



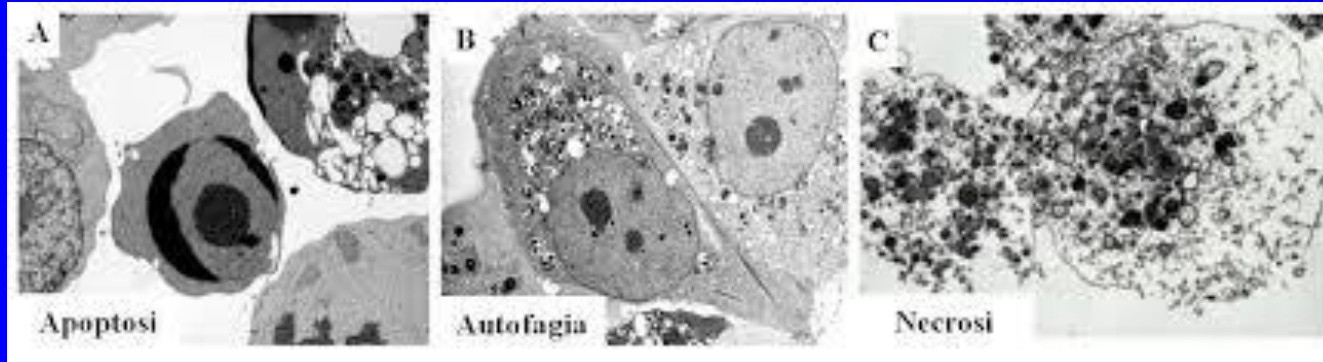
Azienda Ospedaliera Universitaria  
Policlinico Paolo Giaccone Palermo

**AUDIOLOGIA**  
*Policlinico di Palermo*

**Dr Aldo Messina**  
**U.O. Audiologia**  
**Policlinico Palermo**

Aldomes 2017

# Cosa uccide un neurone



**Eccitotossicità PNEI**

**Ossidazione**

**Infiammazione**

**Metalli pesanti**

**Mutazioni geniche**

**Eventi vascolari**

**Traumi**

**Fattori ambientali**

**Diabete**

**Malattia di Parkinson**

**Malattia di Alzheimer**

**Sclerosi laterale**

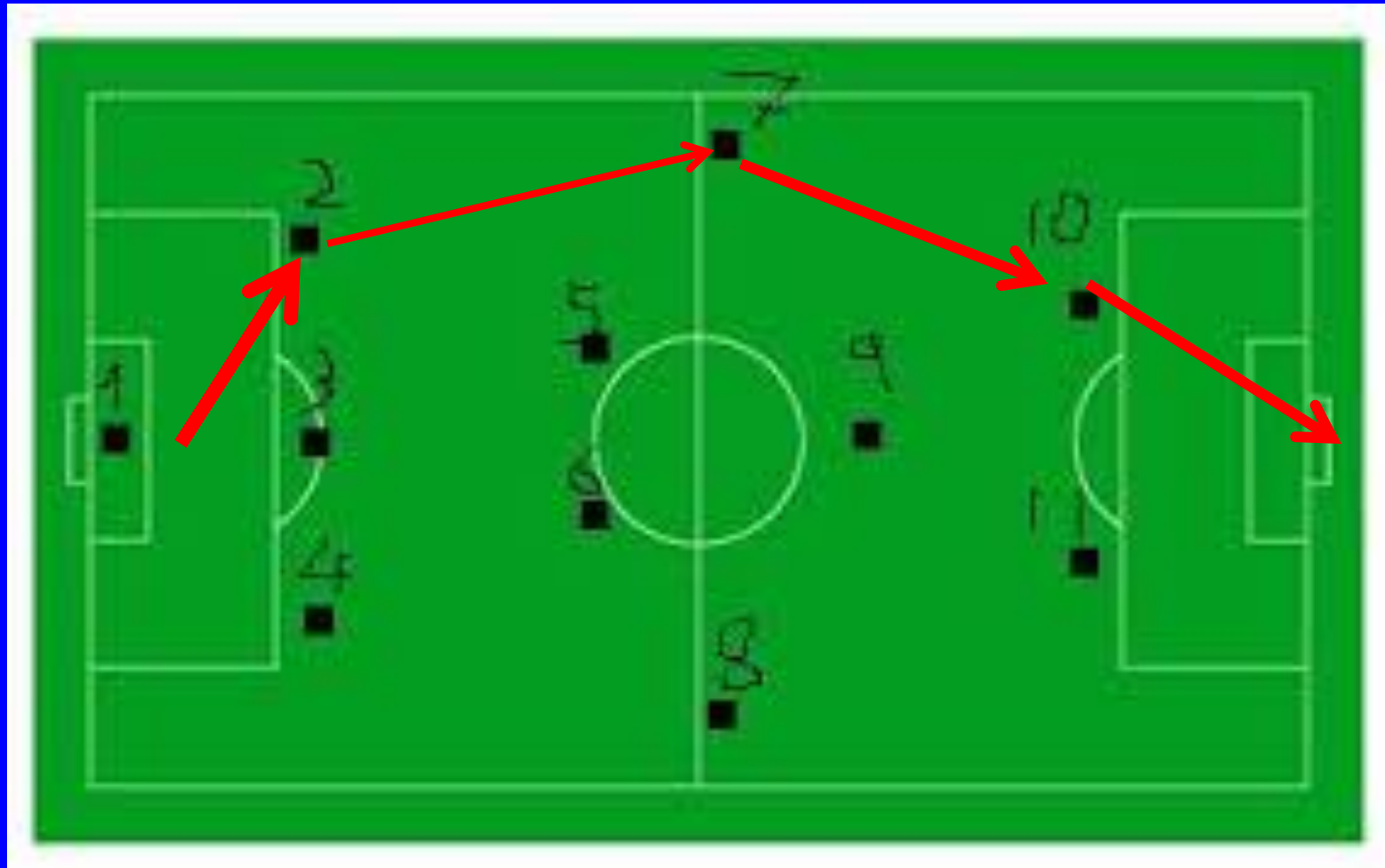
**Corea di Hungtington**

**Demenza da HIV**

**Demenza senile**

**Deficit sensoriali**

Alcune premesse: il SNC non funziona grazie a «stazioni» che inviano la loro informazione a quella successivo



Ma grazie a sinapsi(stazioni) , che pur con la loro individualità, inviano dopo aver « subito» anche le informazioni di altri neurotrasmettitori, nervosi e/o ormonali



# Poichè l'uomo è un animale chimico anzi biochimico.

## La chimica dell'innamoramento

Quando ci innamoriamo si attiva un'autentica tempesta di ormoni, neurotrasmettitori e sostanze chimiche che ci permettono di percepire intense sensazioni fisiche

### Feniletilamina (PEA)

Responsabile dell'euforia e della positività all'inizio di un rapporto amoroso

### Adrenalina

Provoca un aumento del battito cardiaco, della respirazione e della pressione sanguigna, da cui ha origine il rossore del volto

### Ossitocina

Genera sensazioni affettive e protettive rafforzando la componente emotiva dell'innamoramento

### Vasopressina

È l'ormone che spinge alla fedeltà

### Endorfine

Hanno un'azione rilassante, calmante, analgesica. Entrano in gioco quando l'innamoramento si trasforma in una relazione meno passionale e più affettiva

### Estrogeni e androgeni (donna)

Attivano i centri cerebrali capaci di tradurre un desiderio erotico in una risposta anche fisica che si propaga a tutto il corpo

### Testosterone (uomo)

Rilasciato dai testicoli, è l'ormone principe del desiderio sessuale e stimola la libido

### Noradrenalina

Provoca eccitazione, euforia ed entusiasmo. Fa passare l'appetito

### Feromoni

Sono emessi da pelle, capelli, saliva, ghiandole ascellari, urina e flusso mestruale e, percepiti da un organo recettore situato nel vomere nasale, scatenano l'attrazione fisica

### Dopamina

Genera sensazioni piacevoli di benessere

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"Il bacio" di Francesco Hayez

ANSA centimetri



Il risultato è l'individuo, dal latino  
“inseparabile”, l'arma vincente  
dell'evoluzione



# La svolta organicista: Gorman indica la «sede» neurologica di alcuni disturbi ritenuti psichici

- A conferma di una visione prettamente organicista l'ipotesi di Gorman secondo la quale
- gli attacchi di **panico = tronco-encefalo,**
- **l'ansia anticipatoria nel lobo limbico**
- **l'evitamento fobico nelle aree prefrontali**

[Am J Psychiatry](#). 1989 Feb;146(2):148-61.

## **A neuroanatomical hypothesis for panic disorder.**

[Gorman JM](#)<sup>1</sup>, [Liebowitz MR](#), [Fyer AJ](#), [Stein J](#).

[+](#) **Author information**

### **Abstract**

Anxiety disorders, the most common psychiatric conditions in the United States, have generated a great deal of research and scientific debate. Panic disorder, the best-studied anxiety disorder, is often believed to be either a biological disease or a psychological disease. The authors present a neuroanatomical model of panic disorder that attempts to reconcile these views. The model locates the three components of the disease--the acute panic attack, anticipatory anxiety, and phobic avoidance--in three specific sites of the CNS: the brainstem, limbic system, and prefrontal cortex, respectively. The authors suggest experiments to test their model.

# *In questo contesto «olistico» si inserisce la PNEI (Psiconeuroendocrinoimmunologia)*

Rappresenta la vittoria della saggezza popolare che da **molti secoli**, con le sue affermazioni (Es. ho il cuore in gola, stringi i denti ed affronta la vita, un bambino cresce anche dormendo, la notte porta consiglio... )ci ha invitato ad intendere il corpo come organismo.

La PNEI ci fa andare «oltre Galileo», facendoci conoscere un mondo di emozioni e vissuti , non misurabili ma per questo non certo non esperibili.





**ERRORE**

# Sei grasso? «Costituzionalmente predisposto»

E' un termine che si utilizza spesso allorquando si vuol cercar di capire perchè, in condizioni di uguale esposizione, alcuni soggetti si ammalano ed altri no.

In realtà “costituzionalmente predisposto” però ci deve ricordare che l'essere umano è elemento biochimico e che in definitiva ciò che succede o non succede dentro di noi è espressione di una reazione chimica o della prevalenza di un processo biochimico rispetto ad un altro.

**Sono grasso!  
Sarà lo stress**



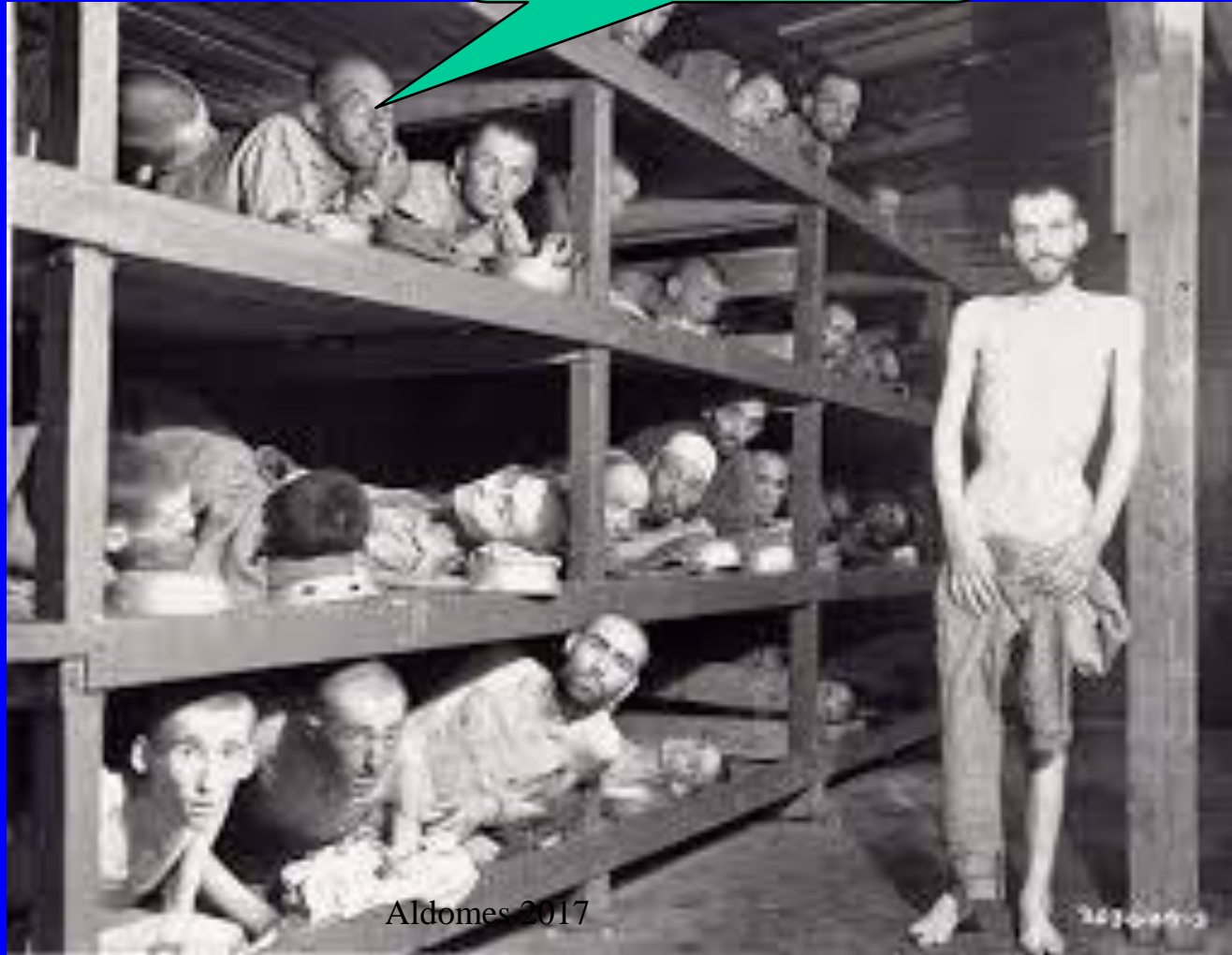
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www.aldomes.it

