

Workshop Atopic Dermatitis Praha 27th May 2006



**Atopic Dermatitis or Neurodermatitis ? –
Neurogenic Inflammation in Atopic Dermatitis**

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Psychodermatology

Justus-Liebig-University Giessen


Germany

My last stay in the Czech Republic was the atopic dermatitis workshop in Novy Jicin 2004

e-mail



Nemocnice s poliklinikou
v Novém Jičíně
Zámek Kunín




I. Moravskoslezské sympozium o atopické dermatitidě a psychodermatologii s mezinárodní účastí - Nový Jičín 2004



Symposium zaměřené na problematiku atopické dermatitidy a psychodermatologie v dětském věku.
Symposium o hledání nových cest k zajištění plnohodnotnějšího života pro vaše pacienty.

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Generálními sponzory jsou společnosti



Organizační servis - CK Jasta
paní Hana Kropíková
100 00 PRAHA, Hestimě, Chudovnické 22/1086



Psychodermatology Dept. Justus-Liebig-University Giessen / Germany



**Outpatient Department
of the Psychosomatic
Clinic**

about 1000 patients /
year, 20 % of them
have dermatological
diagnosis



**Dept. of Psychodermatology –
inpatient ward**

About 180 patients / year (treatment of
40 days in average)

Psychodermatology unit with 8
patients, about 40 patients / year



**Psychodermatology -
Liaison-Clinic**

About 10% of all
dermatological
inpatients and about
150 outpatients / year

Neurodermitis-Akademie

Hessen – Thüringen

Hessen

Giessen

(Gieler/Hennighausen/Niemeier
/Langrock)

Alzenau (Wienke-Graul/Plank)

Bad Soden (Aschoff/Fell)

Bad Homburg (Reimer/Walter)

Darmstadt

(Ahrens/Körper/Seipp)

Frankfurt (Schulze)

Marburg (Hertl)

Thüringen:

Jena (Kaatz)

Eisenach (Weber)



Neurogenic Inflammation - not a new topic

Archives of Dermatology and Syphilology

VOLUME 46

AUGUST 1942

NUMBER 2

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NEUROTIC SYMPTOMS AND EMOTIONAL FACTORS IN ATOPIC DERMATITIS

MAURICE H. GREENHILL, M.D.

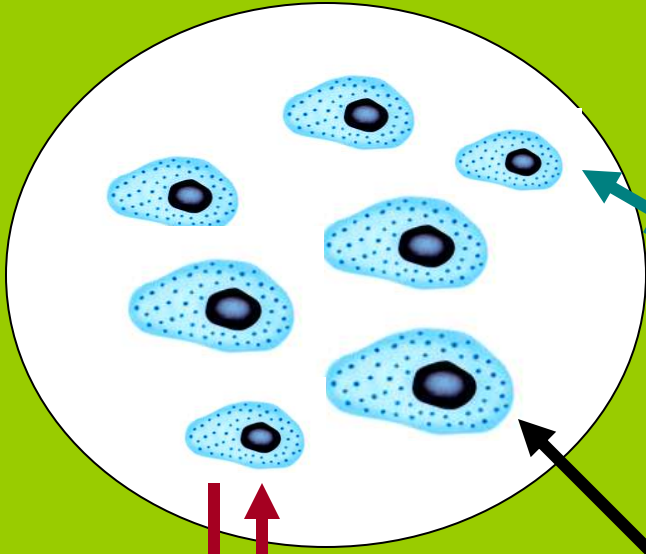
AND

JACOB E. FINESINGER, M.D.

BOSTON

The increasing awareness on the part of physicians of disorders belonging conjointly to the fields of internal medicine and psychiatry has focused attention on the study of emotional states in medical illnesses. Members of the psychiatric department of the Massachusetts General Hospital have been working for some years on these problems, and studies have appeared on rheumatoid arthritis,¹ bronchial asthma² and

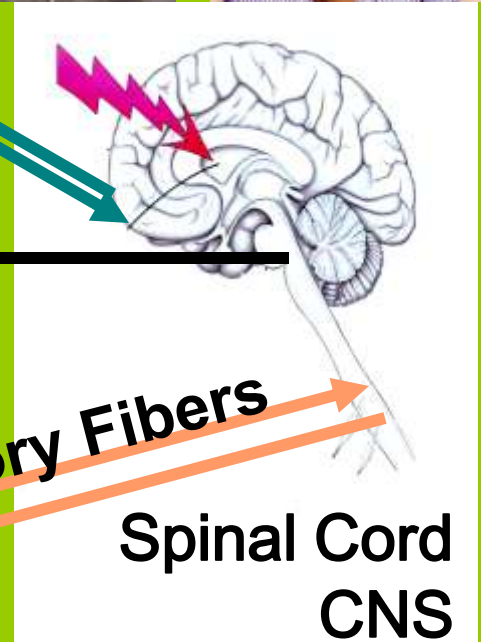
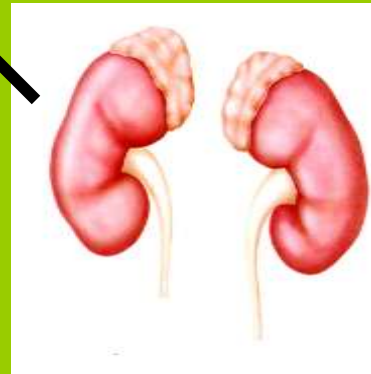
Immune Cells



"Stress"



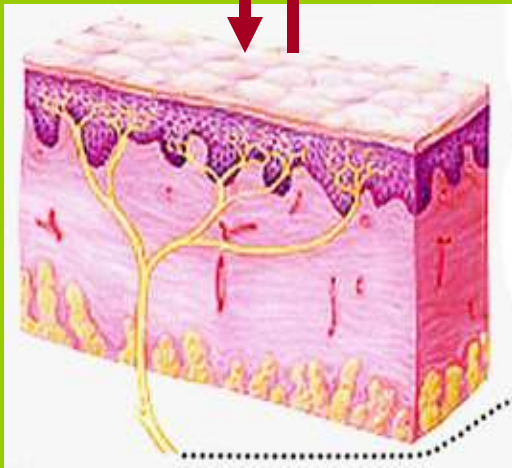
PACAP
MIF



Sensory Fibers

Spinal Cord
CNS

Autonomic Fibers



Skin

Brocq, L. et L. Jacquet: Notes pour servir a l'histoire des neurodermatitis. Annales Dermatologie et Venerologie 97,193-195 (1891)

Atopic Dermatitis as neurogenic inflammatory disease

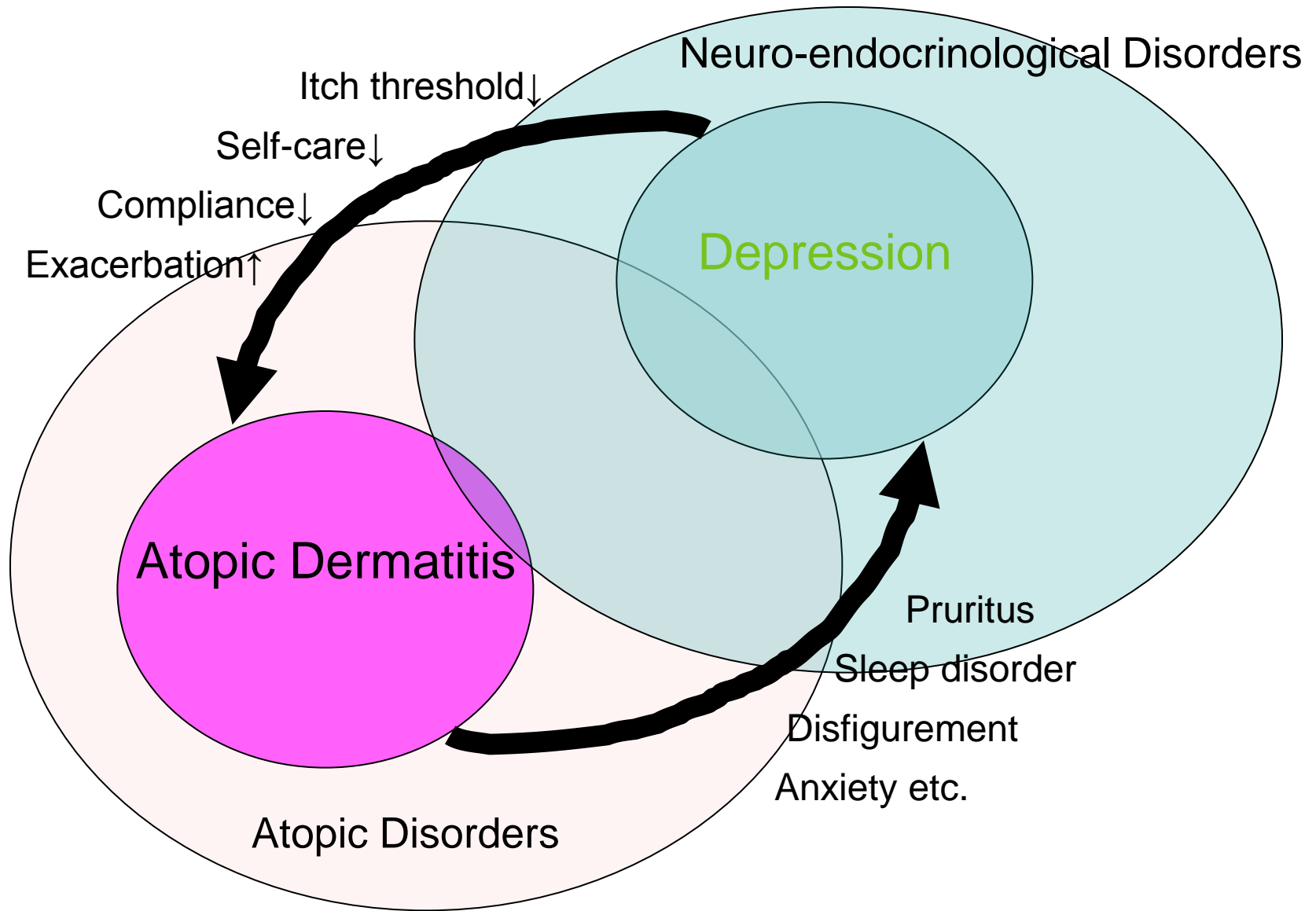
- Was Brocq and Jaquet 1891 correct in her statement „neuro-dermatitis“ ?
- Atopic dermatitis depends from nerves
- Atopic dermatitis and affective disorders interact
- Atopic dermatitis is stress dependend
- Atopic Dermatitis is triggered by peripheral nerves and neuropeptides
 - NGF/BDNF
 - PAR
 - Intermedin - Neuropeptid
- Atopic Dermatitis / Itch correlate with brain activity

Connection between Brain and Skin



Brain and Skin are from the same structure in embryogenesis:

The Ektoderm



„Life-events“ and Atopic Dermatitis

**„Effect of stress on atopic dermatitis:
investigation in patients after the great
hanshin earthquake“**

**Kodama A et al. J Allergy Clin Immunol 104: 173-6
(1999)**

Study-Design: n = 1457 patients with atopic dermatitis (745 m, 712 f)

3 Groups:

A: Severe earthquake disturbances (n= 539)

B: lower earthquake disturbances (n= 757)

C: no disturbances (n= 161)

**Effect of stress on atopic dermatitis: investigation in patients after the
great hanshin earthquake**

Results:

**In 38% increasing symptoms of atopic dermatitis in the
severe earthquake group**

34% increasing symptoms in the slightly disturbed group

Only 7% in patients without earthquake from another area

**But also 9% (A) resp. 5% (B) decreasing symptoms vs 1%
in controls (C)**

**→ Subjectiv recognized stress was most important risk
factor for exacerbation**

Itch depends on the neurological innervation !

