				
PACSLAC	100	67	92	90	87
Abbey scale	81	61	56	93	73
DOLOPLUS	78	53	56	73	65
PADE	56	67	82	53	64
PAINAD	78	50	49	77	63

Limitations

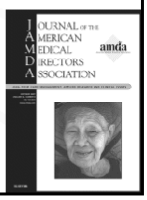
- Although the pain experienced may be excruciating, rubbing or guarding a painful body part may not be physically possible because of contractures or immobility.
- In addition, some researchers have suggested facial expressions of pain may be blunted by physical changes that occur in faces with age

Consequences or Equivalents of Pain (esp in dementia)

- D Delirium
- A Anorexia
- R Restlessness
- N Not taking meds, bath, etc.
- I Insomnia
- H "Help me, help me"
- U Unhappy
- R Rubbing, bracing
- T Tiredness or fatigue

Mental Status is the Vital Sign

6th



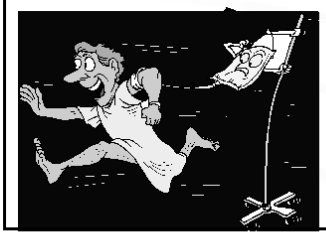
The VA Delirium Working Group, June 2007

Delirium IS NOT Dementia

Although dementia is a risk factor for developing delirium

Why Differentiate?

- Delirium
  >90% Reversible
- Dementia
  ~10% Reversible



Non-treatment →Not an option

If in doubt → Treat

Myths

- Acknowledging pain will lead to loss of independence
- The elderly-especially cognitively impaired-have a higher pain tolerance
- The elderly and cognitively impaired cannot be accurately assessed for pain
- Addiction is common and/or inevitable

Pharmacologic Options

- Nonopioids
- Opiods
- Adjuvant analgesic drugs
- "other" drugs

AGS Guideline on the Pharmacological Management of Persistent Pain in Older Persons
http://www.americangeriatrics.org/
http://www.americangeriatrics.org/education/pharm_management.shtml

Pharmacologic Options

- Quality of evidence
  - High
    - Consistent results from well-designed, well conducted studies (>1 RCTs or multiple observational studies)
  - Moderate
    - "Sufficient but #, size, quality limited"
  - Low
    - Insufficient evidence
- Strength of recommendation
  - Strong
    - Benefits clearly outweigh risks and burden or vice versa
  - Weak
    - Benefits finely balanced with risks and burden
  - Insufficient
    - Insuff. evid to determine benefits vs risks

Nonopioids

- Acetaminophen
  - Initial pharmacotherapy
  - Esp MSK
  - Good safety profile

High quality evidence
Strong recommendation

Nonopioids

- Acetaminophen
  - Absolute contraindications
    - Liver failure
  - Relative contraindications
    - Hepatic insuff, chronic alc use/abuse/dep

Nonopioids

- Acetaminophen- dosing
  - *Routine* if persistent pain
  - Maximum daily dose
    - 3-4 grams per day

Nonopioids

- NSAIDs and COX-2 selective inhibitors
  - "may be considered rarely, and with extreme caution, in highly selected individuals"

High quality evidence
Strong recommendation

Nonopioids

- NSAIDs
  - GI adverse events as high as 20%
  - >100,000 hospitalized yearly
  - 16,500 die yearly from NSAID-related ulcer complications

Katz JD, AGS meeting 2009

Nonopioids

- NSAIDs
  - HTN
  - Renal impairment
  - Edema
  - Cardiovascular

Katz JD, AGS meeting 2009

Opioids

- Which patients?
  - Moderate to severe pain
  - Diminished quality of life

Low quality evidence
Strong recommendation

Opioids

- How?
  - If frequent or continuous, consider around-the-clock

Low quality evidence
Weak recommendation

Opioids

- What else?
  - Anticipate, assess for, and identify side effects…..they're going to happen

Moderate quality evidence
Strong recommendation

Opioids

- Types and dosing

Equianalgesic Potency Conversion

Drug	Equianalgesic Dose Intramuscular[a,b]	Oral
Morphine	10 mg	60 mg[c]
Codeine	130 mg	200 mg
Heroin	5 mg	60 mg
Hydromorphone	1.5 mg	7.5 mg
Levorphanol	2 mg	4 mg
Meperidine	75 mg	300 mg
Methadone	10 mg	20 mg
Oxycodone	15 mg	30 mg
Oxymorphone	1 mg	10 mg (rectal)

Note: All intramuscular and oral doses listed are considered to be equivalent in analgesic effect to 10 mg of intramuscular morphine.

[a]Based on single-dose studies in which an intramuscular dose of each drug listed was compared with morphine to establish relative potency. Oral doses are those recommended when changing from a parenteral to an oral route.

[b]Although no controlled studies are available, in clinical practice it is customary to consider the doses of opioid given intramuscularly, intravenously, or subcutaneously to be equivalent.

[c]The conversion ratio of 10 mg of parenteral morphine to 60 mg of oral morphine is based on a potency study in patients with acute pain.