**ERRORE**

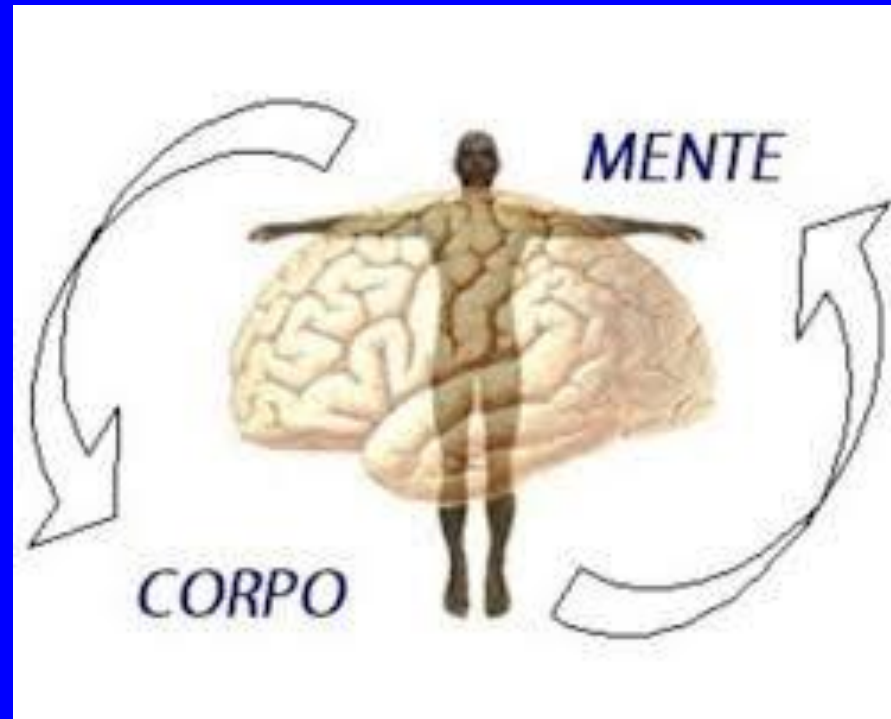
Qui ad Auschwitz  
siamo tutti molto  
stressati. Ma non mi  
pare che siamo grassi!

**Mantenendo il rigore  
scientifico.**



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# PNEI- OLISMO



**LA PNEI è il sistema che regola l'omeostasi globale biochimica- epigenetica (quindi sia strutturale che psichica) del nostro organismo in risposta ad input interni ed esterni.**

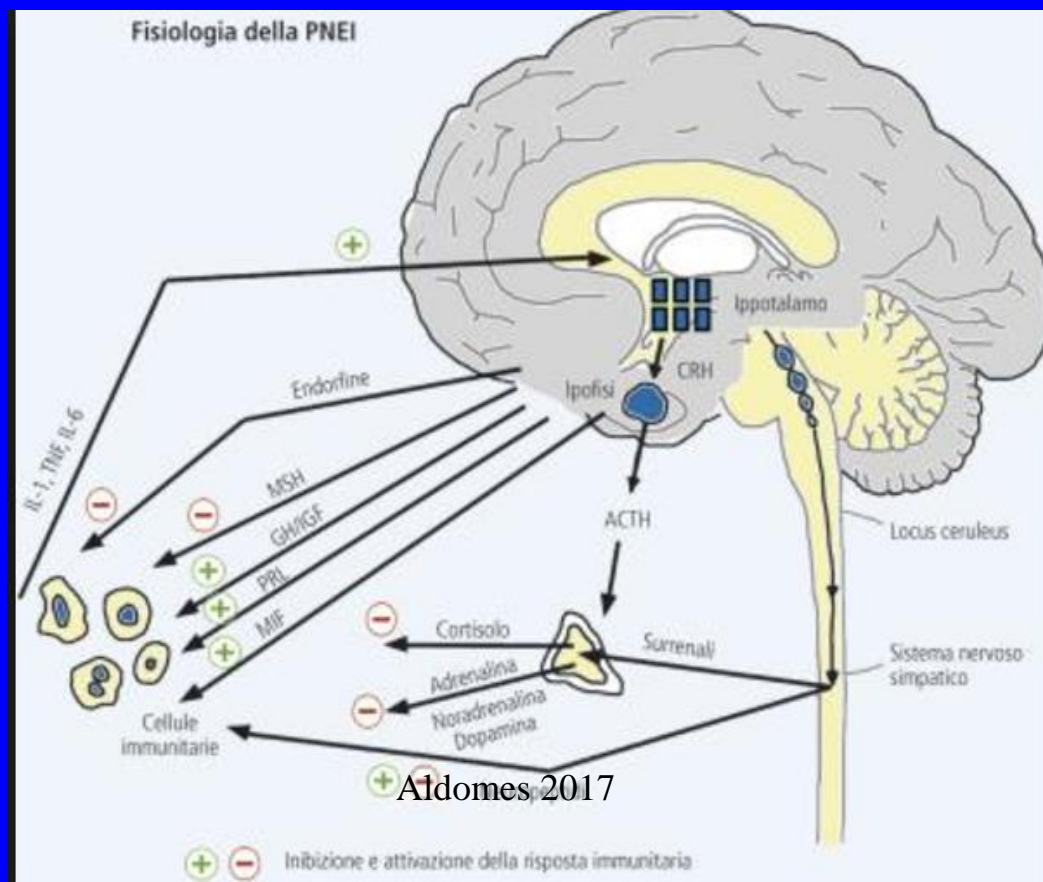
# Per capire meglio, un po' di storia. Cannon e Selye

- E' il fisiologo e psicologo statunitense che per primo ha pubblicato sulle conseguenze emozionali della condizione di stress : **fight or flight** (Combatti o fuggire).
- Ad Hans Hugo **Bruno Selye** (1907-1982), endocrinologo di origine ungherese, si deve la distinzione tra **eustress** (acuto e positivo) e **distress** ( cronicamente presente e negativo)



# Ed ora entra in gioco il sistema immunitario: 1980.

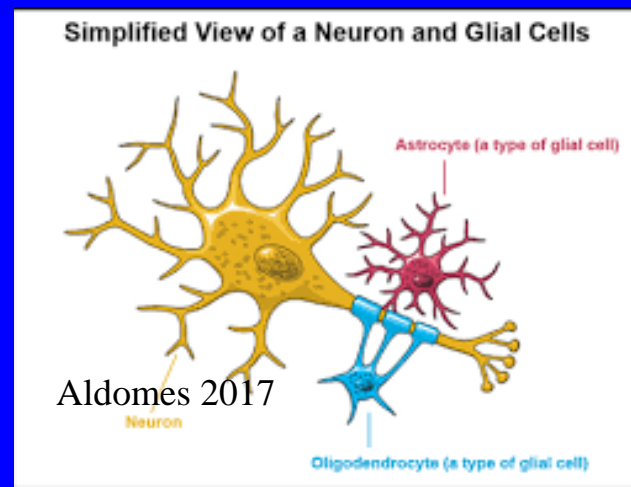
- il linfocita produce **TSH** (tireotropo) e numerose altre molecole ad attività neuroendocrina. Inoltre presenta **recettori specifici per vari mediatori del sistema endocrino e del sistema nervoso centrale**



# Il connubio Neuro- endocrino- immunità non ci sorprende se si considera il ruolo della neuroglia

Scoperta da Ramon Y Cajal (1891) si presenta con un numero di cellule cinque volte superiore a quelle dei neuroni

La **microglia** ha funzione di immuno sorveglianza ed è costituita da macrofagi e astrociti, con un ruolo attivo nella neurotrasmissione e punto di “contatto” tra sistema nervoso e sanguigno, gli **oligodendrociti** (con funzione analoga alle cellule di Schwann del sistema nervoso periferico) che rivestono di mielina le fibre nervose),



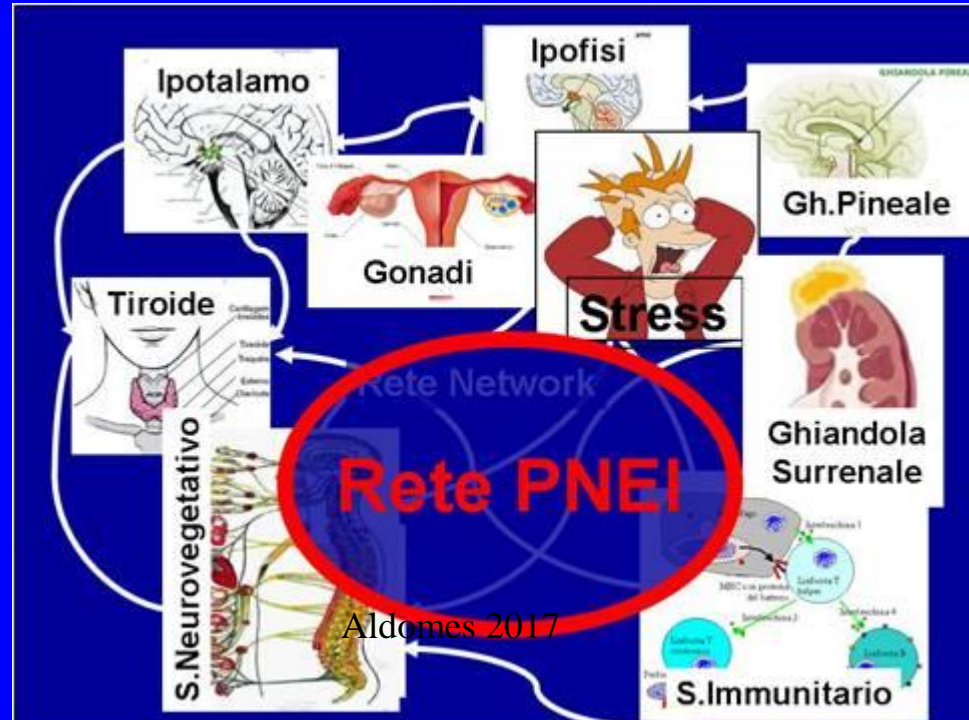
# Alterazioni della Guaina di Schwann da cellulari? Epigenetica

- Nel 1999 Aloisi ha dimostrato che ogni insulto al tessuto cerebrale determina modificazioni sia della microglia che degli astrociti della macroglia. Le cellule microgliali si comportano come i macrofagi della flogosi “non neurologica” e rispondono immediatamente a qualsiasi insulto patogeno a carico del sistema nervoso centrale, riprendendo la funzione dei macrofagi nella flogosi e sui processi immunitari



# 1981. Robert Ader, pubblica Psychoneuroimmunology

- Ader e il suo collega, l'immunologo Nicholas Cohen, dimostrarono che se ai topi veniva somministrato un farmaco immunodepressivo insieme a del succo di mela, in seguito avrebbero gli effetti del farmaco non appena assaggiato il succo anche in assenza del farmaco stesso

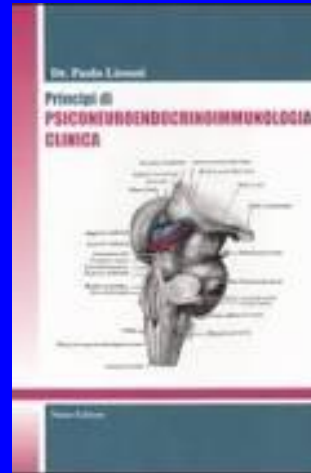




# In Italia.



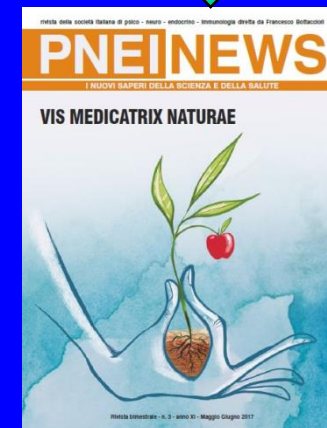
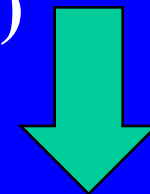
**Umberto Scapagnini  
(1989)**



**Paolo Lissoni  
(2007)**



**Francesco Bottaccioli  
(2014)**



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# Neurotrasmettitori e neuromodulatori

## AMMINOACIDI

Aspartato  
Glutammato  
GABA  
Glicina

## AMINE e SOSTANZE CORRELATE

Acetilcolina  
Dopamina }  
Noradrenalina }  
Adrenalina }  
Istamina  
Serotonina

Catecolamine (derivate dalla tirosina)

## PEPTIDI NEUROATTIVI

Somatostatine  
Peptidi oppioidi  
ACTH  
Sostanza P

Presumibili nuovi v. poi

# In realtà sono molti di più ed includono ormoni

## Neurotrasmettitori comuni

derivati da amminoacidi

- acido aspartico
- acido glutammico
- acido gamma-aminobutirrico (GABA)
- glicina

monoammine (in ordine di sintesi)