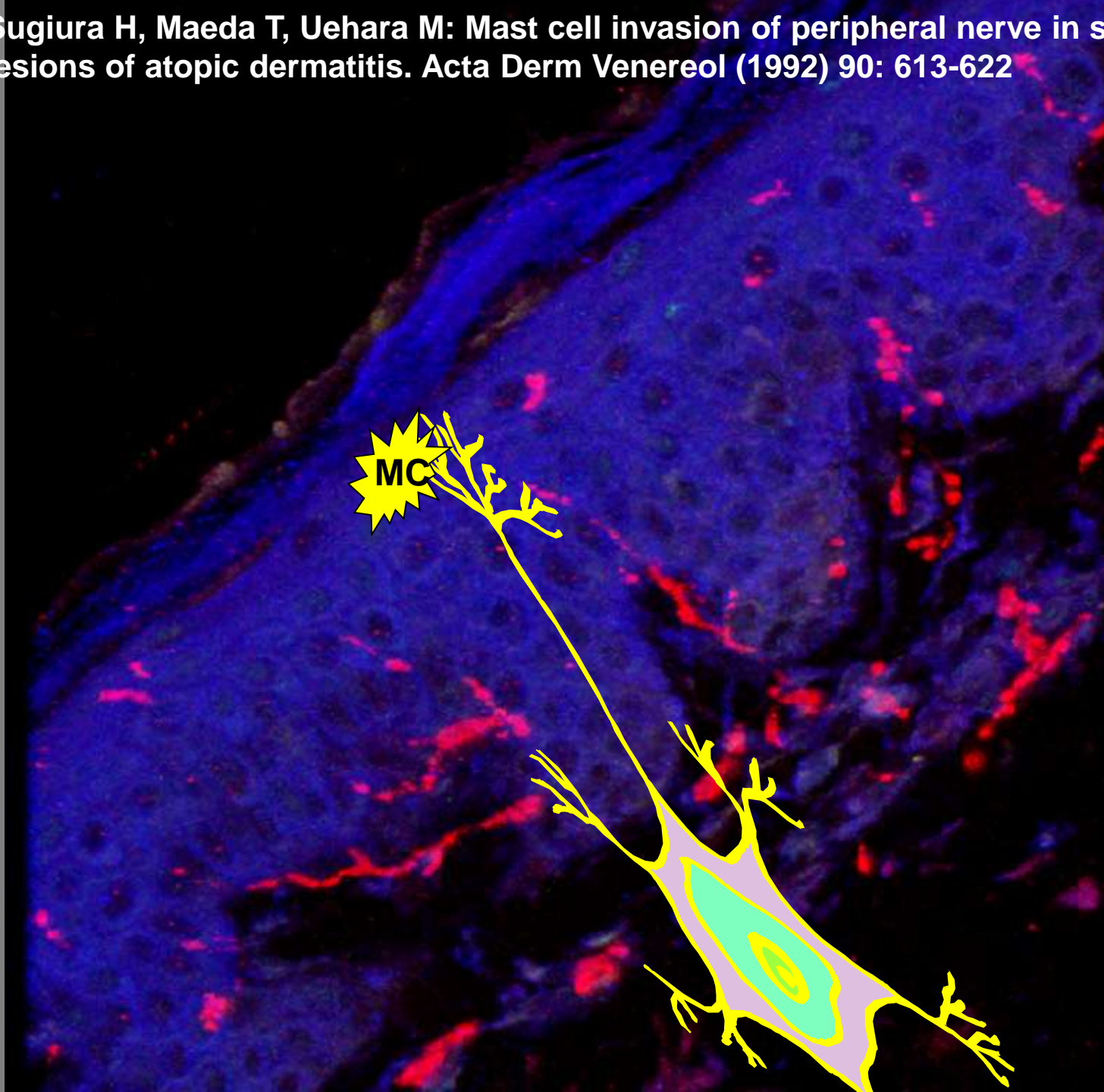
Chowdury et al: Unilateral resolution of palmar eczema and hyperhidrosis complicated by Horner's syndrome following ipsilateral endoscopic cervical sympathectomy. *Brit J Dermatol* 143 (2000) 653-654

Tarkowski et al: Lateralization of cutaneous inflammatory responses in patients with unilateral paresis after poliomyelitis. *J Neuroimmunol* 67 (1996) 1-6

Troilius A, Moller H.
Unilateral eruption of endogenous eczema after hemiparesis.
Acta Derm Venereol 69 (1989) 256-8

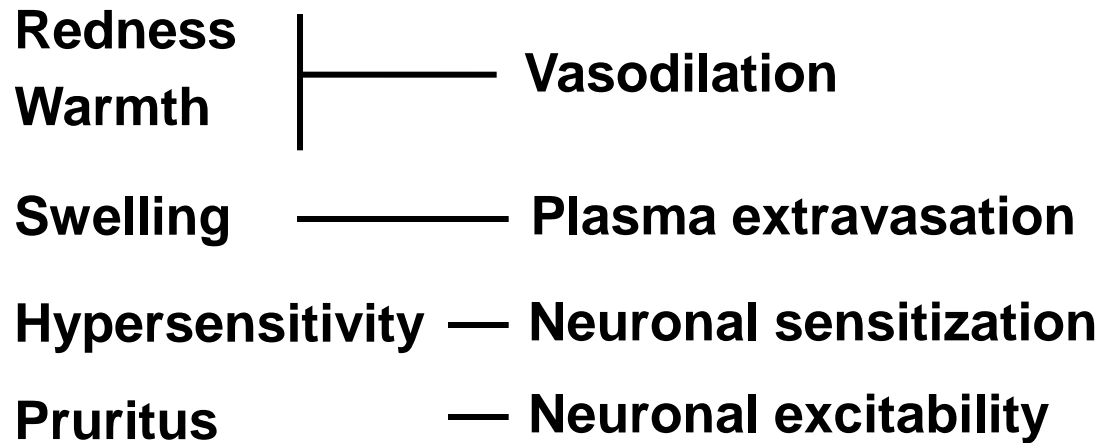


Sugiura H, Maeda T, Uehara M: Mast cell invasion of peripheral nerve in skin lesions of atopic dermatitis. *Acta Derm Venereol* (1992) 90: 613-622



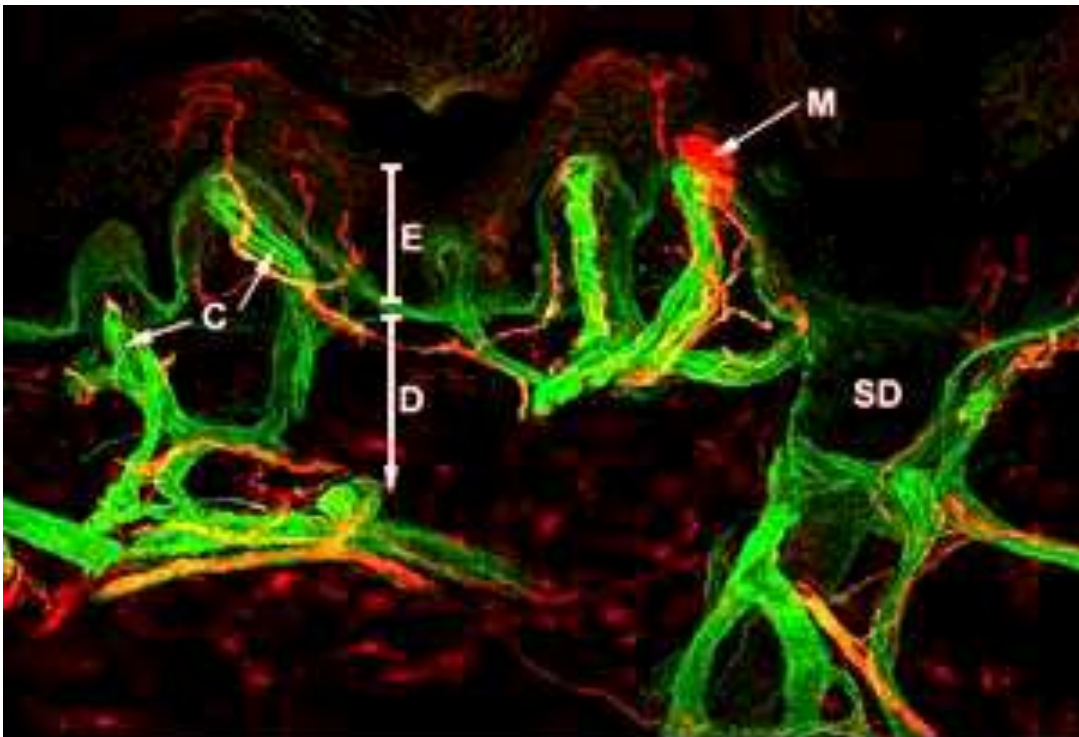
Atopic Eczema – neurogenic inflammation ?