Opioids

- Methadone?
  - Initiated only by clinicians well versed in its use

Moderate quality evidence
Strong recommendation

Opioids

- Meperidine (Demerol)?
  - NEVER
- Propoxyphene
  - AVOID

Adjuvant Analgesic Drugs

- Who?
  - Those with neuropathic pain

Strong quality evidence
Strong recommendation

Adjuvant Analgesic Drugs

- Who?
  - Those with fibromyalgia

Moderate quality evidence
Strong recommendation

Adjuvant Analgesic Drugs

- Who?
  - Other types of refractory persistent pain may be candidates
    - Back pain
    - Headaches
    - Bone pain
    - Temporomandibular disorder

Low quality evidence
Weak recommendation

Adjuvant Analgesic Drugs

- Types?
  - Gabapentin, other anticonvulsants
  - Tramadol
  - Antidepressants

Adjuvant Analgesic Drugs

Class	NNT	NNH (major/minor)	Type of pain
Gabapentin	4.3	NS/3.7	DPN 2.9; PHN 3.9
Carbameza pine	2.5	NS/3.7	TGN; DPN 2.3
Phenytoin	2.1	NS/3.2	DPN
Tramadol	3.8	8.3/?	Neuropathy OA
Venlafexine	3.1	16.2/9.6	Neuropathy

Reisner LA, AGS Meeting, 2009

Adjuvant Analgesic Drugs

- Types?
  - AVOID Tertiary TCAs (amitriptyline, imipramine, doxepin)
  - AVOID benzodiazepines (anxiolytics)

Moderate quality evidence
Strong recommendation

Other Drugs

- Systemic steroids
  - Reserved for pain-associated inflammatory disorders or metastatic bone pain.
  - OA should not be considered inflammatory

Moderate quality evidence
Strong recommendation

Other Drugs

- Topical lidocaine
  - Consider for localized neuropathic pain
- Topical NSAIDS
  - Consider for localized non-neuropathic pain

Moderate quality evidence
Strong recommendation

Oxycodone + Naloxone?

- N =202 patients with chronic cancer- or non-cancer-related pain undergoing stable oxycodone PR therapy (40, 60 or 80 mg/day)
- Randomized to one of four intervention groups:
  - 10, 20 or 40 mg/day naloxone PR or placebo.
- Following a 4-week maintenance phase, patients were followed-up for 2 weeks in which time they received oxycodone PR only.
- At the end of the maintenance phase, patients and investigators were asked to assess treatment efficacy and tolerability, as well as preference for the titration or maintenance phase.

Nadstawek, J. Patient assessment of a novel therapeutic approach for the treatment of severe, chronic pain. International Journal of Clinical Practice. 62(8):1159-67, 2008

Oxycodone + Naloxone?

- Efficacy was ranked as 'good' or 'very good' by 50.0%, 67.4% and 72.5% of patients in the 10, 20 and 40 mg naloxone PR dose groups, respectively, compared with 43.5% of patients in the placebo group.
- Patient assessment of tolerability was similar between treatment groups and placebo, being ranked as 'good' or 'very good' by 83.3%, 79.1% and 82.5% of patients in the 10, 20 and 40 mg/day naloxone PR dose groups, respectively, compared with 71.7% of patients in the placebo group.
- The maintenance treatment phase was preferred by patients in the naloxone groups.

Nadstawek, J. Patient assessment of a novel therapeutic approach for the treatment of severe, chronic pain. International Journal of Clinical Practice. 62(8):1159-67, 2008

Oxycodone + Naloxone?

- A 2 : 1 dose ratio of oxycodone to naloxone was also assessed.
- Efficacy was ranked as 'good' or 'very good' by 70.4% of patients treated with the 2 : 1 dose ratio compared with 43.5% of patients receiving placebo.
- Tolerability of the 2 : 1 dose ratio was ranked as being 'good' or 'very good' by 81.5% of patients compared with 71.1% for the placebo group and patients preferred the maintenance phase.

Nadstawek, J. Patient assessment of a novel therapeutic approach for the treatment of severe, chronic pain. International Journal of Clinical Practice. 62(8):1159-67, 2008

Cannabis without the high?

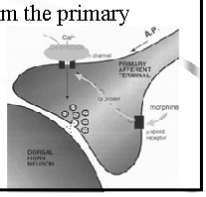
Anand et al. **Cannabinoid receptor CB2 localisation and agonist-mediated inhibition of capsaicin responses in human sensory neurons**. *Pain*, 2008; 138 (3): 667 DOI: 10.1016/j.pain.2008.06.007

Ziconotide

- Type of calcium channel blocker (non-opioid analgesic)
- Ziconotide is derived from the toxin of the cone snail species *Conus magus*.
- Discovered in the early 1980s by Michael McIntosh, at the time barely out of high school and working with Baldomero Olivera.

Ziconotide

- Type of calcium channel blocker (non-opioid analgesic)
- Results in animal model studies suggest that ziconotide (PRIALT) exerts its antinociceptive effect(s) by selectively blocking the pre-synaptic N-type calcium channels and reducing the release of excitatory neurotransmitters from the primary afferent nerve terminals.
- Humans-IT use, mech unkown



Objectives

1. Know the prevalence of the problem, and don't be afraid talk about it.
2. Know your options for assessment tools, and know they work, even for patients with dementia.
3. Know your pharmacological options
4. Remember, function as well as pain control is the goal.

Panel Discussion: Case Study Discussions of Diagnosis, Management and Treatment of Pain in Older Persons

Paul Dougherty, DC
Jane Hart, MD
Joseph Flaherty, MD
David Seaman, DC
Linda Smith, DC

Notes

Notes

Notes

Notes

Notes

Notes

Notes

Notes