- dalla fenilalanina e dalla tirosina
- dopamina (da)
- - norepinefrina (o noradrenalina, ne)
- - - epinefrina (o adrenalina, epi)

dal triptofano

- serotonina (o 5-idrossitriptamina, 5ht)
- melatonina

dall'istidina

- istamina

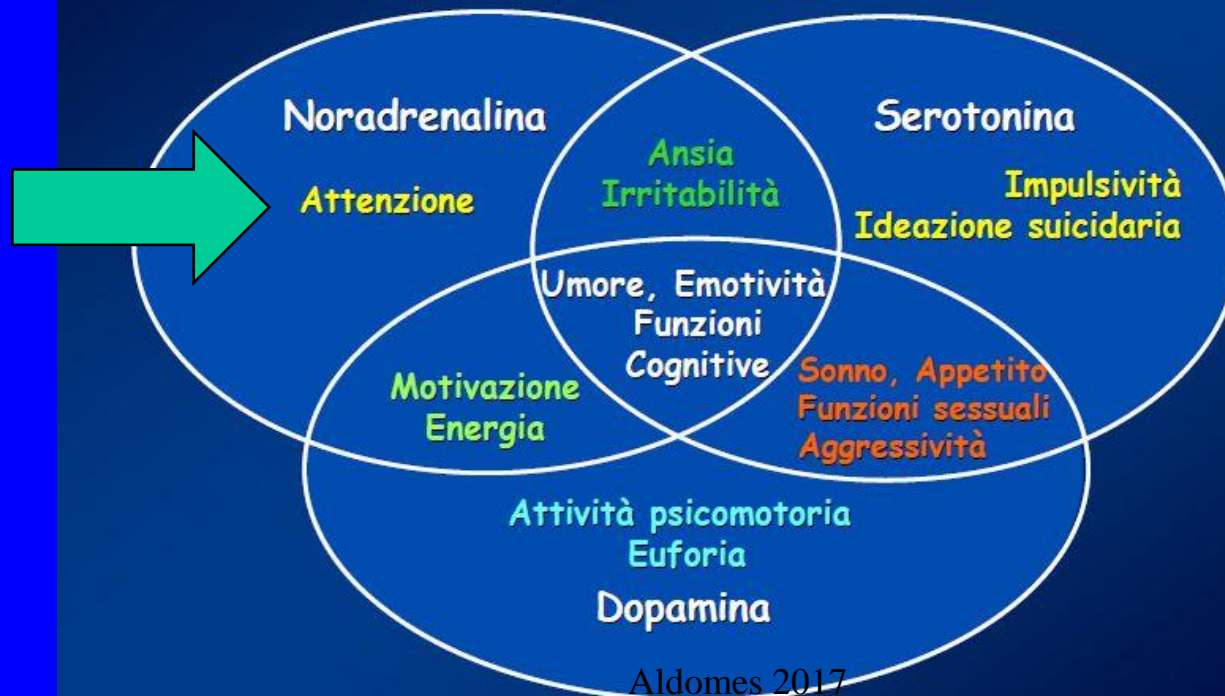
polipeptidi (neuropeptidi)

- neurotensina (NT)
- galanina
- bombesina
- - bombesina
- - peptide rilasciante la gastrina (GRP)
- - neuromedina B
- gastrina
- - gastrina
- - colecistichina (CCK)
- insulina
- - insulina
- neuropofisiali
- - vasopressina
- - ossitocina
- - neurofisina I
- - neurofisina II
- neuropeptide Y
- - neuropeptide Y (NY)
- - polipeptide pancreatico (PP)
- - peptide YY (PYY)
- oppioidi
- - corticotropina (ACTH)
- - beta-llipotropina
- - dinorfina
- - endorfina
- - encefalina
- - leumorfina
- secretine
- - secretina
- - motilina
- - glucagone
- - peptide vasoattivo intestinale (VIP)
- - fattore di rilascio dell'ormone della crescita (GRF)
- somatostatina
- - somatostatina
- tachichinine
- - neurochinina A
- - neurochinina B
- - neuropeptide A
- - neuropeptide gamma
- - sostanza P
- ammine biogeniche
- - acetilcolina (ACh)
- altri
- - ossido di azoto (NO)
- - ossido di carbonio (CO)
- - anandamide

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# Inoltre i Neurotrasmettitori interagiscono in sistemi: sistema monoaminergico

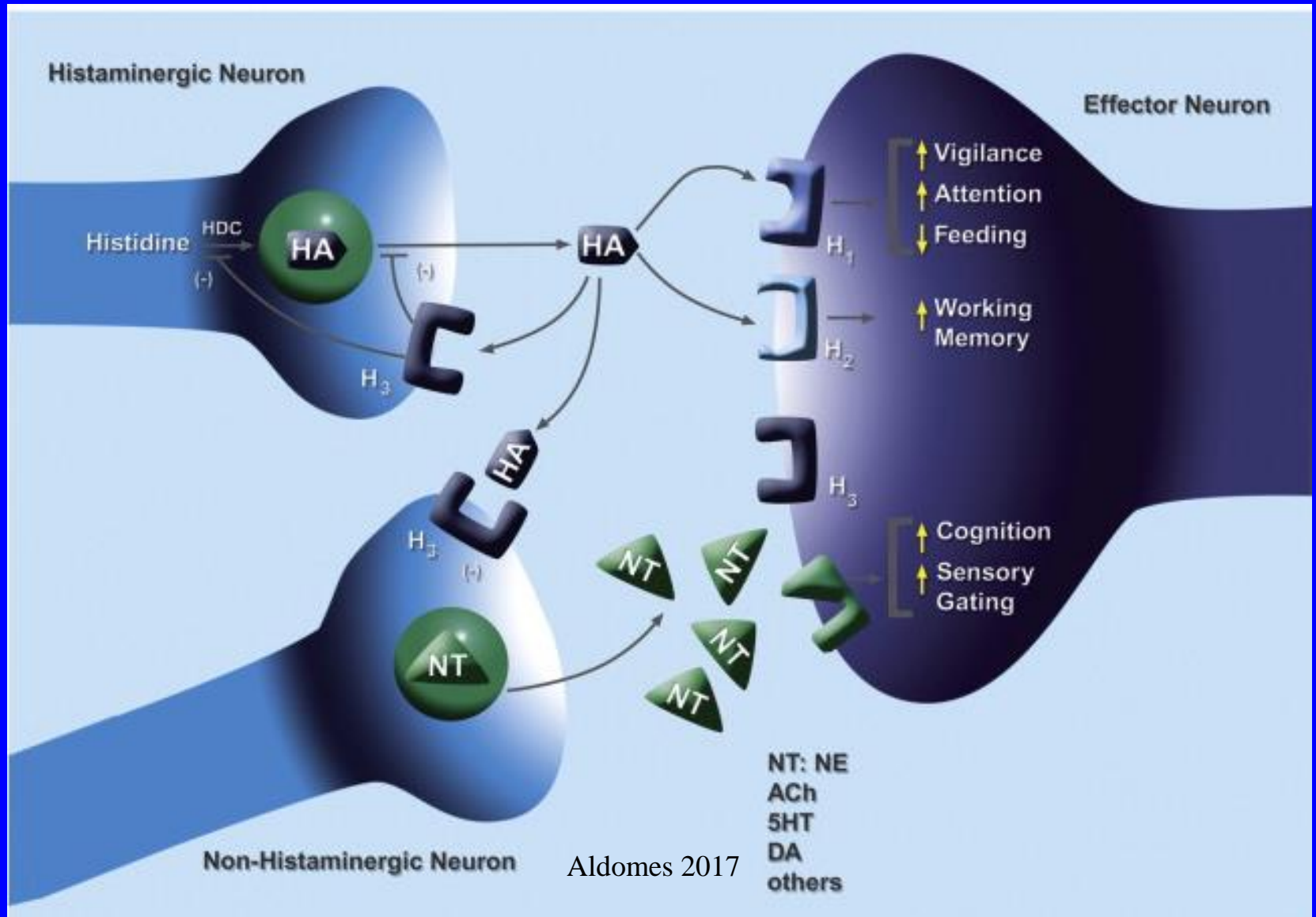
## Sintomi controllati dai sistemi monoaminergici



# I sistemi interagiscono tra loro serotoninerghiche noradrenergiche



# Talvolta il rilascio di uno di essi determina la contemporanea liberazione di altri





**BETAISTINA**

nuclei vestibolari  
Vie vestibolo spinali

**DIMENIDRINATO  
SCOPOLAMINA**

nuclei vestibolari  
Vie vestibolo spinali  
Reticolare  
**ATTIVANTE**

- vie cerebello-  
vestibolari  
- Azione sulla  
reticolare  
attivante  
colinergica

**H**

**Ach**

**FENOTIAZINE**

dell'asse  
rubro-nigro-  
striato  
Area trigger  
zone

**DA**

**TRIMETOBENZAMIDE**

**GABA**

**Au INTERNO**

Locus coeruleus  
Reticolare  
pontina  
**INIBENTE**

**benzodiazepine**

**5HT**

**NA**

**Anti  
depressivi**

Aldomes 2011 **tronco encefalico**

# Cosa stimola la neuroplasticità

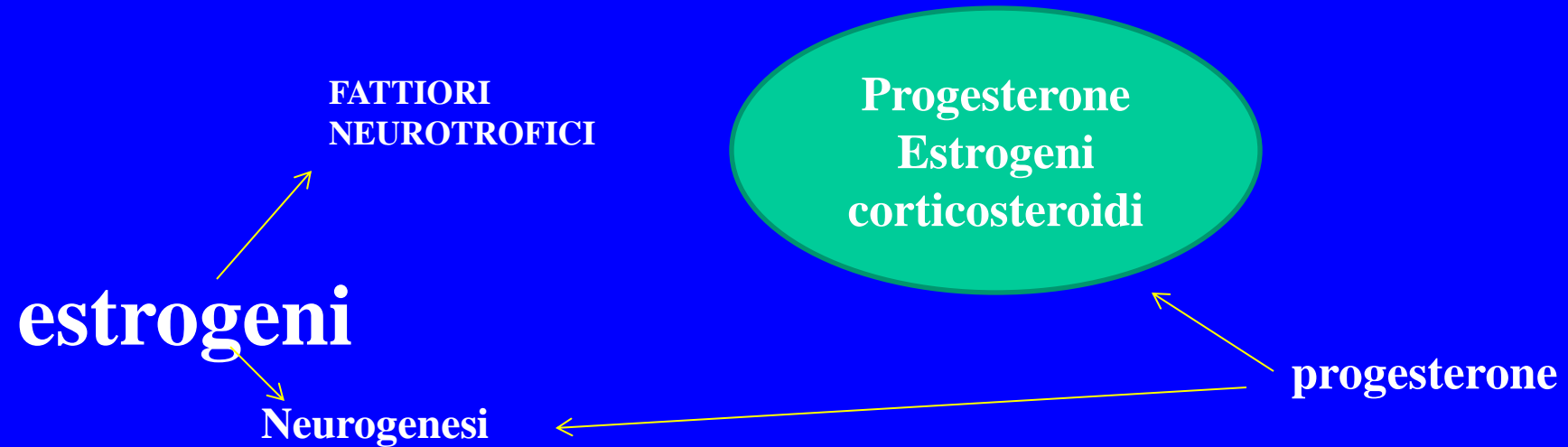
- Ambiente arricchito
- Sonno melatonina
- Esercizio
- Apprendimento
- Memoria
- Traumi-ischemia
- Neurosteroidi
- litio

**EUSTRESS**





# Estrogeni e progesterone inducono neurogenesi



**Il fine è quello di adattarsi al ciclo vitale la mamma deve inventarsi mille strategie per allattare ed accudire i piccoli**

# Pubertà ciclo mestruale gravidanza menopausa

- Le fluttuazioni ormonali determinano modificazioni cicliche di trofismo ed eccitabilità neuronale

Un altro ormone sessuale femminile, il progesterone, sembra svolgere molteplici funzioni centrali non legate alla funzione riproduttiva: la regolazione dei processi cognitivi, la funzione mitocondriale della cellula neuronale, la neurogenesi e la riparazione del tessuto nervoso danneggiato. Le risposte neuronali regolate dal progesterone sono mediate dai recettori PR-A e PR-B, incluse alcune varianti derivate da *splicing* alternativo del gene di PR.

A livello del sistema nervoso centrale (SNC), quindi, gli estrogeni e il progesterone agiscono di concerto nel regolare diverse funzioni neuronali, come la neuroprotezione e diversi processi cognitivi. Il gene di PR contiene sequenze promotore capaci di legare ER; pertanto, l'espressione genica di PR presuppone l'esistenza di una (efficiente) stimolazione estrogenica.

# Ciclo e neuroplasticità

*J Neurosci.* 2003 May 1;23(9):3790-5.

## **Menstrual cycle-dependent neural plasticity in the adult human brain is hormone, task, and region specific.**

Fernández G<sup>1</sup>, Weis S, Stoffel-Wagner B, Tendolkar I, Reuber M, Beyenburg S, Klaver P, Fell J, de Greiff A, Ruhlmann J, Reul J, Elger CE.