Neurogenic inflammation



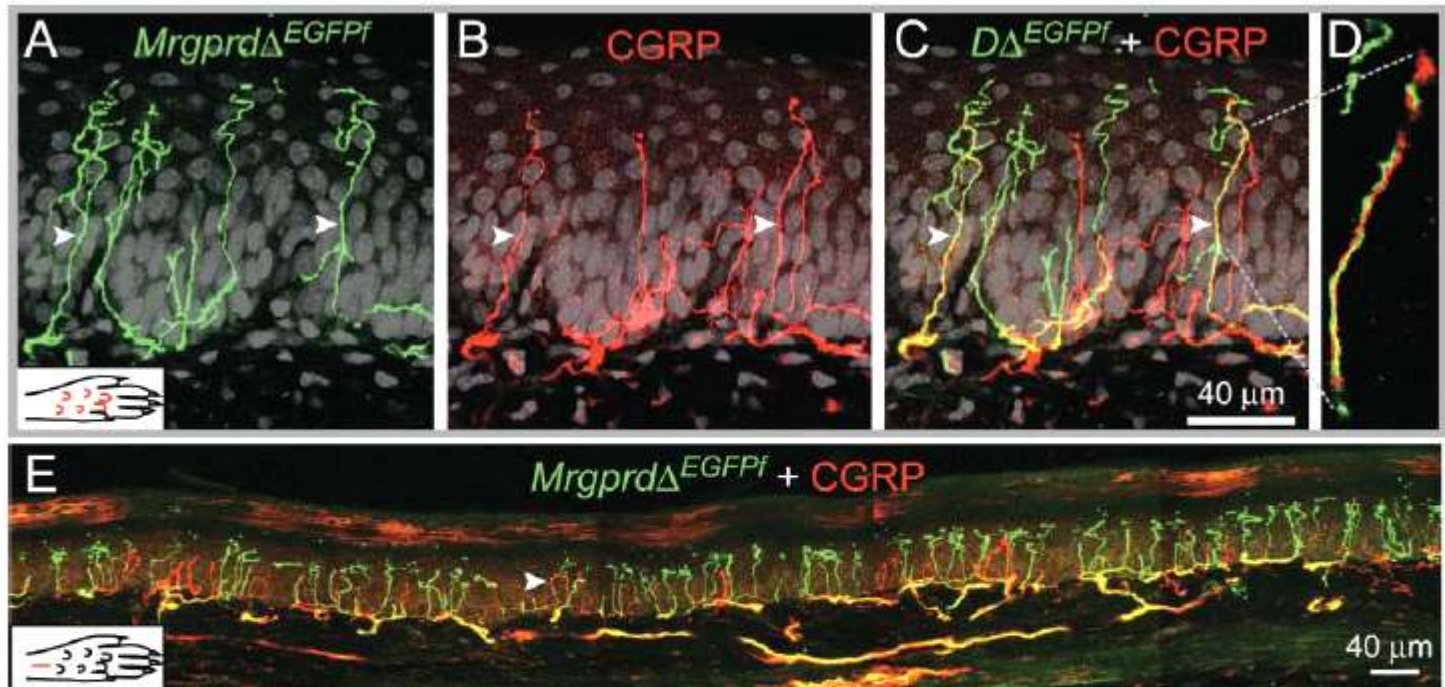
Neurogenic inflammation

Innervation of the skin



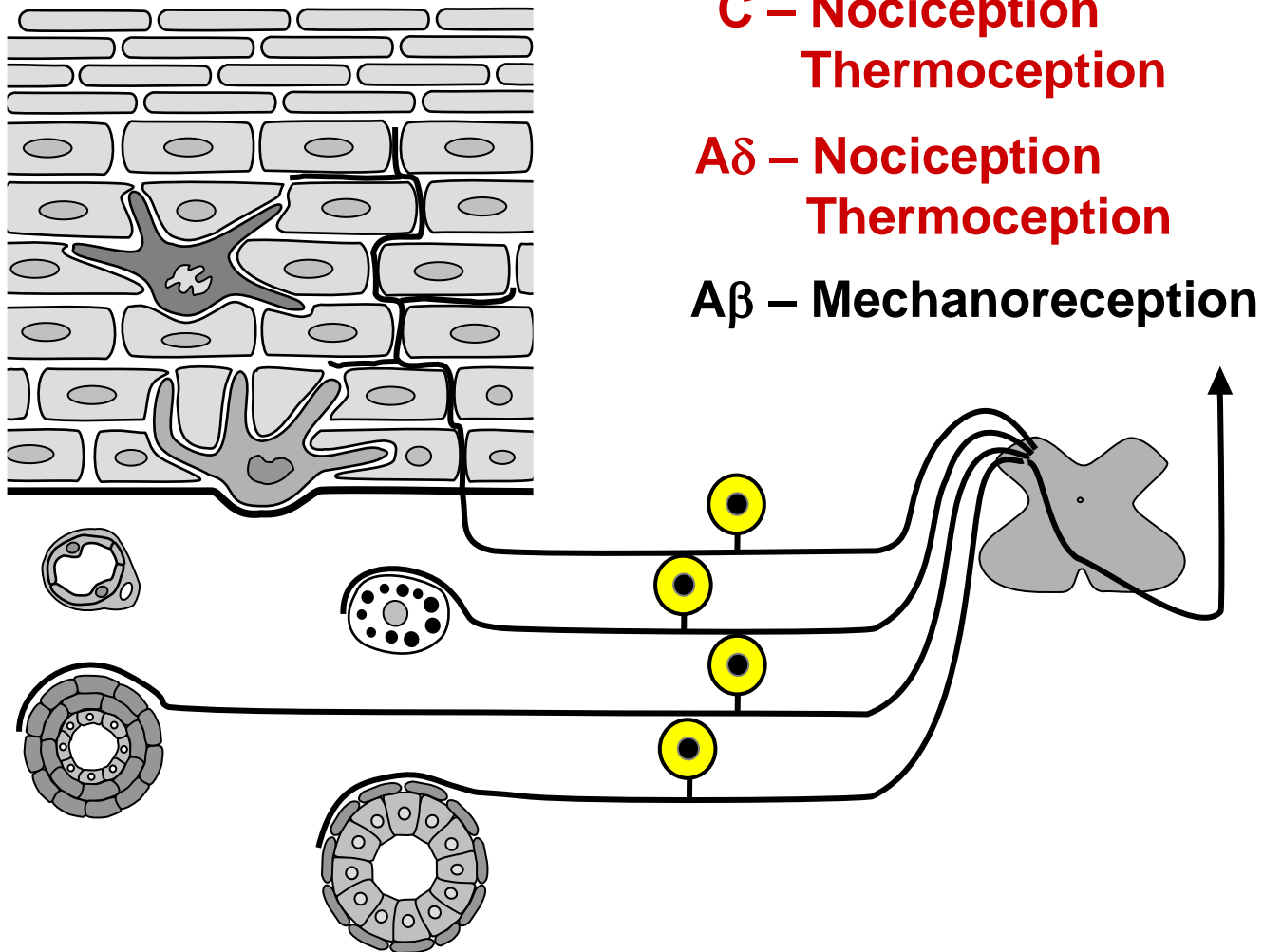
Neurogenic inflammation

Innervation of the skin



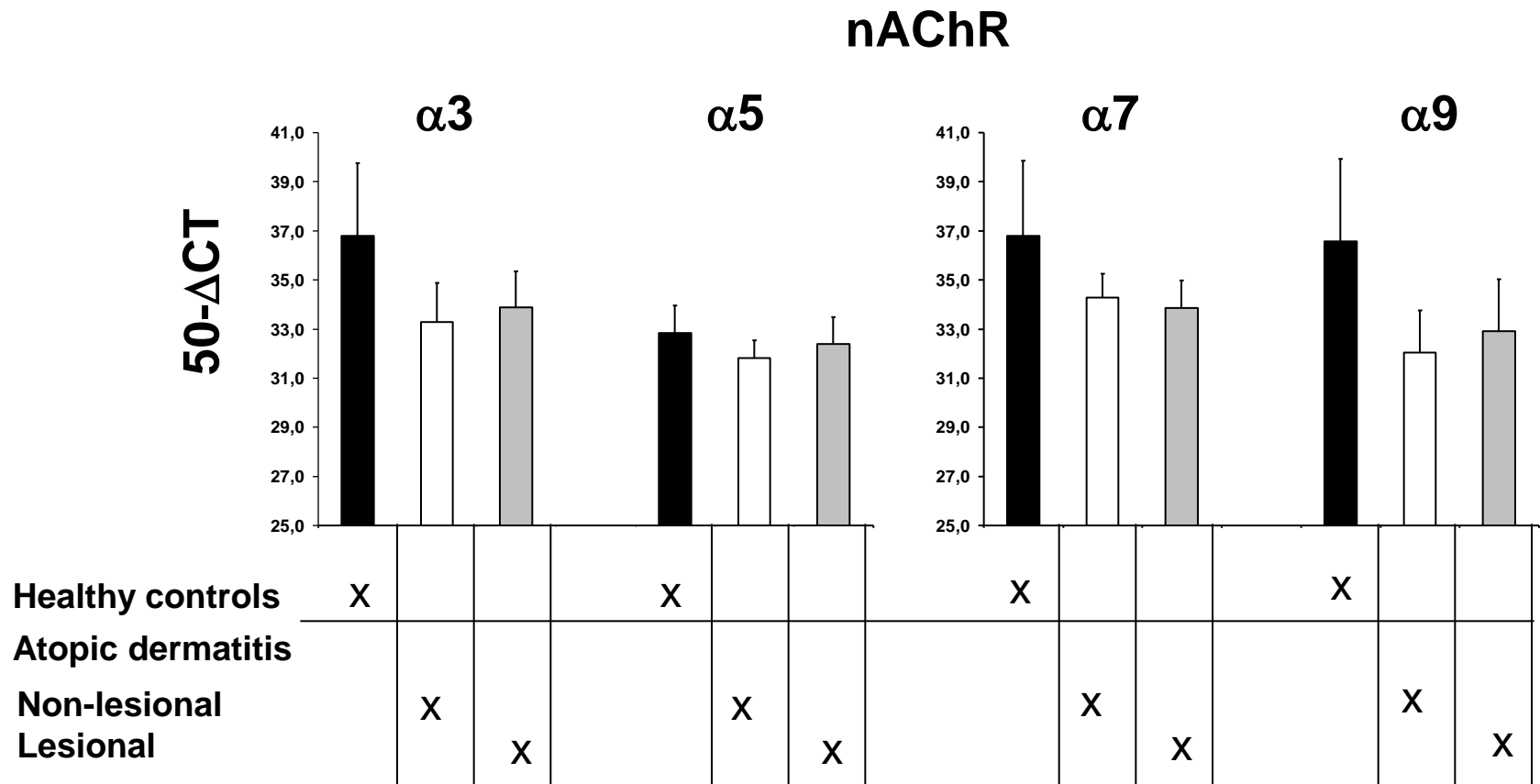
Neurogenic inflammation

Classification of neurons



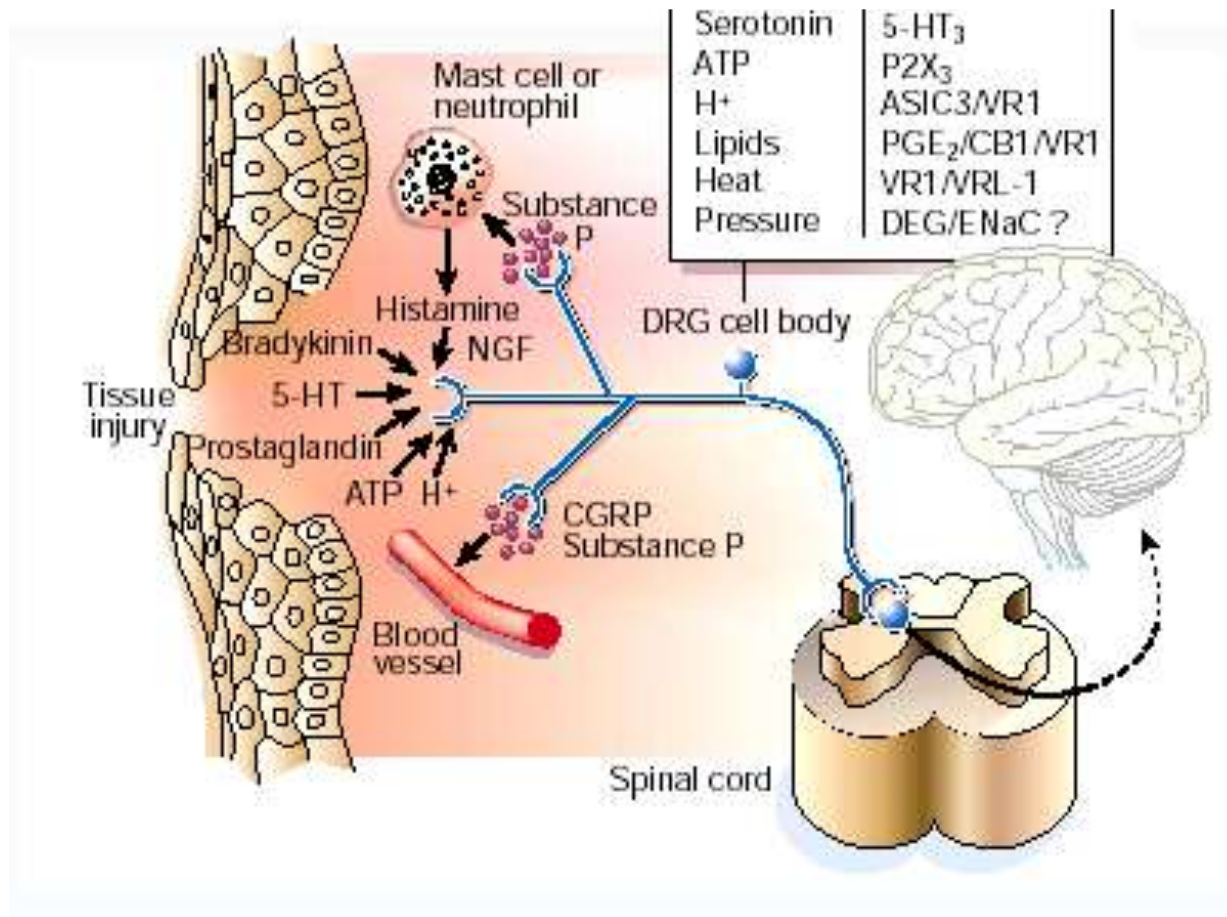
Neurogenic inflammation

The cholinergic system

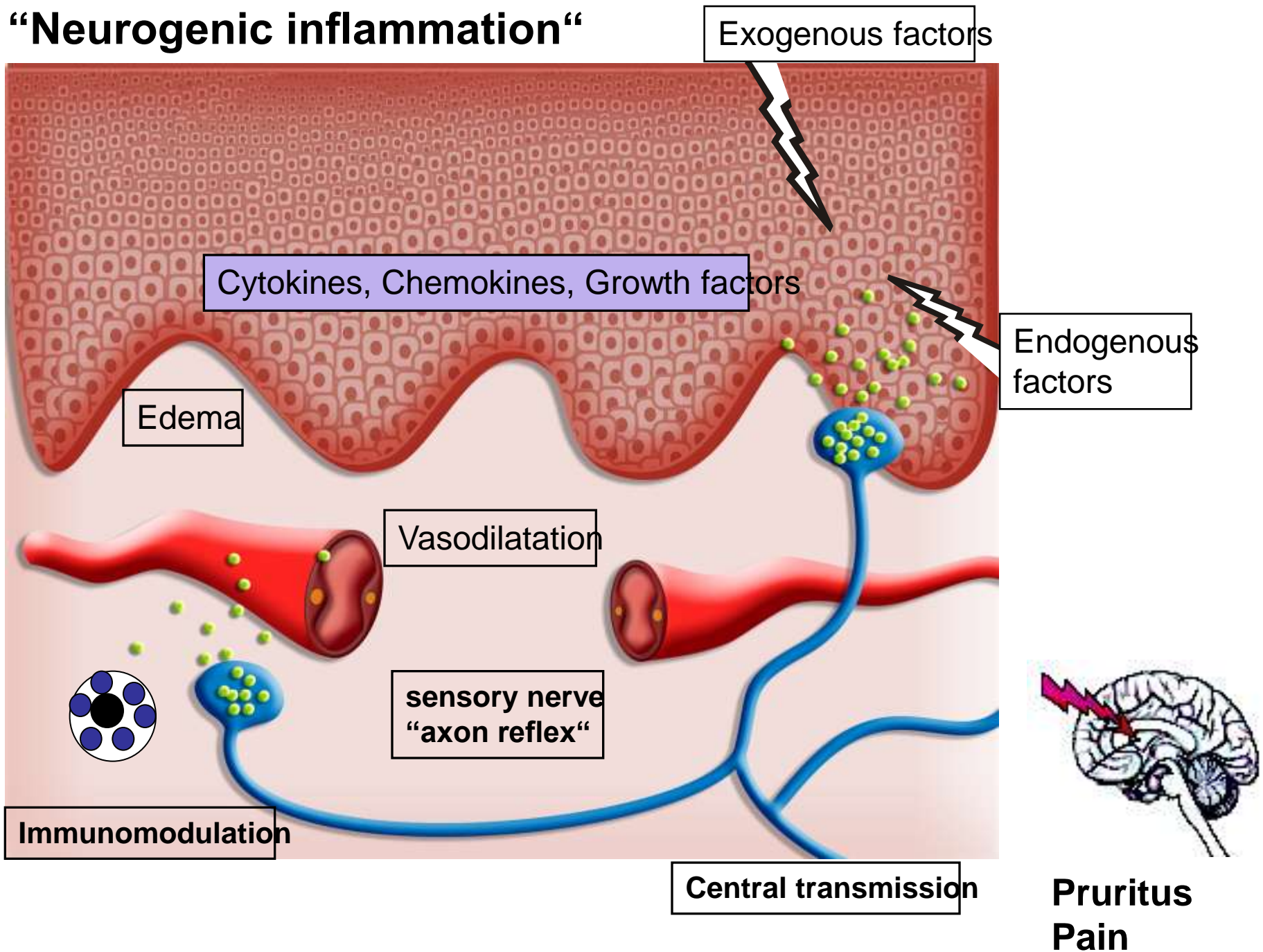


Neurogenic inflammation

Transmitters/mediators/receptors



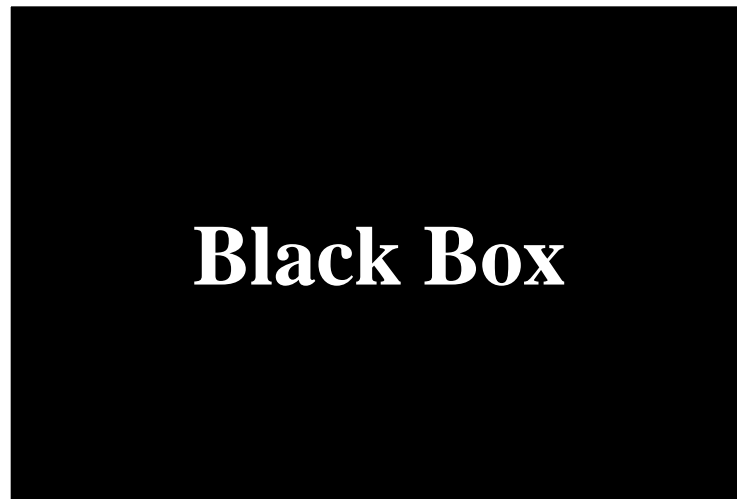
“Neurogenic inflammation“



STRESS



???



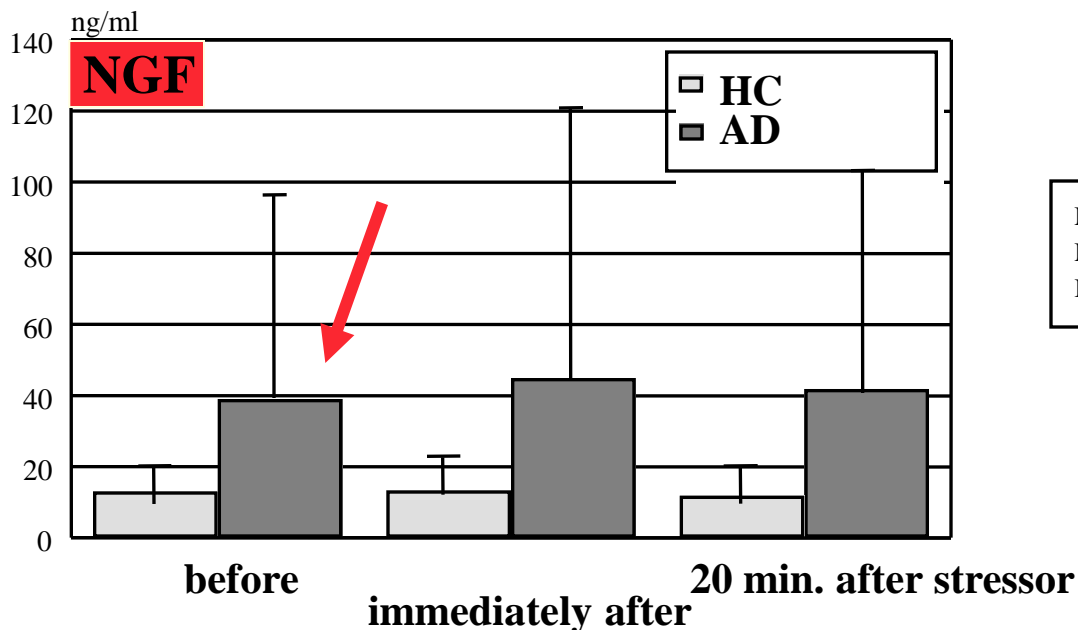
SYMPTOMS

TSST

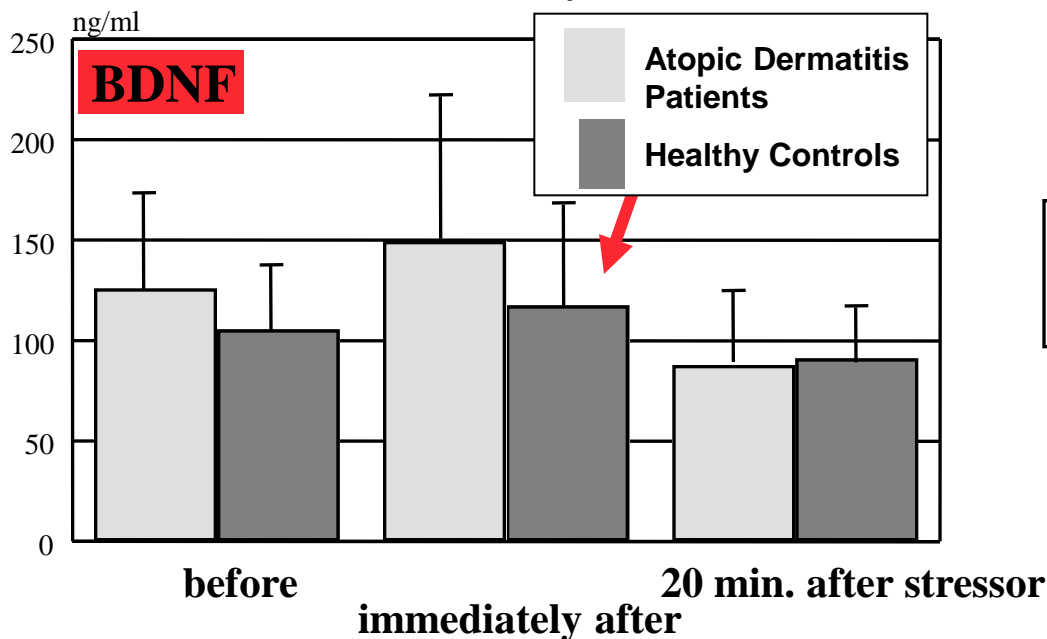
(Kirschbaum et al. 1993)



NGF / BDNF and Stress (TSST)