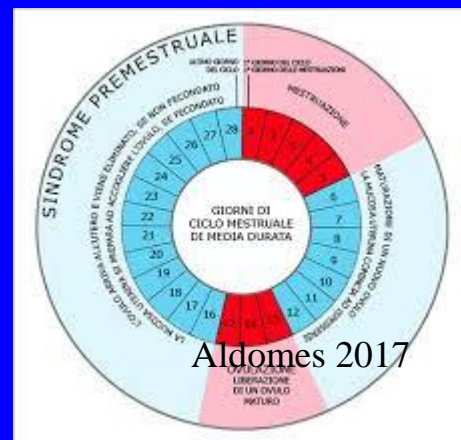
### **⊕ Author information**

#### **Abstract**

In rodents, cyclically fluctuating levels of gonadal steroid hormones modulate neural plasticity by altering synaptic transmission and synaptogenesis. Alterations of mood and cognition observed during the menstrual cycle suggest that steroid-related plasticity also occurs in humans. Cycle phase-dependent differences in cognitive performance have almost exclusively been found in tasks probing lateralized neuronal domains, i.e., cognitive domains such as language, which are predominantly executed by one hemisphere. To search for neural correlates of hormonally mediated neural plasticity in humans, we thus conducted a functional magnetic resonance imaging study measuring brain activity related to a semantic decision task in the language domain. This was contrasted with a letter-matching task in the perceptual domain, in which we expected no steroid hormone-mediated effect. We investigated 12 young healthy women in a counterbalanced repeated-measure design during low-steroid menstruation and high-steroid midluteal phase. Steroid serum levels correlated with the volume and lateralization of particular brain activations related to the semantic task but not with brain activity related to the perceptual task. More specifically, bilateral superior temporal recruitment correlated positively with progesterone and medial superior frontal recruitment with both progesterone and estradiol serum levels, whereas activations in inferior and middle frontal cortex were unaffected by steroid levels. In contrast to these specific interactions, testosterone levels correlated nonselectively with overall activation levels by neural and/or vascular factor(s). In conclusion, our data demonstrate steroid hormone responsivity in the adult human brain by revealing neural plasticity in the language domain, which appears hormone, task, and region specific.

# IN PARTICOLARE

- Nelle donne in fase luteinica sia l'emisfero destro che il sinistro raddoppiano il loro volume (più il destro) non solo limitatamente all'ippocampo.
- Nel maschio il cervello non si modifica



[J Neurosci](#). 2003 May 1;23(9):3790-5.

## Menstrual cycle-dependent neural plasticity in the adult human brain is hormone, task, and region specific.

[Fernández G](#)<sup>1</sup>, [Weis S](#), [Stoffel-Wagner B](#), [Tendolkar I](#), [Reuber M](#), [Beyenburg S](#), [Klaver P](#), [Fell J](#), [de Greiff A](#), [Ruhlmann J](#), [Reul J](#), [Elger CE](#).

### Author information

#### Abstract

In rodents, cyclically fluctuating levels of gonadal steroid hormones modulate neural plasticity by altering synaptic transmission and synaptogenesis. Alterations of mood and cognition observed during the menstrual cycle suggest that steroid-related plasticity also occurs in humans. Cycle phase-dependent differences in cognitive performance have almost exclusively been found in tasks probing lateralized neuronal domains, i.e., cognitive domains such as language, which are predominantly executed by one hemisphere. To search for neural correlates of hormonally mediated neural plasticity in humans, we thus conducted a functional magnetic resonance imaging study measuring brain activity related to a semantic decision task in the language domain. This was contrasted with a letter-matching task in the perceptual domain, in which we expected no steroid hormone-mediated effect. We investigated 12 young healthy women in a counterbalanced repeated-measure design during low-steroid menstruation and high-steroid midluteal phase. Steroid serum levels correlated with the volume and lateralization of particular brain activations related to the semantic task but not with brain activity related to the perceptual task. More specifically, bilateral superior temporal recruitment correlated positively with progesterone and medial superior frontal recruitment with both progesterone and estradiol serum levels, whereas activations in inferior and middle frontal cortex were unaffected by steroid levels. In contrast to these specific interactions, testosterone levels correlated nonselectively with overall activation levels by neural and/or vascular factor(s). In conclusion, our data demonstrate steroid hormone responsivity in the adult human brain by revealing neural plasticity in the language domain, which appears hormone, task, and region specific.

# durante la gravidanza

Pregnancy brain::questa “riscolpisce” il cervello per almeno due anni

- In gravidanza si riduce il volume di molte aree cerebrali della **corteccia parietale posteriore**, e in particolare specifiche sezioni della **corteccia prefrontale e temporale**. . Un’attività di prouning (simile a quella che studieremo nello sviluppo del cervello) che avvantaggia le funzioni limbiche
- Omeostasi sinaptica pulire il cervello e lasciare spazio a nuovi apprendimenti

Nonostante la perdita di **materia grigia**, i ricercatori, comunque, non hanno osservato alcun **deficit cognitivo** come un calo della memoria o altre funzioni cognitive. Ma anzi, “i nostri risultati indicano un processo di adattamento del cervello relativo ai benefici dovuti a una migliore comprensione dei bisogni del bambino, come comprendere lo stato emotivo. Inoltre, forniscono indizi per quanto riguarda le basi neurali della maternità, della salute mentale perinatale e della plasticità del cervello in generale”, conclude l’autore Oscar Vilarroya.

## **Pregnancy leads to long-lasting changes in human brain structure.**

Hoekzema E<sup>1,2,3</sup>, Barba-Müller E<sup>1</sup>, Pozzobon C<sup>4</sup>, Picado M<sup>1</sup>, Lucco F<sup>4</sup>, García-García D<sup>5</sup>, Soliva JC<sup>1</sup>, Tobefía A<sup>1</sup>, Descro M<sup>5</sup>, Crone EA<sup>2,3</sup>, Ballesteros A<sup>4</sup>, Carmona S<sup>1,5,6</sup>, Villarroya O<sup>1,7</sup>.

### **⊕ Author information**

### **Abstract**

Pregnancy involves radical hormone surges and biological adaptations. However, the effects of pregnancy on the human brain are virtually unknown. Here we show, using a prospective ('pre'-'post' pregnancy) study involving first-time mothers and fathers and nulliparous control groups, that pregnancy renders substantial changes in brain structure, primarily reductions in gray matter (GM) volume in regions subserving social cognition. The changes were selective for the mothers and highly consistent, correctly classifying all women as having undergone pregnancy or not in-between sessions. Interestingly, the volume reductions showed a substantial overlap with brain regions responding to the women's babies postpartum. Furthermore, the GM volume changes of pregnancy predicted measures of postpartum maternal attachment, suggestive of an adaptive process serving the transition into motherhood. Another follow-up session showed that the GM reductions endured for at least 2 years post-pregnancy. Our data provide the first evidence that pregnancy confers long-lasting changes in a woman's brain.

# Lo sviluppo cerebrale dipende anche dal sonno

eNeuro. 2016 Jun 20;3(2). pii: ENEURO.0053-16.2016. doi: 10.1523/ENEURO.0053-16.2016.

## Effects of Chronic Sleep Restriction during Early Adolescence on the Adult Pattern of Connectivity of Mouse Secondary Motor Cortex.

Billeh YN<sup>1</sup>, Rodriguez AV<sup>2</sup>, Bellesi M<sup>3</sup>, Bernard A<sup>4</sup>, de Vivo L<sup>5</sup>, Funk CM<sup>6</sup>, Harris J<sup>4</sup>, Honjoh S<sup>5</sup>, Mihalas S<sup>4</sup>, Ng L<sup>4</sup>, Koch C<sup>4</sup>, Cirelli C<sup>5</sup>, Tononi G<sup>5</sup>.

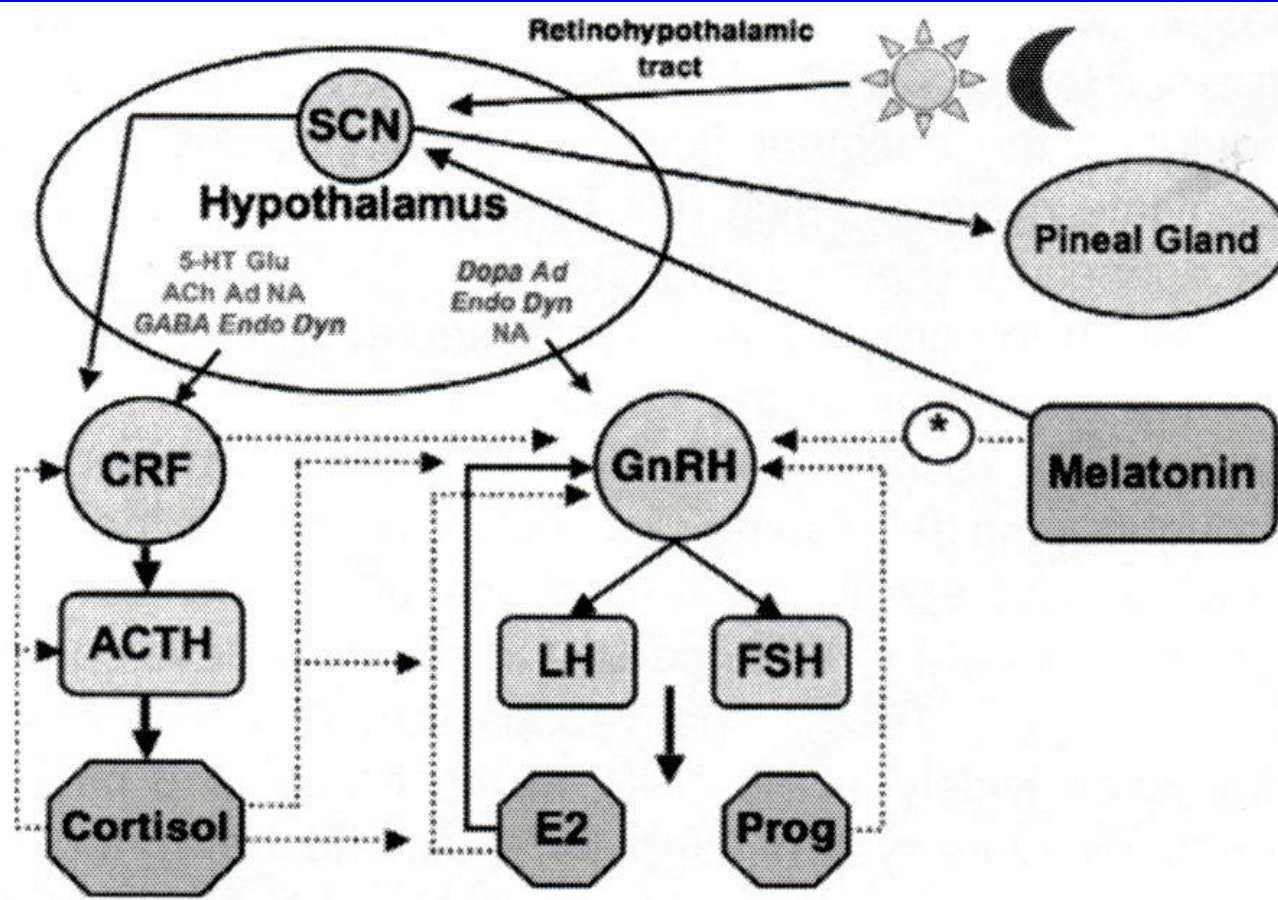
### Author information

#### Abstract

Cortical circuits mature in stages, from early synaptogenesis and synaptic pruning to late synaptic refinement, resulting in the adult anatomical connection matrix. Because the mature matrix is largely fixed, genetic or environmental factors interfering with its establishment can have irreversible effects. Sleep disruption is rarely considered among those factors, and previous studies have focused on very young animals and the acute effects of sleep deprivation on neuronal morphology and cortical plasticity. Adolescence is a sensitive time for brain remodeling, yet whether chronic sleep restriction (CSR) during adolescence has long-term effects on brain connectivity remains unclear. We used viral-mediated axonal labeling and serial two-photon tomography to measure brain-wide projections from secondary motor cortex (MOs), a high-order area with diffuse projections. For each MOs target, we calculated the projection fraction, a combined measure of passing fibers and axonal terminals normalized for the size of each target. We found no homogeneous differences in MOs projection fraction between mice subjected to 5 days of CSR during early adolescence (P25-P30,  $\geq 50\%$  decrease in daily sleep, n=14) and siblings that slept undisturbed (n=14). Machine learning algorithms, however, classified animals at significantly above chance levels, indicating that differences between the two groups exist, but are subtle and heterogeneous. Thus, sleep disruption in early adolescence may affect adult brain connectivity. However, because our method relies on a global measure of projection density and was not previously used to measure connectivity changes due to behavioral manipulations, definitive conclusions on the long-term structural effects of early CSR require additional experiments.

**KEYWORDS:** adolescence; secondary motor cortex; sensitive period; sleep loss





**Fig. 2.** Hypothalamic pituitary adrenal and gonadal axis and the circadian cycle. Light effect on the SCN leads to inhibition of melatonin synthesis from the pineal gland. \* The inhibitory effect of melatonin on GnRH is only seen before puberty and in certain pathological conditions in humans (Silman, 1991; Kadva et al., 1998). Solid lines: Excitatory effect, Dashed lines: inhibitory effect. CRF: corticotropin releasing factor, E<sub>2</sub>: estrogen, Prog: progesterone, ACTH: adrenocorticotrophic hormone, Endo:  $\beta$ -endorphin, Dyn: dynorphin, ACh: acetylcholine, Ad: adrenalin and, NA: nor adrenalin. (Italics indicate inhibitory action.)

# OSAS e ABR

Acta Otorhinolaryngol Ital. 1995 Apr;15(2 Suppl 47):15-7.

## **[Brain stem auditory evoked potentials in obstructive sleep apnea syndrome].**

[Article in Italian]

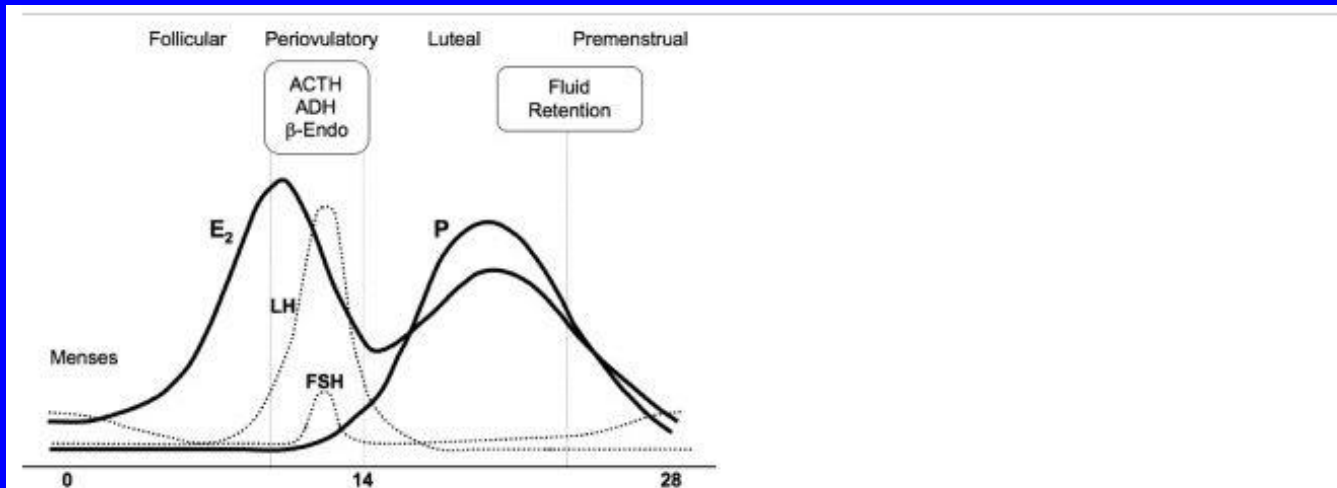
Cimino A<sup>1</sup>, Speciale R, Gallina S, Cimino M, Chillura M, Lo Presti GM, Ciulla L.

### **⊕ Author information**

#### **Abstract**

To evaluate a possible brainstem role in pathogenesis of obstructive sleep apnea syndrome, a study on brainstem auditory evoked potentials (BAEP), has been conducted. 15 OSAS patients, medium and severe form, with organic pathologies of the upper respiratory tract have been evaluated. 15 normal subjects were compared as control. All the patients were subjected to audiometry, including total liminal audiometry, tympanometry, acoustic reflex, and BAEP study. BAEP evoked with trains of clicks at 11 and 51 periods/sec., showed morphological alterations and a longer central conductance of time interval (I-V interval) in only four patients. BAEP alterations noted in the OSAS-affected patients are neither constant nor specific. Therefore, the observed BAEP alterations might be due to apneas, as a consequence of the chronic hypoxic- hypercapnic status occurring in the brain-stem.

# ORMONI SESSUALI E ORMONI DELLO STRESS SPESSE INTERAGISCONO

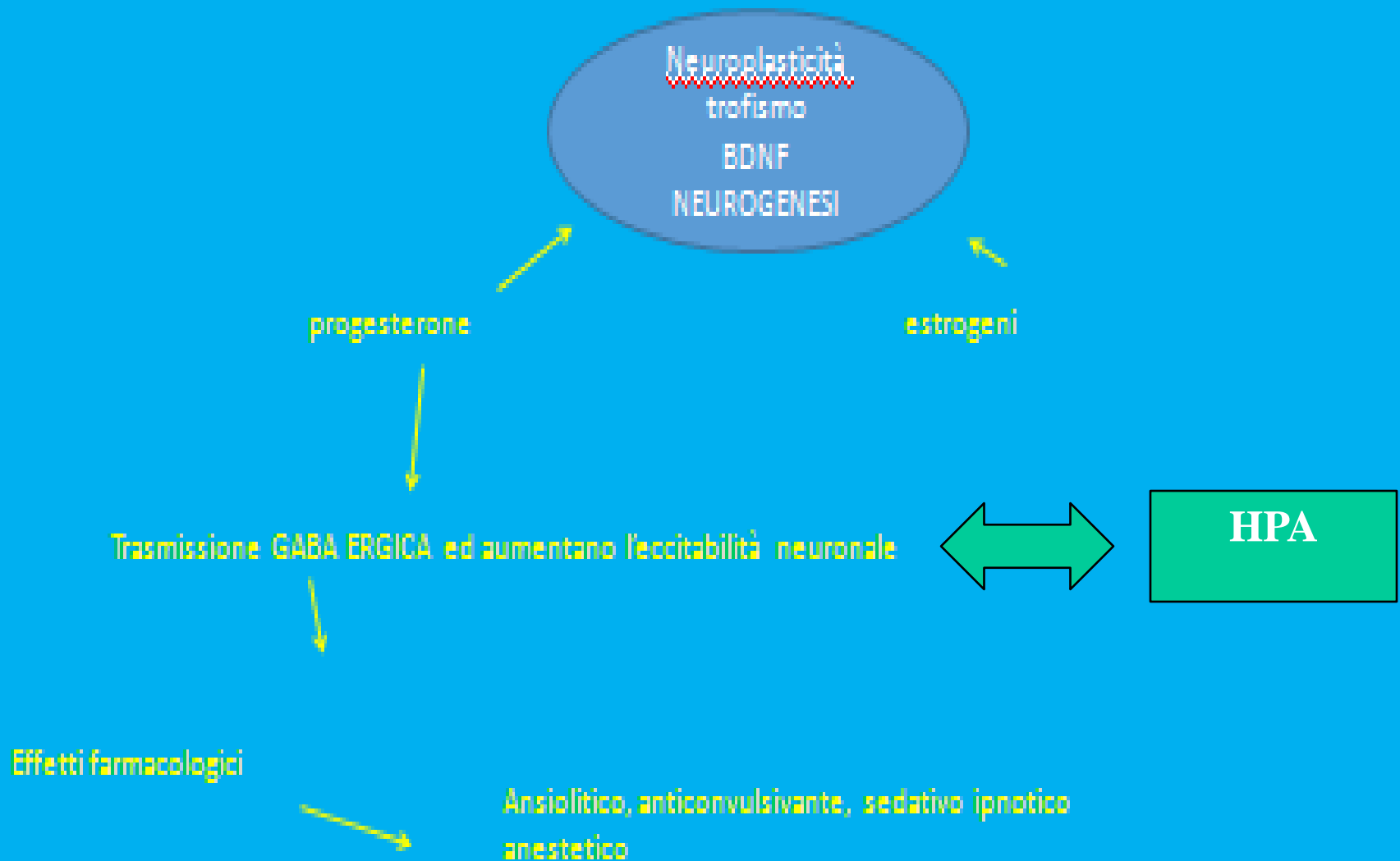


[Scarica l'immagine ad alta risoluzione \(66KB\)](#)

[Scarica l'immagine a grandezza intera](#)

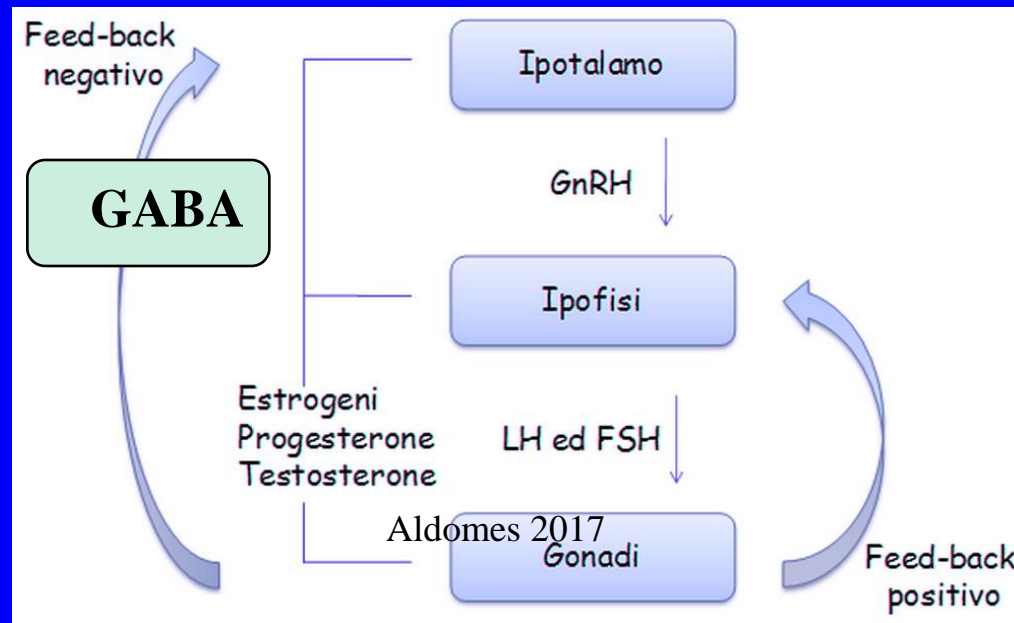
Fig. 3 . Rappresentazione schematica dei cambiamenti negli ormoni riproduttivi durante il ciclo mestruale medio e l'aumento associato di altri ormoni nella fase periovulatoria. Il grafico non rispecchia il rilascio pulsionale di estrogeni e LH nella fase periovulatoria ( Djahanbakhch et al., 1984 ), ma ha ridotto i cambiamenti complessivi nei livelli degli ormoni. E<sub>2</sub> : estrogeno, P: progesterone, ACTH: ormone adrenocorticotropico ADH: ADH (vasopressina), Endo: β-endorfina.

# Estrogeni-progesterone e GABA



# STEROIDI ED ASSE IPOTALAMO IPOFISARIO (HPA)

- GABA agisce nella modulazione dell'asse ipotalamo ipofisario surrene(HPA) ed i neurosteroidi partecipano a questo schema .
- I neurosteroidi giocano un ruolo nel limitare il grado e la durata della diminuzione della funzione GABAergica indotta dallo stress acuto(aspetti emozionali dello stress)
- Nello stress cronico l'asse HPA gioca un ruolo importante nel determinare le concentrazioni periferiche e centrali di neurosteroidi



# «Stress»

- E' un termine inglese, ma deriva dal latino: strictus. Tutto ciò che ci fa «stare stretti» con la vita dà stress. Pertanto il problema non è l'agente stressante ma come lo si vive.

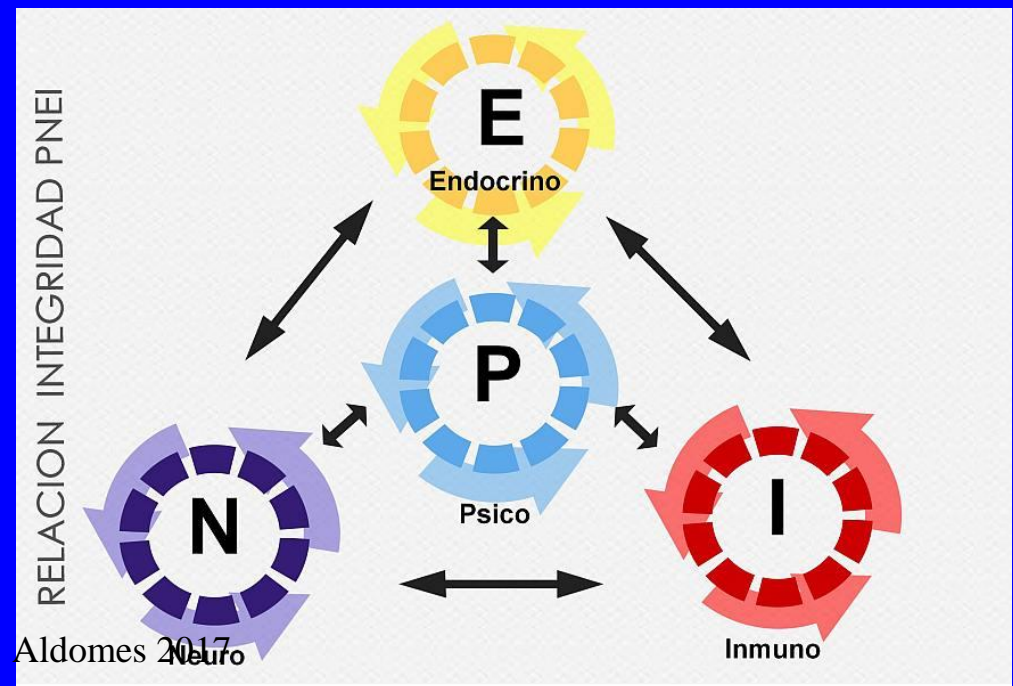
- Stressor Tipo fisico

- --dolore intenso o prolungato;
- --caldo o freddo estremi;
- --traumi o abusi;
- -- infezioni e processi infiammatori;

- Stresso di Tipo psicologico:

- -- paura;
- -- senso di sconfitta;
- -- umiliazione;
- --delusione

- --gioia estrema.



# IL VERO STRESS

## Lo Stress che può determinare conseguenze per tutta la vita:asse Ipotalamo ipofisario e traumi infantili

[Am J Psychiatry](#). 2001 Apr;158(4):575-81.

### Altered pituitary-adrenal axis responses to provocative challenge tests in adult survivors of childhood abuse.

Heim C<sup>1</sup>, Newport DJ, Bonsall R, Miller AH, Nemeroff CB.

#### Author information

#### Abstract

**OBJECTIVE:** Early adverse life events may predispose individuals to the development of mood and anxiety disorders in adulthood, perhaps by inducing persistent changes in corticotropin-releasing factor (CRF) neuronal systems. The present study sought to evaluate pituitary-adrenal responses to standard hypothalamic-pituitary-adrenal axis challenge tests in adult female survivors of childhood abuse with and without major depressive disorder.