Main effect group	F(1)=4,80;	p<.05
Main effect time	F(2)=1,45; ns	
Interaction g x t	F(2)=1,20; ns	



Main effect group	F(1)=2,41; ns	
Main effect time	F(2)=25,95;	p<.001
Interaction g x t	F(2)=4,28;	p<.05

Kupfer J, Gieler U, Braun A, Niemeier V, Huzler C, Renz H. Stress and Atopic Eczema. Int Arch Allergy Immunol 2001; 124: 353-5

Intermedin – Neuropeptid seems to play a significant role in the immunologic network in atopic dermatitis (Haberberger et al 2005)

Fig. 5

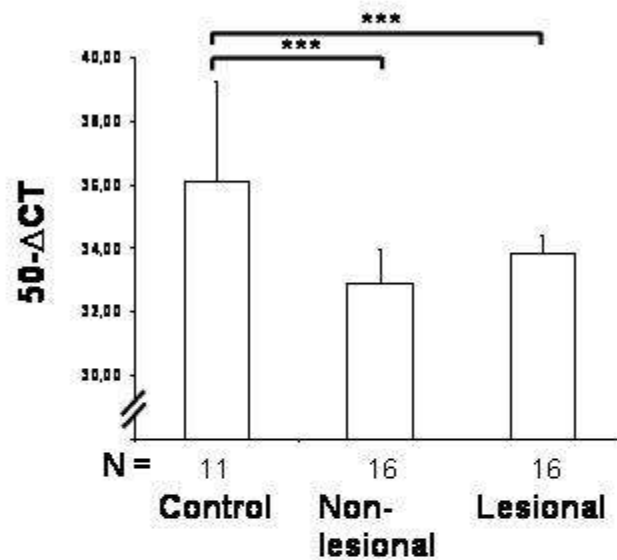
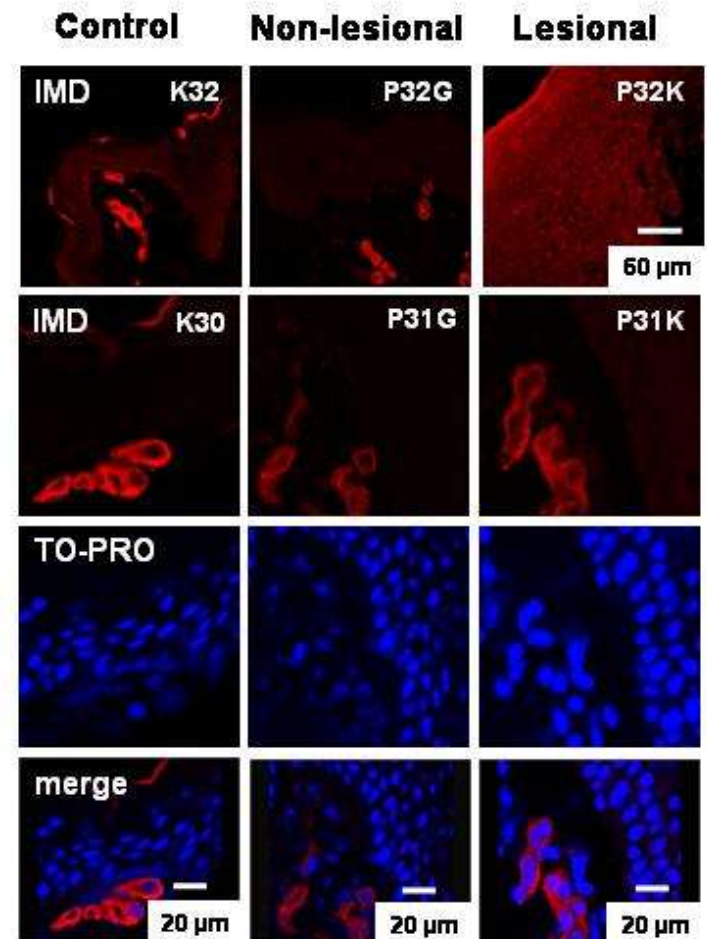


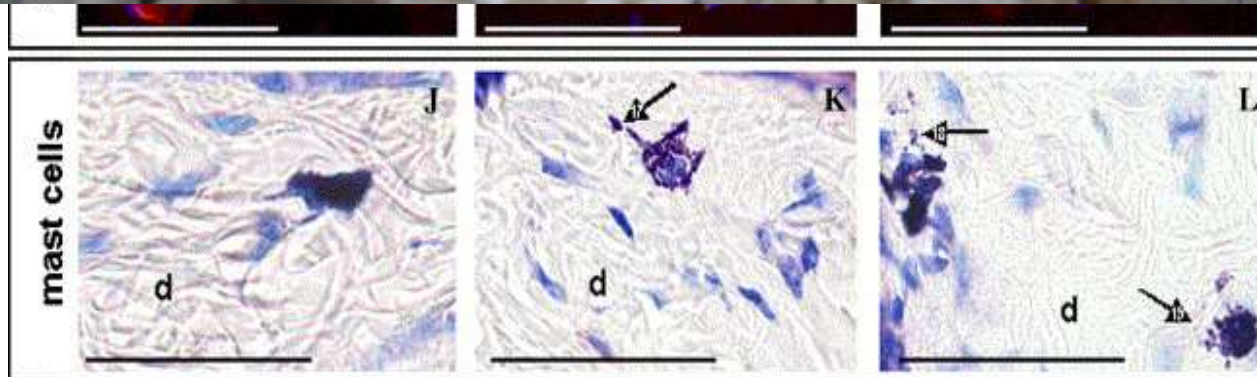
Fig. 7



Sonic stress modulates mast-cell nerve interactions

Enhanced SP+ fibers
Mast-cell nerve contact
Mast cell
Degranulation.