**METHOD:** Plasma ACTH and cortisol responses to the administration of 1 microg/kg ovine CRF and plasma cortisol responses to the administration of 250 microg ACTH(1-24) were measured in healthy women without early life stress (N=20), women with childhood abuse without major depressive disorder (N=20), women with childhood abuse and major depressive disorder (N=15), and women with major depression but no early life stress (N=11).

**RESULTS:** Abused women without major depressive disorder exhibited greater than usual ACTH responses to CRF administration, whereas abused women with major depressive disorder and depressed women without early life stress demonstrated blunted ACTH responses. In the ACTH(1-24) stimulation test, abused women without major depressive disorder exhibited lower baseline and stimulated plasma cortisol concentrations. Abused women with comorbid depression more often suffered from posttraumatic stress disorder and reported more recent life stress than abused women without major depressive disorder.

**CONCLUSIONS:** These findings suggest sensitization of the anterior pituitary and counterregulative adaptation of the adrenal cortex in abused women without major depressive disorder. On subsequent stress exposure, women with a history of childhood abuse may hypersecrete CRF, resulting in down-regulation of adenohipophyseal CRF receptors and symptoms of depression and anxiety.

# Identificato un periodo critico

*Proc Natl Acad Sci U S A*. 2016 May 17;113(20):5742-7. doi: 10.1073/pnas.1601443113. Epub 2016 Apr 25.

## **Preschool is a sensitive period for the influence of maternal support on the trajectory of hippocampal development.**

Luby JL<sup>1</sup>, Belden A<sup>2</sup>, Harms MP<sup>2</sup>, Tillman R<sup>2</sup>, Barch DM<sup>3</sup>.

### **⊕ Author information**

#### **Abstract**

Building on well-established animal data demonstrating the effects of early maternal support on hippocampal development and adaptive coping, a few longitudinal studies suggest that early caregiver support also impacts human hippocampal development. How caregiving contributes to human hippocampal developmental trajectories, whether there are sensitive periods for these effects, as well as whether related variation in hippocampal development predicts later childhood emotion functioning are of major public health importance. The current study investigated these questions in a longitudinal study of preschoolers assessed annually for behavioral and emotional development, including observed caregiver support. One hundred and twenty-seven children participated in three waves of magnetic resonance brain imaging through school age and early adolescence. Multilevel modeling of the effects of preschool and school-age maternal support on hippocampal volumes across the three waves was conducted. Hippocampal volume increased faster for those with higher levels of preschool maternal support. Subjects with support 1 SD above the mean had a 2.06 times greater increase in total hippocampus volume across the three scans than those with 1 SD below the mean (2.70% vs. 1.31%). No effect of school-age support was found. Individual slopes of hippocampus volume were significantly associated with emotion regulation at scan 3. The findings demonstrate a significant effect of early childhood maternal support on hippocampal volume growth across school age and early adolescence and suggest an early childhood sensitive period for these effects. They also show that this growth trajectory is associated with later emotion functioning.

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**KEYWORDS:** emotions; hippocampus; maternal support; preschool; sensitive period



# La mancanza di cure materne

- Sviluppa meno PFC e lascia libera l'amigdala, la paura

[Proc Natl Acad Sci U S A. 2011 Aug 23;108\(34\):14324-9. doi: 10.1073/pnas.1105371108. Epub 2011 Aug 15.](#)

## **Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth.**

[Lupien SJ<sup>1</sup>](#), [Parent S](#), [Evans AC](#), [Tremblay RE](#), [Zelazo PD](#), [Corbo V](#), [Pruessner JC](#), [Séguin JR](#).

### **⊕ Author information**

#### **Abstract**

Maternal separation and poor maternal care in animals have been shown to have important effects on the developing hippocampus and amygdala. In humans, children exposed to abuse/maltreatment or orphanage rearing do not present changes in hippocampal volumes. However, children reared in orphanages present enlarged amygdala volumes, suggesting that the amygdala may be particularly sensitive to severely disturbed (i.e., discontinuous, neglectful) care in infancy. Maternal depressive symptomatology has been associated with reductions in overall sensitivity to the infant, and with an increased rate of withdrawn, disengaged behaviors. To determine if poor maternal care associated with maternal depressive symptomatology has a similar pattern of association to the volumes of the hippocampus and amygdala in children, as is the case for severely disturbed infant care (orphanage rearing), we measured hippocampal and amygdala volumes as well as stress hormone (glucocorticoid) levels in children exposed ( $n = 17$ ) or not ( $n = 21$ ) to maternal depressive symptomatology since birth. Results revealed no group difference in hippocampal volumes, but larger left and right amygdala volumes and increased levels of glucocorticoids in the children of mothers presenting depressive symptomatology since birth. Moreover, a significant positive correlation was observed between mothers' mean depressive scores and amygdala volumes in their children. The results of this study suggest that amygdala volume in human children may represent an early marker of biological sensitivity to quality of maternal care.

l'attività non controllata dell'amigdala scatena l'instaurarsi di atteggiamenti di paura . Documentato una significativa correlazione positiva tra il punteggio medio depressivo delle madri e il volume degli amigdala nei loro figli. I risultati di questo studio suggeriscono che il volume degli amigdala nei bambini umani può rappresentare un marcatore precoce della sensibilità biologica alla qualità della cura materna..

## Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth

Sonia J. Lupien<sup>a,b,c,1</sup>, Sophie Parent<sup>d</sup>, Alan C. Evans<sup>e</sup>, Richard E. Tremblay<sup>c,f,g,h</sup>, Philip David Zelazo<sup>i</sup>, Vincent Corbo<sup>j</sup>, Jens C. Pruessner<sup>j</sup>, and Jean R. Séguin<sup>b,c</sup>

Author Affiliations 

Edited\* by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved July 21, 2011 (received for review April 04, 2011)

Abstract Full Text Authors & Info Figures SI Metrics Related Content PDF PDF + SI

### Abstract

Maternal separation and poor maternal care in animals have been shown to have important effects on the developing hippocampus and amygdala. In humans, children exposed to abuse/maltreatment or orphanage rearing do not present changes in hippocampal volumes. However, children reared in orphanages present enlarged amygdala volumes, suggesting that the amygdala may be particularly sensitive to severely disturbed (i.e., discontinuous, neglectful) care in infancy. Maternal depressive symptomatology has been associated with reductions in overall sensitivity to the infant, and with an increased rate of withdrawn, disengaged behaviors. To determine if poor maternal care associated with maternal depressive symptomatology has a similar pattern of association to the volumes of the hippocampus and amygdala in children, as is the case for severely disturbed infant care (orphanage rearing), we measured hippocampal and amygdala volumes as well as stress hormone (glucocorticoid) levels in children exposed ( $n = 17$ ) or not ( $n = 21$ ) to maternal depressive symptomatology since birth. Results revealed no group difference in hippocampal volumes, but larger left and right amygdala volumes and increased levels of glucocorticoids in the children of mothers presenting depressive symptomatology since birth. A significant positive correlation was observed between mothers' mean depressive scores and amygdala volumes in their children. The results of this study suggest that amygdala volume in human children may represent an early marker of biological sensitivity to quality of maternal care.

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# Tutto questo potrebbe comportare atteggiamenti depressivi nell'adulto. Lo affermano ER Murphy et al in uno studio condotto nel 2015 in soggetti con disturb depressive maggiore

[Dev Cogn Neurosci](#). 2016 Apr;18:89-100. doi: 10.1016/j.dcn.2015.11.003. Epub 2015 Nov 28.

## Functional connectivity of the amygdala and subgenual cingulate during cognitive reappraisal of emotions in children with MDD history is associated with rumination.

Murphy ER<sup>1</sup>, Barch DM<sup>2</sup>, Pagliaccio D<sup>3</sup>, Luby JL<sup>4</sup>, Belden AC<sup>4</sup>.

### ⊕ Author information

#### Abstract

Major Depressive Disorder (MDD) is characterized by poor emotion regulation. Rumination, a maladaptive strategy for dealing with negative emotions, is common in MDD, and is associated with impaired inhibition and cognitive inflexibility that may contribute to impaired emotion regulation abilities. However, it is unclear whether rumination is differently associated with emotion regulation in individuals with MDD history (MDD-ever) and healthy individuals. In this study, children (8-15 years old) performed a cognitive reappraisal task in which they attempted to decrease their emotional response to sad images during fMRI scanning. Functional connectivity (FC) between both the amygdala and subgenual anterior cingulate (sACC) increased with cortical control regions during reappraisal as rumination increased in MDD-ever, while connectivity between those regions decreased during reappraisal as rumination increased in healthy controls. As the role of cortical control regions is to down-regulate activity of emotion processing regions during reappraisal, this suggests that rumination in MDD-ever, but not controls, is associated with inefficient regulation. This finding suggests that rumination may be particularly associated with poor emotion regulation in MDD-ever, and may also indicate qualitative group differences in whether rumination is maladaptive. These differences in rumination may provide important insight into depressive risk and potential avenues for treatment.

# Lo sviluppo dell'ippocampo e del nucleo dentato è condizionato dalle cure materne ricevute.

[Proc Natl Acad Sci U S A](#). 2012 Feb 21; 109(8): 2854–2859.  
Published online 2012 Jan 30. doi: [10.1073/pnas.1118003109](https://doi.org/10.1073/pnas.1118003109)  
Psychological and Cognitive Sciences

PMCID: PMC3286943

## Maternal support in early childhood predicts larger hippocampal volumes at school age

[Joan L. Luby](#),<sup>a,1</sup> [Deanna M. Barch](#),<sup>a,b,c</sup> [Andy Belden](#),<sup>a</sup> [Michael S. Gaffrey](#),<sup>a</sup> [Rebecca Tillman](#),<sup>a</sup> [Casey Babb](#),<sup>a</sup> [Tomoyuki Nishino](#),<sup>a</sup> [Hideo Suzuki](#),<sup>a</sup> and [Kelly N. Botteron](#)<sup>a,c</sup>

[Author information](#) ► [Copyright and License information](#) ►

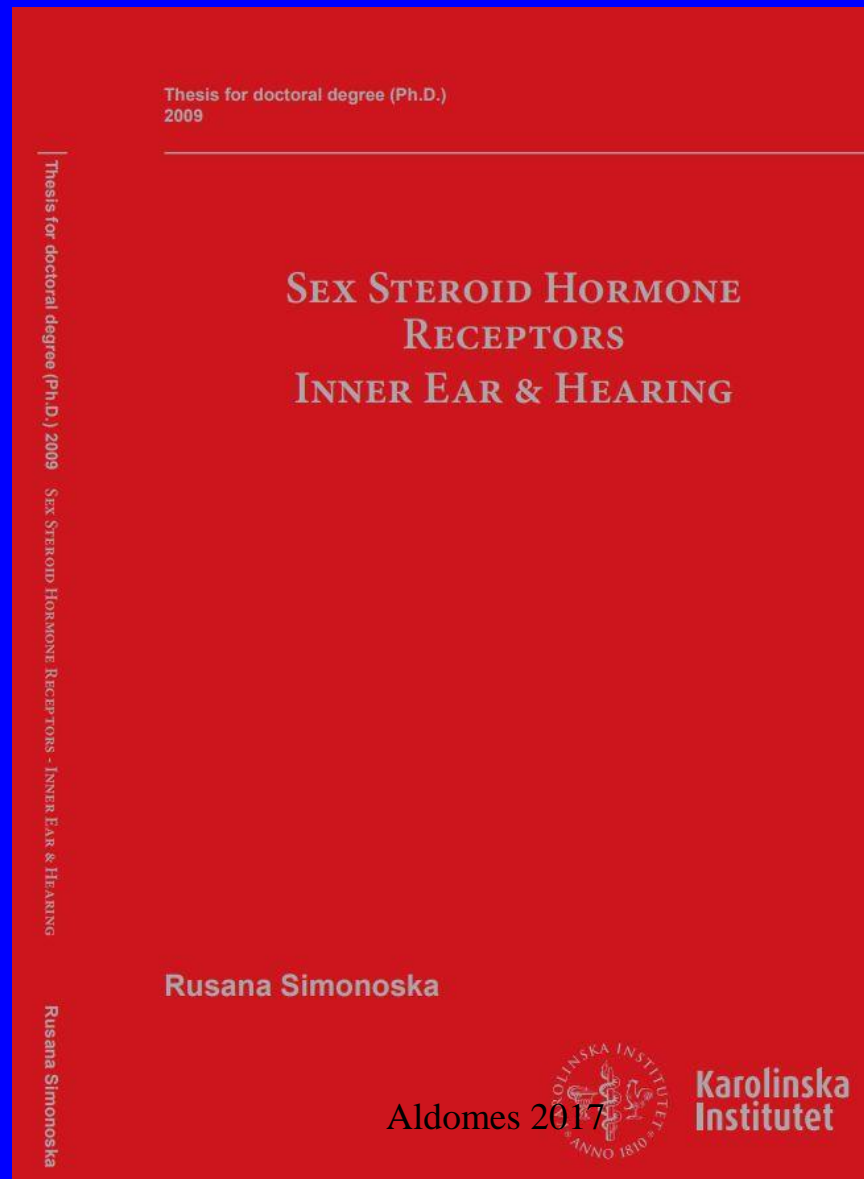
This article has been [cited by](#) other articles in PMC.

### ABSTRACT

[Go to:](#) 

Early maternal support has been shown to promote specific gene expression, neurogenesis, adaptive stress responses, and larger hippocampal volumes in developing animals. In humans, a relationship between psychosocial factors in early childhood and later amygdala volumes based on prospective data has been demonstrated, providing a key link between early experience and brain development. Although much retrospective data suggests a link between early psychosocial factors and hippocampal volumes in humans, to date there has been no prospective data to inform this potentially important public health issue. In a longitudinal study of depressed and healthy preschool children who underwent neuroimaging at school age, we investigated whether early maternal support predicted later hippocampal volumes. Maternal support observed in early childhood was strongly predictive of hippocampal volume measured at school age. The positive effect of maternal support on hippocampal volumes was greater in nondepressed children. These findings provide prospective evidence in humans of the positive effect of early supportive parenting on healthy hippocampal development, a brain region key to memory and stress modulation.

# Un volume di riferimento



# Una review completa

*Neuroscience* 153 (2008) 881–900

## REVIEW

### HORMONES AND THE AUDITORY SYSTEM: A REVIEW OF PHYSIOLOGY AND PATHOPHYSIOLOGY

D. AL-MANA,<sup>a,d</sup> B. CERANIC,<sup>b\*</sup> O. DJAHANBAKHCH<sup>c</sup>  
AND L. M. LUXON<sup>a,d</sup>

<sup>a</sup>*Department of Neuro-Otology, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, UK*

<sup>b</sup>*Department of Audiology, St. George's Hospital, Blackshaw Road, London SW17 0QT, UK*

<sup>c</sup>*Newham University Hospital, Academic Department of Obstetrics & Gynaecology, Barts and The London Queen Mary's School of Medicine and Dentistry, Glen Road, London E13 8SL, UK*

<sup>d</sup>*Academic Unit of Audiological Medicine, University College London, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK*

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[Neuroscience](#), 2008 Jun 2;153(4):881-900. doi: 10.1016/j.neuroscience.2008.02.077. Epub 2008 Mar 15.

#### Hormones and the auditory system: a review of physiology and pathophysiology.

[Al-Mana D<sup>1</sup>](#), [Ceranac B](#), [Djahanbakhch O](#), [Luxon LM](#).

#### Ⓜ Author information

#### Abstract

This review explores the potential role of hormones in modulating the auditory function. The review describes four groups of hormones (the hormones of the circadian cycle, reproduction, stress response and the fluid and electrolyte balance), their physiological variations, interactions, as well as the physiological basis for their effect on the auditory system. Possible contribution of hormones to pathophysiology of auditory dysfunctions, including hyperacusis, tinnitus, Menière's disease and pre-menstrual auditory dysfunction, has also been discussed.

PMID: 18440718 DOI: [10.1016/j.neuroscience.2008.02.077](#)

[Indexed for MEDLINE]



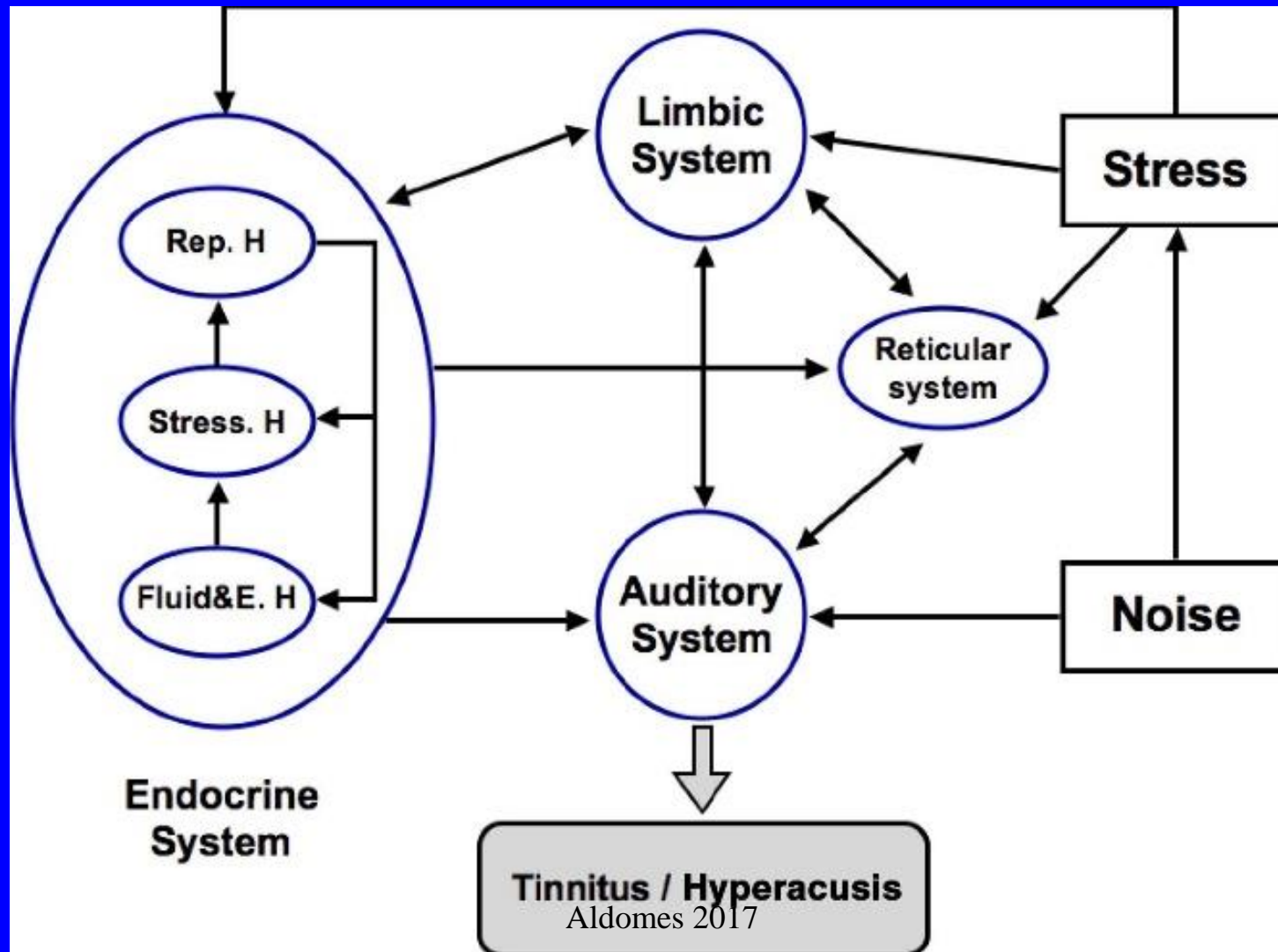
Aldomes 2017

# PNEI ED ACUFENI



Aldomes 2017

# Il sistema otoneurologico





# GABA Ormoni sessuali ed acufeni

- L'estrogeno è generalmente considerato un ruolo **eccitatorio** e ha un effetto neuroprotettivo, e vi è una forte relazione **tra estrogeni e vie serotoninergiche** (Rubinow et al., 1998). D'altra parte, il progesterone e i suoi metaboliti sono noti per avere un potente effetto inibitorio, attraverso l'interazione con i recettori **GABA**. Pertanto, le alterazioni di questi ormoni, sia fisiologiche che patologiche, possono portare ad una maggiore suscettibilità allo sviluppo di acufene.



# L'acufene provoca stress

- Trattando di acufeni ci interessa solo ricordare che un suono, specie se fastidioso, attiva il sistema limbico emozionale ed in particolare l'amigdala e scatenerà le conseguenti reazioni del sistema neurovegetativo, il sistema surrenale con conseguente produzione degli ormoni dello stress, le catecolamine(adrenalina e nordadrenalina).
- Questi stessi centri nervosi inoltre saranno si di per sé iperattivi dai fenomeni neuroplastici conseguenti alla lesione uditiva.



# Lo stress provoca acufeni

- Elevati valori di **cortisolo** possono **danneggiare le cc interne**, le sinapsi del ganglio spirale della coclea , deficit funzionali di **ippocampo** ed **amiugdala**



# Stress ed acufeni

- Infatti L'HPA è influenzato dal rumore e dallo stress

[Int J Hyg Environ Health](#). 2009 Jan;212(1):37-44. doi: 10.1016/j.ijheh.2007.11.005. Epub 2008 Feb 20.

## Salivary cortisol levels, subjective stress, and tinnitus intensity in tinnitus sufferers during noise exposure in the laboratory.

Hébert S<sup>1</sup>, Lupien SJ.

### ⊕ Author information

#### Abstract

Tinnitus, a chronic internal noise, is thought to increase in intensity during or following external noise exposure. Yet there is no empirical evidence for this complaint in the extant literature. Recently, cortisol has been advanced as a useful tool for studying the physiological effects of noise on stress, but few, if any, studies have examined the short-term effects of noise on cortisol levels in tinnitus sufferers. This study assesses the effects of noise exposure on cortisol levels and subjective stress in tinnitus participants and controls without tinnitus. Twenty tinnitus participants and 20 controls without tinnitus were exposed to a 20-min broadband noise with amplified low frequencies. Saliva samplings for cortisol analysis and subjective stress and tinnitus intensity ratings (for tinnitus participants) were performed at regular intervals throughout testing. Results show higher cortisol levels for both groups immediately before, immediately after, and 10min after the end of noise than at other time points. The tinnitus group had lower overall cortisol levels than controls. In contrast, subjective stress ratings were higher for the tinnitus group, and higher at midpoint and immediately after the noise ended. Tinnitus subjective intensity increased throughout testing, especially for the group with high tinnitus-related distress. Overall results show that noise exposure influences cortisol response,

# Stress cronico: recettori NMDA

Brain Res. 2013 Mar 7;1499:80-108. doi: 10.1016/j.brainres.2013.01.006. Epub 2013 Jan 10.

## **Endogenous dynorphins, glutamate and N-methyl-d-aspartate (NMDA) receptors may participate in a stress-mediated Type-I auditory neural exacerbation of tinnitus.**

Sahley TL<sup>1</sup>, Hammonds MD, Musiek FE.

### **⊕ Author information**

#### **Abstract**

Tinnitus is the phantom perception of sounds occurring in the absence of an external auditory stimulus. Tinnitus: [1] affects 50 million individuals, [2] often results from acoustic trauma and, [3] is very often exacerbated under stressful conditions. Tinnitus may result from lesions occurring at any location in the auditory system, but its mechanisms are poorly understood. Evidence is provided supporting an endogenous dynorphin-mediated potentiation of glutamate excitotoxicity at cochlear Type-I auditory dendrites that may well exacerbate chronic subjective neural-generated tinnitus during periods of heightened stress. The proposed mechanism is based on the following: [1] lateral efferent olivocochlear (LEOC) axon terminals contain endogenous dynorphin neuromodulators and are presynaptic to cochlear Type-I auditory dendrites that bear both  $\kappa$ -opioid and N-methyl-d-aspartate (NMDA) receptors/binding sites; [2] the release of presynaptic LEOC dynorphins is likely to be triggered by sympathetic stress via the locus coeruleus; [3] sodium salicylate induces an acute excitotoxicity by potentiating glutamate neurotransmitter effects at cochlear NMDA receptors, resulting in a Type-I auditory neural-generated tinnitus; [4] dynorphins participate in central NMDA-receptor-mediated excitotoxic inflammation; and [5]  $\kappa$ -opioid receptor ligands also modulate Type-I auditory neural activity by potentiating glutamate at cochlear NMDA receptors. A stress-activated release of dynorphins into the cochlea could potentiate the already excitotoxic effects of glutamate, producing: [1] hyperacusis, together with an acute exacerbation of [2] chronic aberrant Type-I neural activity and [3] a worsening of the activity-dependent central auditory neural plasticity changes that must certainly generate the perception of tinnitus. Treatment options are discussed.



# Come pure l'amigdala

## Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth

Sonia J. Lupien<sup>a,b,c,1</sup>, Sophie Parent<sup>d</sup>, Alan C. Evans<sup>e</sup>, Richard E. Tremblay<sup>c,f,g,h</sup>, Philip David Zelazo<sup>i</sup>, Vincent Corbo<sup>j</sup>, Jens C. Pruessner<sup>j</sup>, and Jean R. Séguin<sup>b,c</sup>

Author Affiliations 

Edited\* by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved July 21, 2011 (received for review April 04, 2011)

[Abstract](#) [Full Text](#) [Authors & Info](#) [Figures](#) [SI](#) [Metrics](#) [Related Content](#) [PDF](#) [PDF + SI](#)

### Abstract

Maternal separation and poor maternal care in animals have been shown to have important effects on the developing hippocampus and amygdala. In humans, children exposed to abuse/maltreatment or orphanage rearing do not present changes in hippocampal volumes. However, children reared in orphanages present enlarged amygdala volumes, suggesting that the amygdala may be particularly sensitive to severely disturbed (i.e., discontinuous, neglectful) care in infancy. Maternal depressive symptomatology has been associated with reductions in overall sensitivity to the infant, and with an increased rate of withdrawn, disengaged behaviors. To determine if poor maternal care associated with maternal depressive symptomatology has a similar pattern of association to the volumes of the hippocampus and amygdala in children, as is the case for severely disturbed infant care (orphanage rearing), we measured hippocampal and amygdala volumes as well as stress hormone (glucocorticoid) levels in children exposed ( $n = 17$ ) or not ( $n = 21$ ) to maternal depressive symptomatology since birth. Results revealed no group difference in hippocampal volumes, but larger left and right amygdala volumes and increased levels of glucocorticoids in the children of mothers presenting depressive symptomatology since birth. Moreover, a significant positive correlation was observed between mothers' mean depressive scores and amygdala volumes in their children. The results of this study suggest that amygdala volume in human children may represent an early marker of biological sensitivity to quality of maternal care.

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# Amigdala e acufeni

Int Arch Otorhinolaryngol. 2015 Jul;19(3):259-65. doi: 10.1055/s-0035-1548671. Epub 2015 Mar 30.