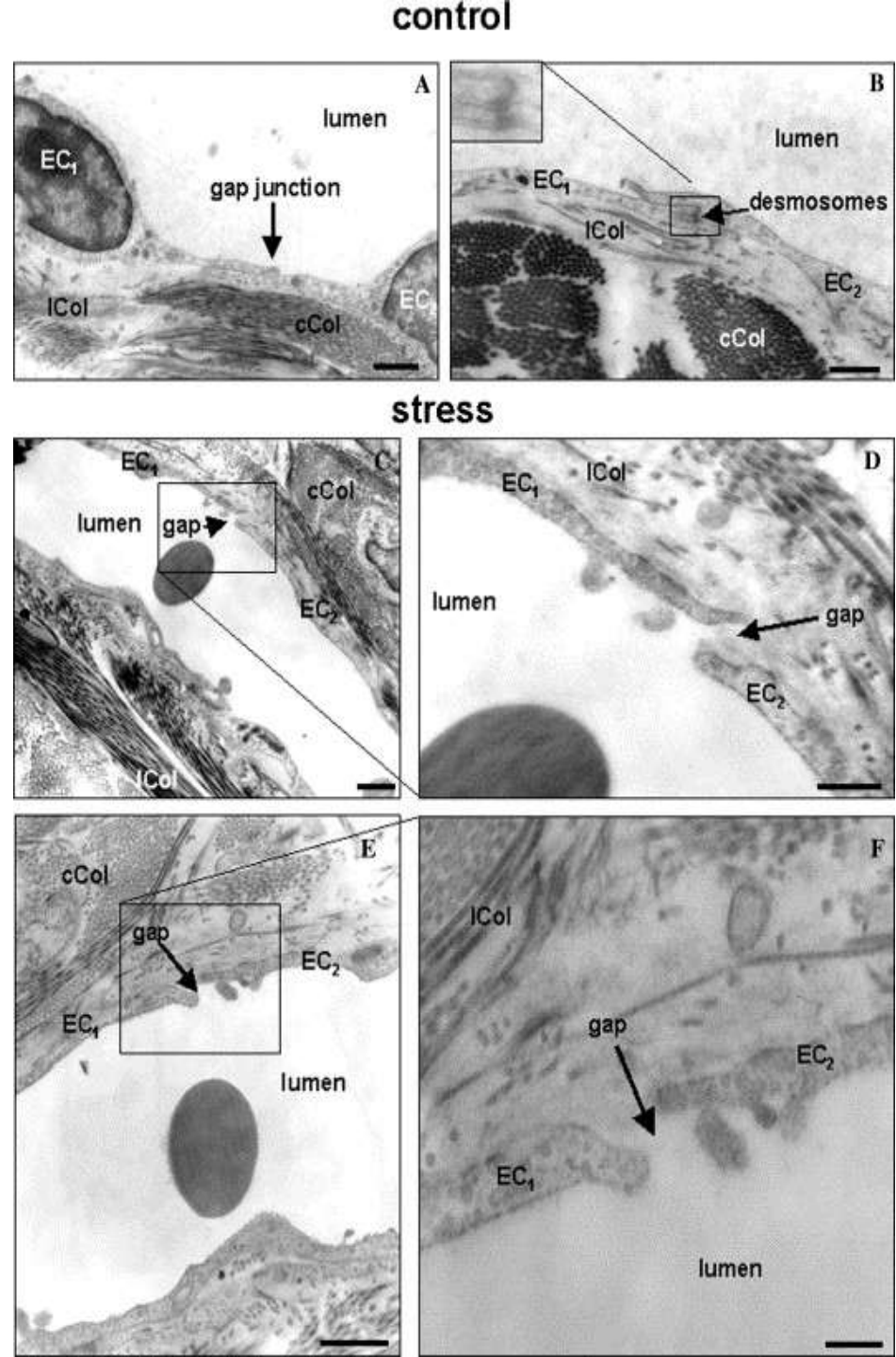
Peters E et al.
Brain, Behav Immun 2005



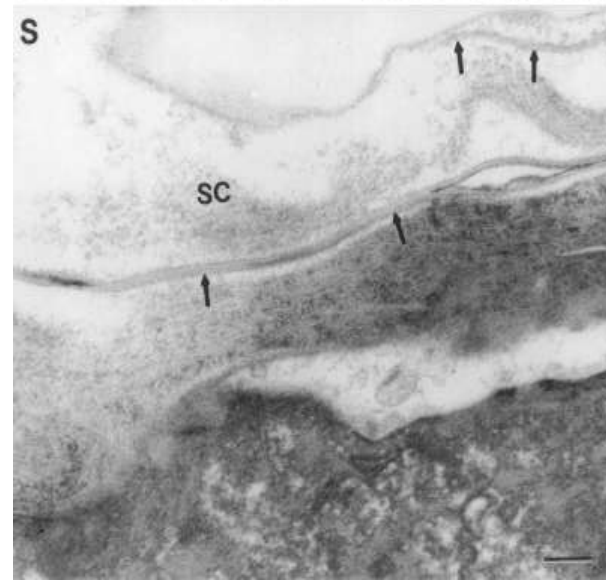
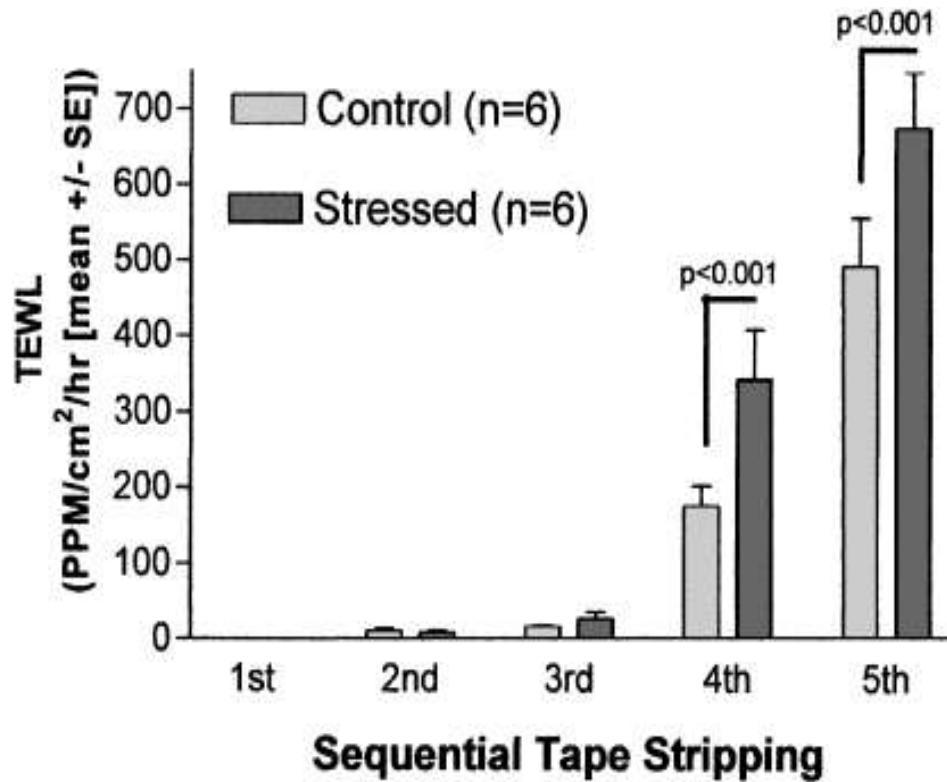
Sonic stress modulates Vascular Permeability

Enhanced SP+ fibers,
Mast-cell nerve contacts
Mast cell
Degranulation.

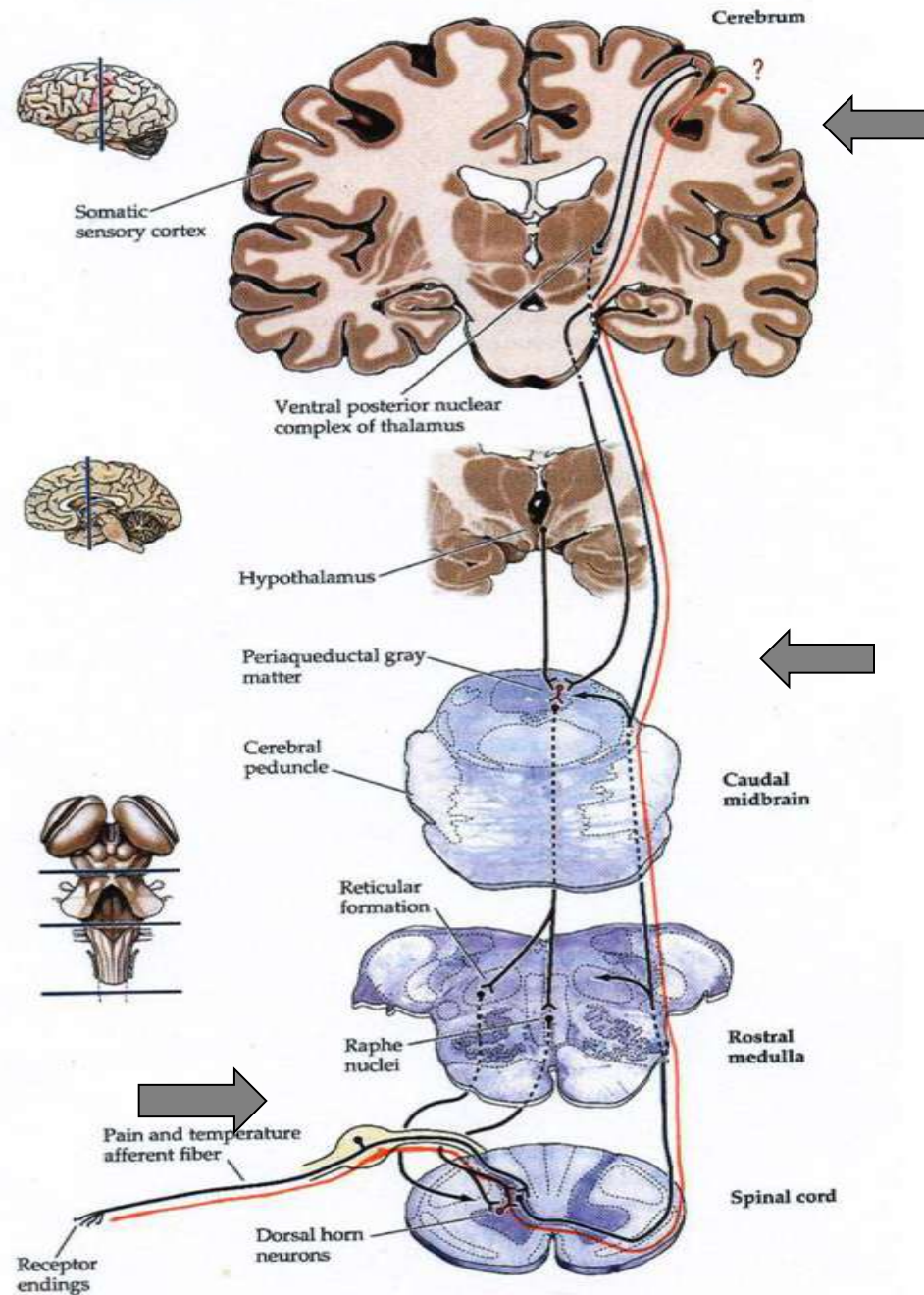
Peters E et al.
Brain, Behav Immun 2005



Stress modulates skin barrier function and epithelial integrity



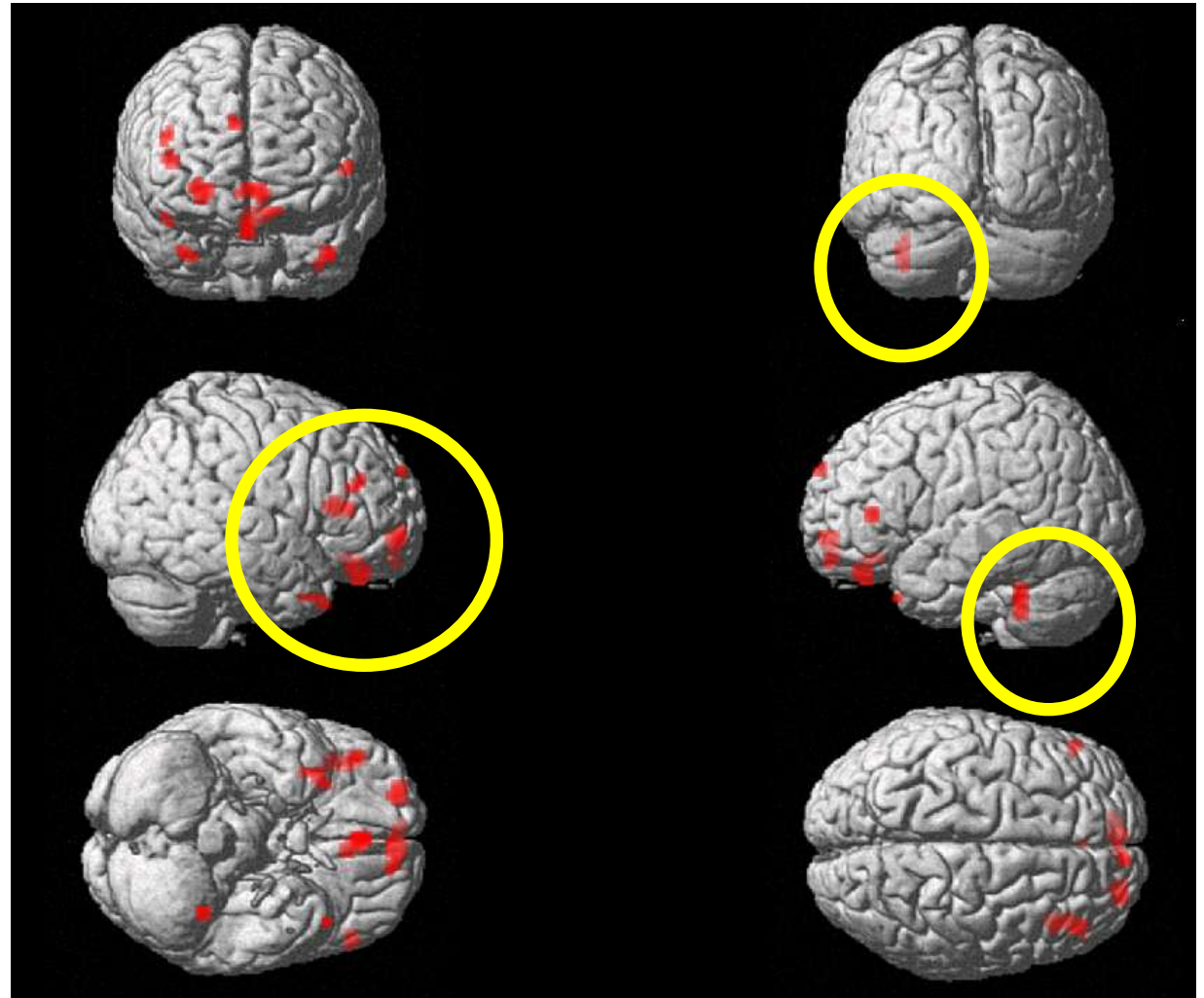
CENTRAL MECHANISM OF INHIBITION OF HISTAMINE INDUCED ITCH AND HYPEREMIA



In which areas are activities in brain after histamin itch ?

5 healthy male were stimulated by normal histamin prick test and NaCl-control-prick-test

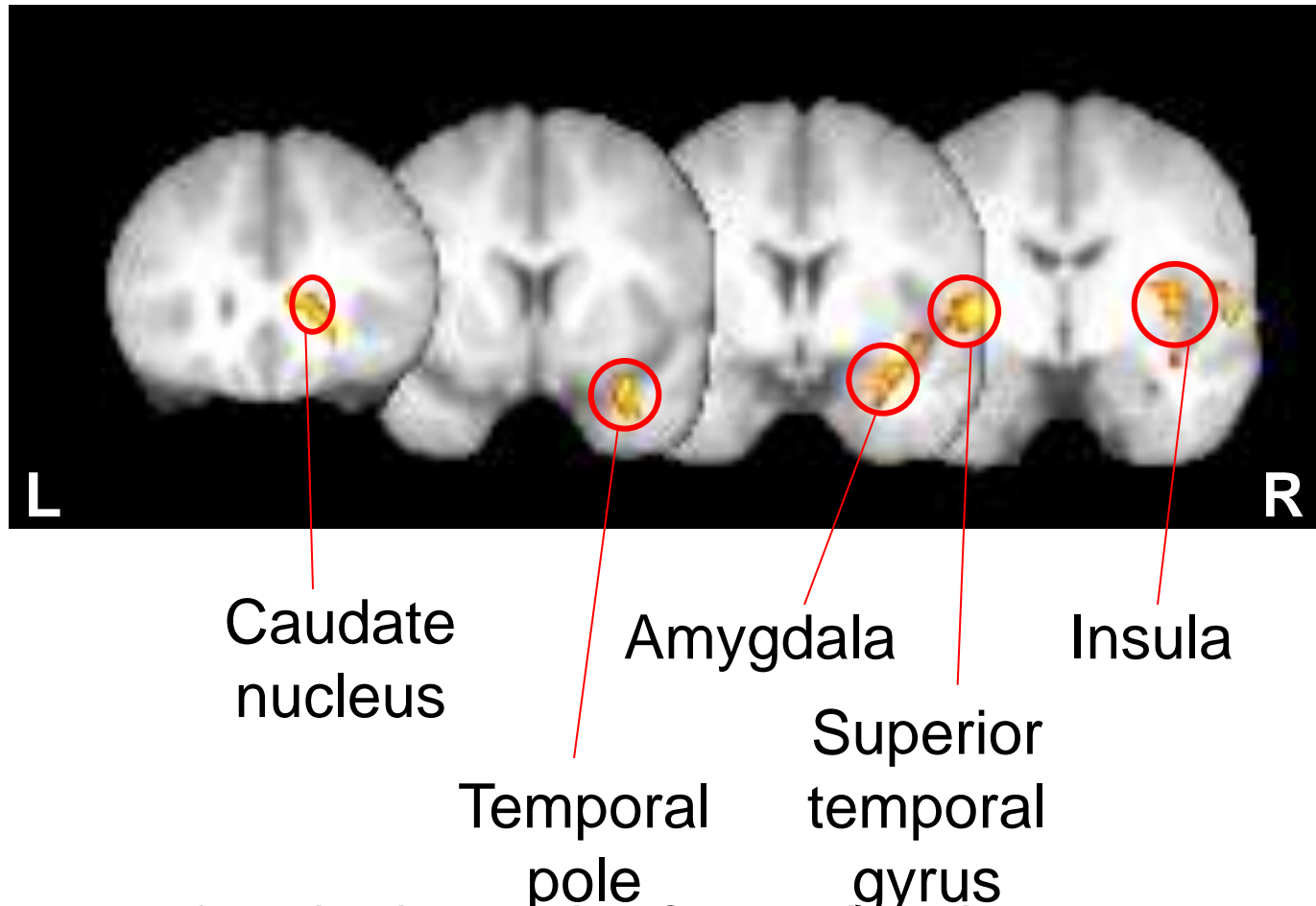
Brain activities were measured by f-MRT analysis (BION-Institut for Psychology: Prof. Vaitl; Dr.B.Walter; Gießen/Germany) and statistical analysis of significant acitivation by SPM99.



Walter B, Sadlo MN, Kupfer J, Niemeier V, Brosig B, Stark R, Vaitl D, Gieler U (2005) Brain Activation by Itch Induced by Histamine Prick Test. Journal of Investigative Dermatology 125:380-382

Work in progress: Results

31 – 150 secs after prick



Walter B, Sadlo MN, Kupfer J, Niemeier V, Brosig B, Stark R, Vaitl D, Gieler U
(2005) Brain Activation by Itch Induced by Histamine Prick Test.
Journal of Investigative Dermatology 125:380-382

Thank you very much for your attention !



- **Was Brocq and Jaquet 1891 correct in her statement „neuro-dermatitis“ ? – Yes, but not „neuro-dermatitis, but neurogenic dermatitis“**
- **Atopic dermatitis depends from nerves**
- **Atopic dermatitis and affective disorders interact**
- **Atopic dermatitis is stress dependend**
- **Atopic Dermatitis is triggered by peripheral nerves and neuropeptides**
 - **NGF/BDNF**
 - **PAR**
 - **Non-cholinergic Acetylcholin-Receptors**
 - **Intermedin - Neuropeptid**
- **Atopic Dermatitis / Itch correlate with brain activity**
- **Possible Therapy approach by Anti-neuropeptides or with psychotherapy to change brain reaction !**

The Psychodermatology Research Team Giessen-Germany



Centre for Psychosomatic
Medicine – University of Giessen:

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Dipl.-Psych. S.Schallmayer

PD Dr. Volker Niemeier

Bender Institute for Neuroimaging
– Clinical Psychology Institute
University of Giessen:

Dr. Dipl.-Psych. Bertram Walter

Prof. Dr. Dieter Vaitl

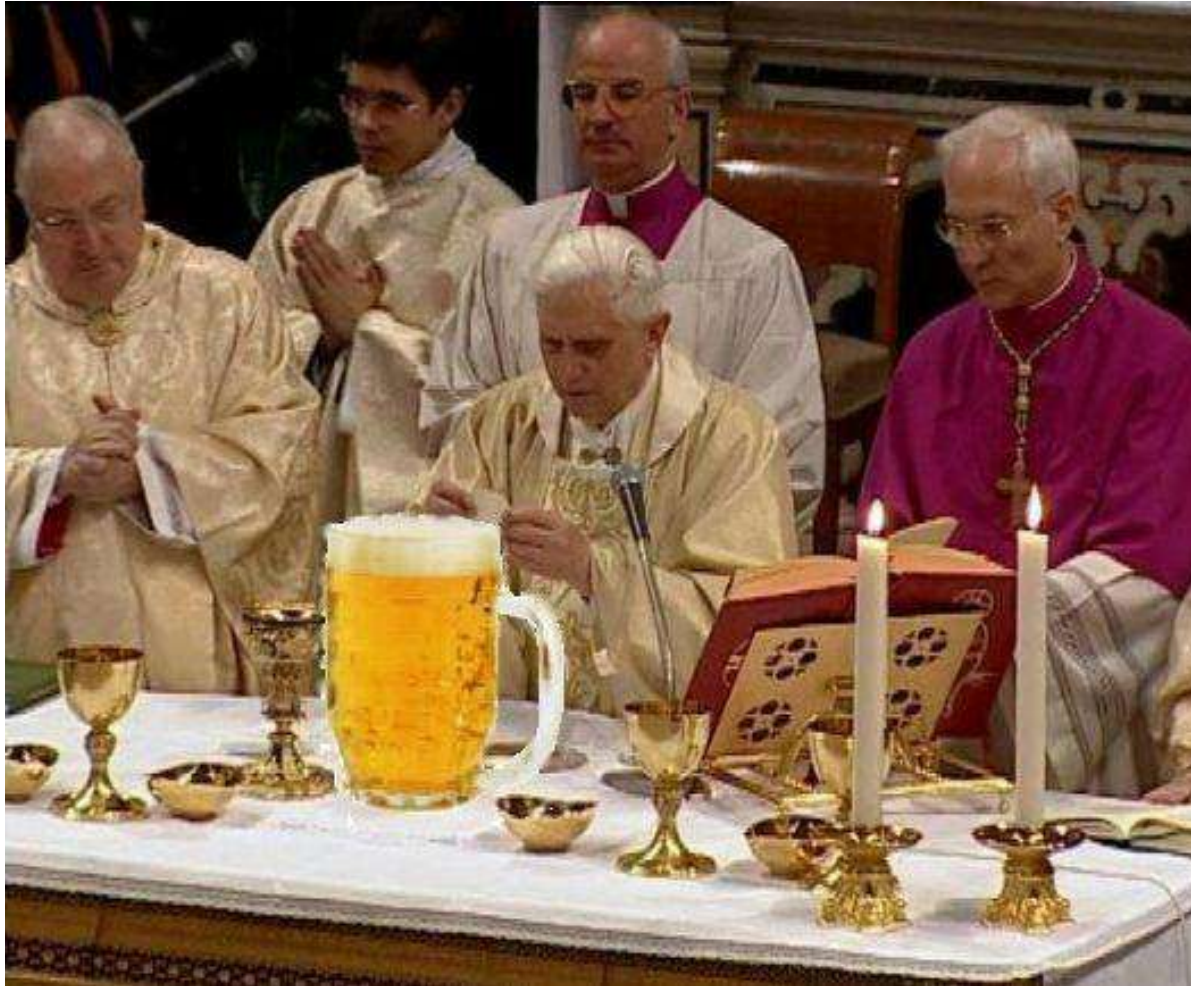
Institute for Anatomy and Cell
Biology – University of Giessen:

PD Dr. Rainer Haberberger

Cand.med. Frederike Kindt

Prof. Dr. Wolfgang Kummer

Thank you very much for the
Pilsener Urquell !



www.ESDP2007.org

University Department of
Dermatology in Wrocław (1892)



12th Congress of the
European Society for
Dermatology and Psychiatry

June 14 – June 17, 2007
Hotel Mercure Panorama
Wrocław, Poland



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**Do not forget
the next
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June 14 - 17**

**МОСКОВСКАЯ МЕДИЦИНСКАЯ АКАДЕМИЯ
XXIII РАХМАНОВСКИЕ ЧТЕНИЯ ПРОГРАММА
26 – 27 ЯНВаРЯ 2006 гОда**



Уве ГИЛеР

**ПСИХОСОМАТИКА АТОПИЧЕСКОГО ДЕРМАТИТА:
ОТ РЕЦЕПТОРОВ К ИНДИВИДУАЛЬНОЙ ТЕРАПИИ**



Dr. Veronica Frolova

P.-D. Andrej Lvov MD PhD

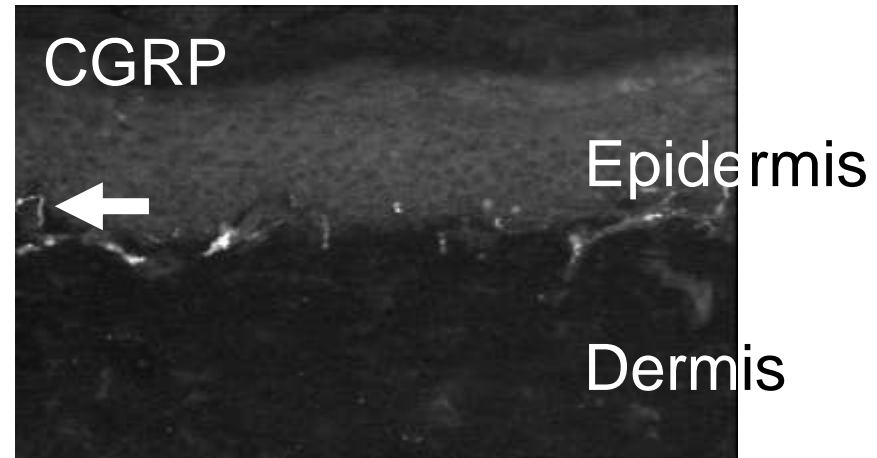
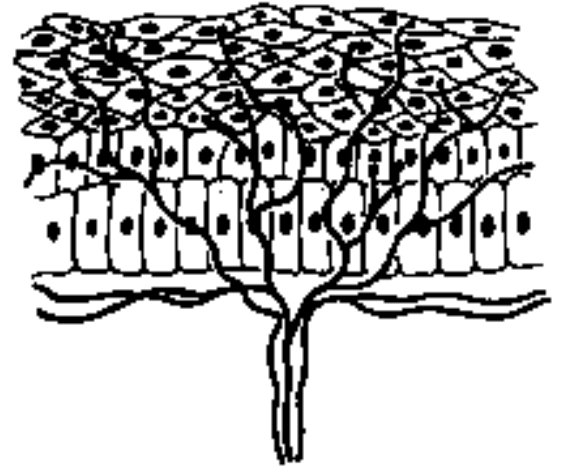
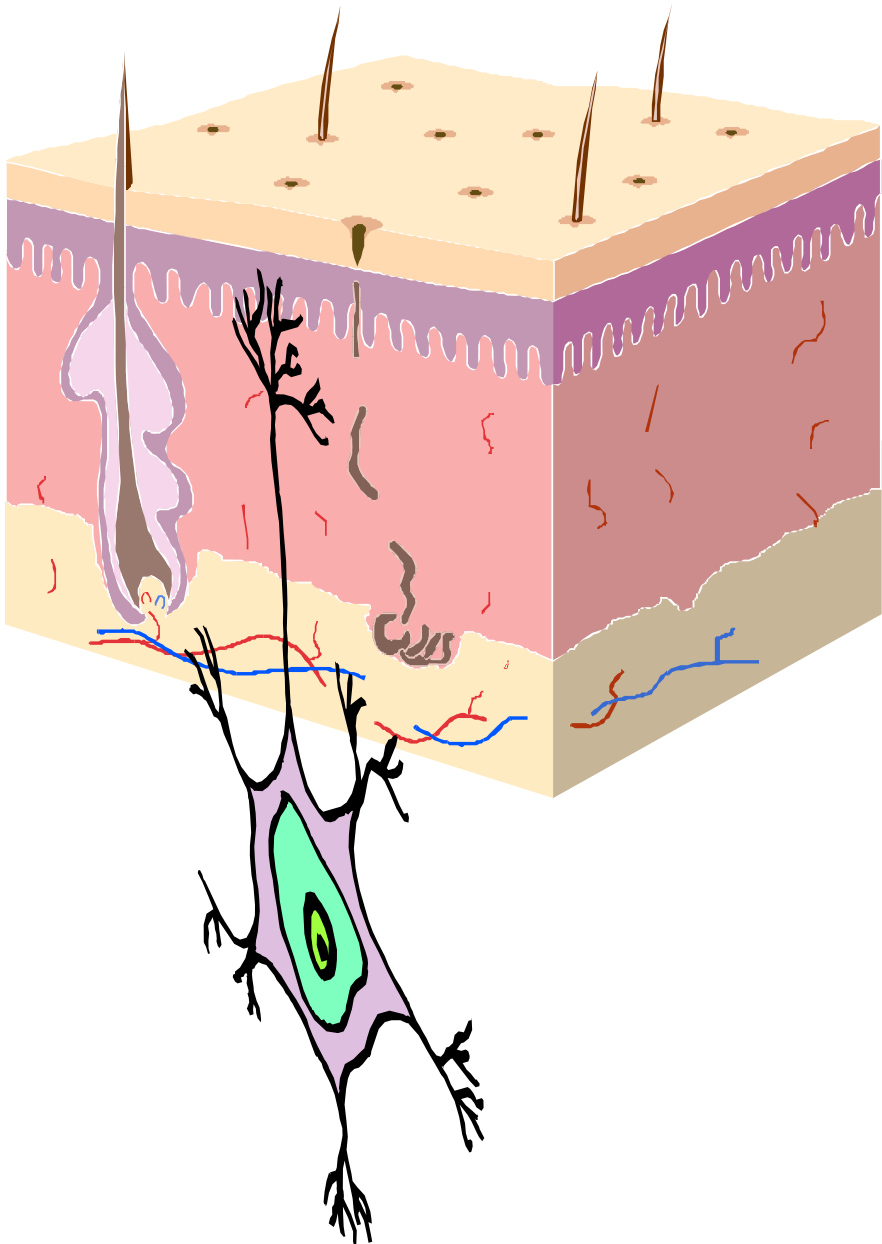
Tactile Development of Human Being

- Mice and other animals including apes who are separated from their mothers in early childhood developed more somatic reactions to stress. Especially tactile stimulation are one of the most important factor for a healthy development.

Levine (1957) Science 126:405-406

Hofer (1984) Psychosomatic Medicine 46:183-187

Rosenblum&Andrews (1994) Acta Paediatrica
397:57-63



Sugiura H, Maeda T, Uehara M: Mast cell invasion of peripheral nerve in skin lesions of atopic dermatitis. *Acta Derm Venereol* (1992) 90: 613-622

Gupta MA et al.

Depression modulates pruritus perception: A study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria.

Psychosom Med 56:36-40, 1994

Kovacs M et al.

Severity of allergic complaints:
the importance of depressed mood.

J Psychosom Res 54: 549-57, 2003

Timonen M et al.

Association between atopic disorders and depression: findings from the northern finland 1966 birth cohort study.

Am J Med Gene 105:216-217, 2001

Mojtabai R.

Parental Psychopathology and Childhood Atopic Disorders in the Community.

Psychosomatic Medicine 67:448-453, 2005

Mojtabai R.

Parental Psychopathology and Childhood Atopic Disorders in the Community.

Psychosomatic Medicine 67:448-453, 2005

- Parental major depression and panic attacks were associated with childhood atopic disorders only in biological parent-child dyads, and among these more strongly in mother-child dyads.



adjusted odds ratios =

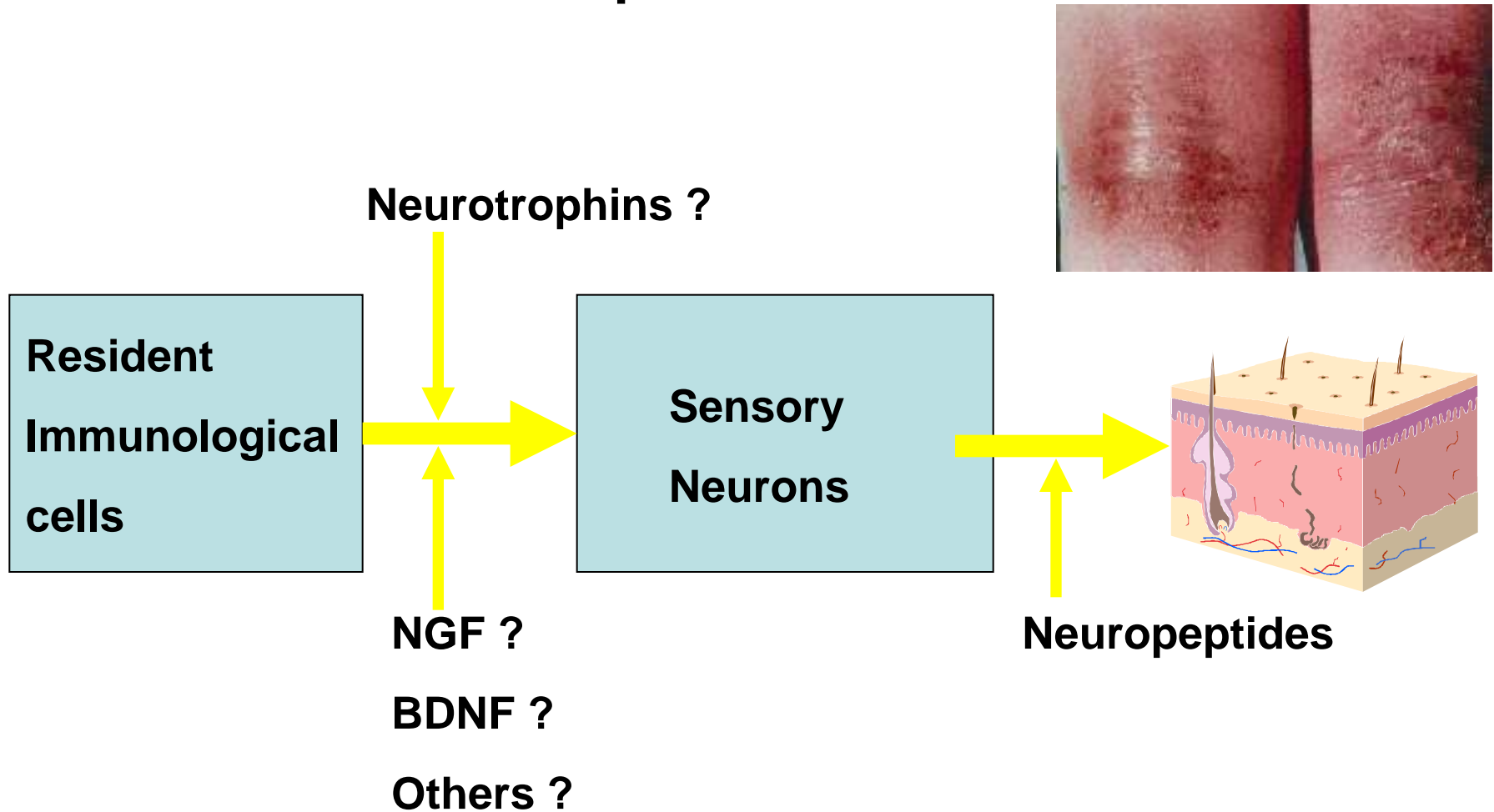
1.67 for major depression and
1.46 for panic attacks

Mechanisms by which psychologic stress alters cutaneous permeability barrier homeostasis and stratum corneum integrity.

Choi EH, Brown BE, Crumrine D, Chang S, Man MQ, Elias PM, Feingold KR.

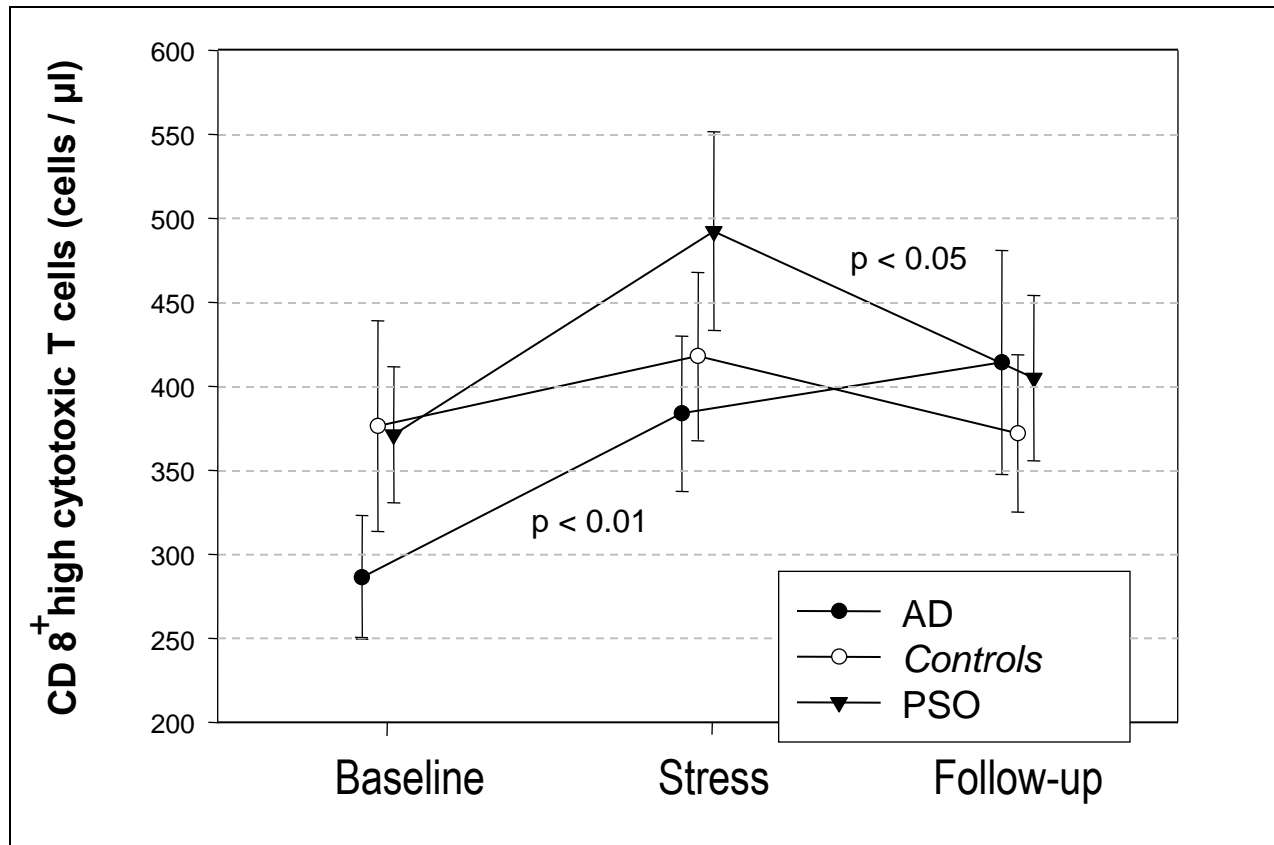
- Insomniac psychologic stress (IPS) altered both barrier homeostasis and SC integrity. IPS decreased epidermal cell proliferation, impaired epidermal differentiation, and decreased the density and size of corneodesmosomes (CD), which was linked to degradation of CD proteins (e.g., desmoglein1).

Neurogenic Inflammation in atopic eczema



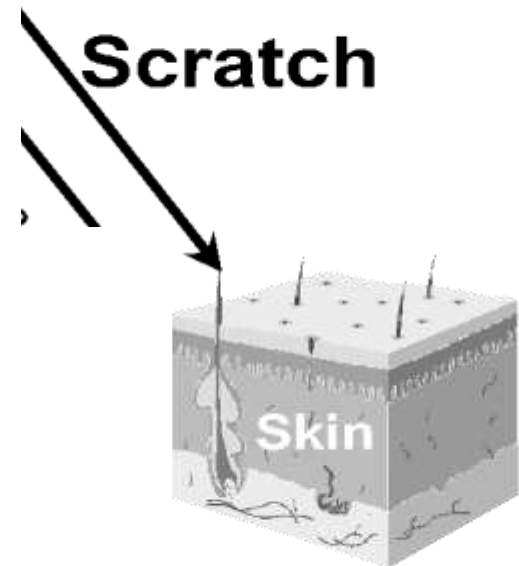
Number of CD8⁺ cytotoxic T lymphocytes

(Schmid-Ott et al. JACI 2001)

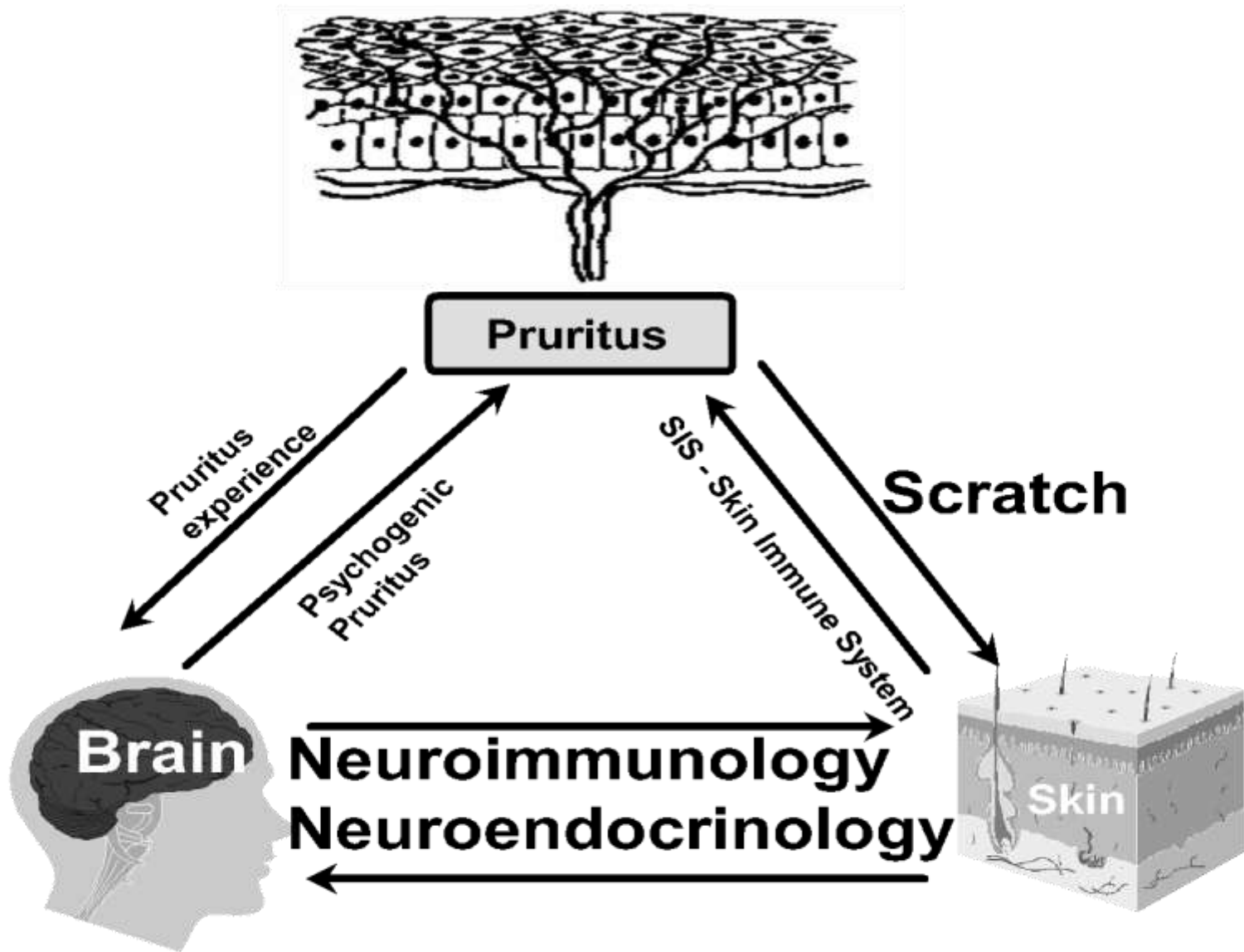


Schmid-Ott G, Jäger B, Meyer S et al (2001) Different expression of cytokine and membrane molecules by circulating lymphocytes on acute mental stress in patients with atopic dermatitis in comparison with healthy controls. *J Allergy Clin Immunol* 108:455—462

Schmid-Ott G, Jaeger B, Adamek C et al (2001) Levels of circulating CD8+ T lymphocytes, natural killer cells and eosinophils increase upon acute psychosocial stress in patients with atopic dermatitis. *J Allergy Clin Immunol* 107:171--177



Brocq, L. et L. Jacquet: Notes pour servir a l'histoire des neurodermatitis. Annales Dermatologie et Venerologie 97,193-195 (1891)



Brocq, L. et L. Jacquet: Notes pour servir a l'histoire des neurodermatitis. Annales Dermatologie et Venerologie 97,193-195 (1891)