## Tinnitus Neural Mechanisms and Structural Changes in the Brain: The Contribution of Neuroimaging Research.

Simonetti P<sup>1</sup>, Oiticica J<sup>1</sup>.

### ⊕ Author information

#### Abstract

**Introduction** Tinnitus is an abnormal perception of sound in the absence of an external stimulus. Chronic tinnitus usually has a high impact in many aspects of patients' lives, such as emotional stress, sleep disturbance, concentration difficulties, and so on. These strong reactions are usually attributed to central nervous system involvement. Neuroimaging has revealed the implication of brain structures in the auditory system. **Objective** This systematic review points out neuroimaging studies that contribute to identifying the structures involved in the pathophysiological mechanism of generation and persistence of various forms of tinnitus. **Data Synthesis** Functional imaging research reveals that tinnitus perception is associated with the involvement of the nonauditory brain areas, including the front parietal area; the limbic system, which consists of the anterior cingulate cortex, anterior insula, and amygdala; and the hippocampal and parahippocampal area. **Conclusion** The neuroimaging research confirms the involvement of the mechanisms of memory and cognition in the persistence of perception, anxiety, distress, and suffering associated with tinnitus.

**KEYWORDS:** auditory cortex; functional neuroimaging; limbic system; neural networks; tinnitus

PMID: 26157502 [PubMed] PMCID: PMC4490922 [Free PMC Article](#)



Images from this publication. [See all images \(1\)](#) [Free text](#)



# Sistema limbico e acufeni

See 1 citation found by title matching your search:

[Neuron](#). 2010 Jun 24;66(6):819-26. doi: 10.1016/j.neuron.2010.04.032.

## Tuning out the noise: limbic-auditory interactions in tinnitus.

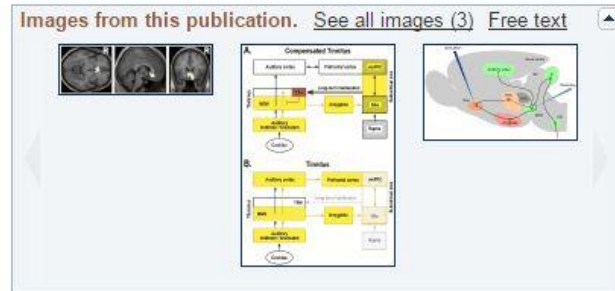
[Rauschecker JP](#)<sup>1</sup>, [Leaver AM](#), [Mühlau M](#).

[Author information](#)

### Abstract

Tinnitus, the most common auditory disorder, affects about 40 million people in the United States alone, and its incidence is rising due to an aging population and increasing noise exposure. Although several approaches for the alleviation of tinnitus exist, there is as of yet no cure. The present article proposes a testable model for tinnitus that is grounded in recent findings from human imaging and focuses on brain areas in cortex, thalamus, and ventral striatum. Limbic and auditory brain areas are thought to interact at the thalamic level. While a tinnitus signal originates from lesion-induced plasticity of the auditory pathways, it can be tuned out by feedback connections from limbic regions, which block the tinnitus signal from reaching auditory cortex. If the limbic regions are compromised, this "noise-cancellation" mechanism breaks down, and chronic tinnitus results. Hopefully, this model will ultimately enable the development of effective treatment.

PMID: 20620868 [PubMed - indexed for MEDLINE] PMCID: PMC2904345 [Free PMC Article](#)





# Abituarsi agli acufeni

- L'abitudine al tinnito comprende circuiti complessi neuronali e sistemi multipli di trasmissione ( Mesulam, 1990; Kandel, 2001 ), inclusi sistemi **acetilcolinergici** , dopaminergici, **GABA** ergici, ossido di azoto e sistemi **serotoninergici**.



# PNEI E SISTEMA VESTIBOLARE



# Il ciclo ormonale altera i riflessi ottococinetici(Tramite GABA) i fluidi labirintici

- *It is important to note that estrogen and progesterone levels in the premenstrual phase may affect central nervous system functioning, indirectly altering the optokinetic function. This may occur especially in those areas related to the visual-vestibular interaction, such as GABAA (gamma-aminobutyric acid) receptors, which is an inhibitory neurotransmitter that binds to specific receptors. Progesterone metabolism may modulate these receptors, altering the transmission in the vestibular nuclei that are involved with the optokinetic, vestibuloocular and vestibulospinal reflexes.*
- *Increased DPN values in the upper semicircular canals in the DPRT test during the postmenstrual phase were statistically significant. We may assume that this occurred due to a possible effect of sex hormones on bodily fluids. Thus, as the volume and pressure of endolymph and perilymph increased during the premenstrual phase, stimulation during the test would have a milder effect when we positioned the head for the DPRT of the vertical canals to the right and left.*

# Effetti del ciclo ormonale femminile sul sistema vestibolare

[Braz J Otorhinolaryngol](#). 2009 May-Jun;75(3):375-80.

## Vestibular characterization in the menstrual cycle.

[Article in English, Portuguese]

Ishii C<sup>1</sup>, Nishino LK, Campos CA.

### ⊕ Author information

#### Abstract

Hormonal disorders in the menstrual cycle can affect labyrinthine fluid homeostasis, causing balance and hearing dysfunctions.

**STUDY DESIGN:** Clinical prospective.

**AIM:** compare the results from vestibular tests in young women, in the premenstrual and postmenstrual periods.

**MATERIALS AND METHODS:** twenty women were selected with ages ranging from 18 to 35 years, who were not using any kind of contraceptive method for at least six months, and without vestibular or hearing complaints. The test was carried out in each subject before and after the menstrual period, respecting the limit of ten days before or after menstruation.

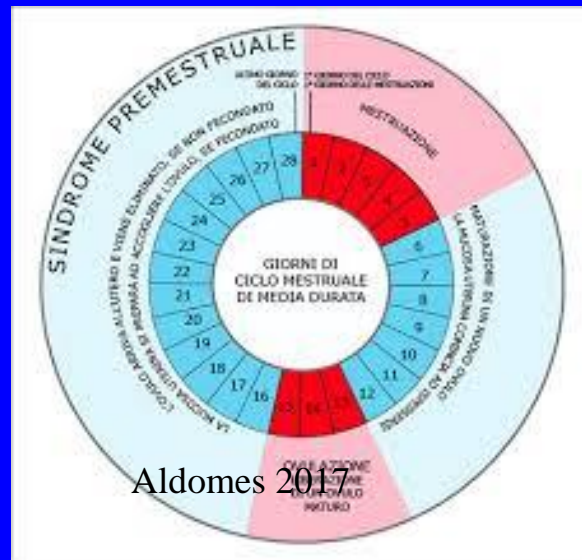
**RESULTS:** there was a statistically significant difference in the menstrual cycle phases only in the following vestibular tests: calibration, saccadic movements, PRPD and caloric-induced nystagmus. We also noticed that age; a regular menstrual cycle; hearing loss or dizziness cases in the family; and premenstrual symptoms such as tinnitus, headache, sleep disorders, anxiety, nausea and hyperacusis can interfere in the vestibular test.

**CONCLUSION:** there are differences in the vestibular tests of healthy women when comparing their pre and postmenstrual periods.

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# CICLO e Acufeni, mal di testa, disturbi del sonno, ansia, nausea e ipersensibilità al suono e prove vestibolari alterate, poiché il periodo premenstruale altera la pressione perilinfatica ed endolinfatica nonché la viscosità del sangue

- Tinnitus, headaches, sleep disorders, anxiety, nausea, and hypersensitivity to sound may alter the vestibular tests (PT type and frequency, ON gain and SCAV, DPRT velocity and DPN, and CT SCAV), since the premenstrual period alters perilymph and endolymph pressure and blood viscosity. Additionally, some studies have shown that there are psychic symptoms in the PMS that decrease the concentration ability, which also reduces attention during testing.



# Ormoni e Menière.- La sindrome di Ohresser

Si manifesta nella donna, nel periodo premenstruale per uno squilibrio nella quantità di endolinfa circolante all'interno delle cavità del labirinto su base ormonale



Aldomes 2017



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Brain Research Bulletin 66 (2005) 1–8

www.elsevier.com

Review

# Stress hormones in Ménière's disease and acoustic neuroma

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Received 7 January 2005; received in revised form 1 April 2005; accepted 7 April 2005  
Available online 25 April 2005

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## Abstract

Stress has been postulated to trigger or contribute to inner ear pathologies but there is little objective evidence. We measured stress hormones in Ménière's patients and patients with acoustic neuroma. Data were compared with those from a control group with facial spasm. We assayed classic stress hormones including adrenocorticotrophic hormone, cortisol, growth hormone, and prolactin.

We found a strong positive correlation between cortisol and adrenocorticotrophic hormone in Ménière patients and acoustic neuroma but no correlation in patients with facial spasm. The data also revealed in female patients with Ménière's disease an unexpected significant positive correlation between cortisol and prolactin. The data showed the expected positive or no correlation between cortisol and prolactin associated with males and females in the other patient groups. Prolactin increases are known to represent alternative strategies to cope with stress, and our data point to prolactin being particularly elevated in Ménière's disease and cortisol in acoustic neuroma. These data provide further evidence for modification of di-

# Analysis of Cortisol and Other Stress-Related Hormones in Patients with Ménière's Disease

\*Nynke van Crujisen, †Robin P. F. Dullaart, \*Hero P. Wit,  
and \*Frans W. J. Albers

*\*Departments of Otorhinolaryngology, and †Endocrinology, University Medical Centre Groning  
Groningen, The Netherlands*

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**Objective:** To evaluate cortisol and catecholamine levels in patients with Ménière's disease.

**Study Design:** Prospective, controlled study.

**Setting:** Tertiary referral center.

**Patients:** Thirty patients with Ménière's disease and 18 healthy controls.

**Main Outcome Measures:** Serum and saliva cortisol, serum cortisol after the dexamethasone suppression test, urine free cortisol, and urine catecholamines.

**Results:** The serum and saliva cortisol levels were higher in Ménière's patients compared with their control group:  $440 \pm 127$  (n = 28) versus  $366 \pm 90$  (nmol/L) (n = 18) and  $17.2 \pm 6.1$

using a serum cortisol level cutoff point (median). The total Ménière's disease time of tinnitus tended to be longer in the high-cortisol group (p = 0.07, two-tailed). The total Ménière's disease duration was  $13.5 \pm 9.9$  years in the high-cortisol group and  $13.5 \pm 9.9$  years in the low-cortisol group (n = 14 for both). The groups were matched for age, gender, and unilaterally or bilaterally affected ears.

**Conclusion:** Patients with Ménière's disease have higher serum cortisol levels. It is suggested that the elevated cortisol levels are rather the result than the cause of the disease, because patients affected longer se



## Hyperprolactinemia in some Ménière patients even in the absence of incapacitating vertigo <sup>☆</sup>

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Received 13 October 2004; accepted 26 November 2004

Available online 22 December 2004

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### Abstract

Stress can be a significant factor influencing ear pathologies and is often reported to trigger the symptoms of Ménière's disease. Both physiological and psychological stress provokes the release of prolactin from the pituitary thus allowing the classification of prolactin as a major stress hormone. We investigated the level of the stress hormone prolactin in a Swedish population with early symptoms of Ménière's disease. The median prolactin level in the Ménière patients ( $n = 33$ ) was not significantly different from that of non-Ménière patients ( $n = 23$ ). However, in the Ménière group one female (90 year old) had prolactin levels in the upper normal range for women, one male (77 year old) had prolactin levels above the normal limit for men, and a third patient (76 year old female) presented hyperprolactinemia with more than twice the normal level. MRI confirmed a pituitary adenoma in this patient. This study provides further support for the recent report of hyperprolactinemia in some patients with long-standing Ménière's disease and presenting incapacitating vertigo in France. The data emphasize the likely implication of stress in this pathology where the stress hormone prolactin is likely to represent one actor in a complex hormonal imbalance affecting the inner ear.

# Disorder of the saliva melatonin circadian rhythm in patients with Meniere's disease

Aoki M, Yokota Y, Hayashi T, Kuze B, Murai M, Mizuta K, Ito Y. Disorder of the saliva melatonin circadian rhythm in patients with Meniere's disease.

Acta Neurol Scand 2006; 113: 256–261. © Blackwell Munksgaard 2006.

*Objectives* – Stress is involved in the development of symptoms of Meniere's disease (MD). Stress-related disease has been reported to be associated with disorders in the circadian rhythm of melatonin (MEL) which regulates that rhythm. We therefore investigated MEL circadian rhythm of patients with MD. *Patients and methods* – A comparison of 13 MD patients was made with age-matched controls. Saliva samples were collected every 3 h. A statistical analysis of the circadian rhythm of saliva MEL was performed for a circadian rhythm by the fit of a 24- and 12-h composite cosine model. In addition, we assessed the stress and depression status of the two groups. *Results* – The rhythmic amplitude of MEL in the MD group was significantly lower than that in the control group ( $P < 0.05$ ). The acrophase in the MD group was significantly earlier than that in the control group ( $P < 0.05$ ). MD patients had significantly higher stress score and depression score than control subjects ( $P < 0.05$ ). The amplitude in MD patients had no significant correlation with their otologic clinical data. *Conclusions* – These results suggest that MD patients have a MEL deficiency, which is related to their stress and depression status rather than the otologic pathological status of MD.

**M. Aoki, Y. Yokota, T. Hayashi,  
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Key words: melatonin; Meniere's disease; stress

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Accepted for publication November 16, 2005

# Lo sviluppo dell'ippocampo e del n dentato è condizionato dalle cure materne ricevute

## Maternal support in early childhood predicts larger hippocampal volumes at school age

[Joan L. Luby](#),<sup>a,1</sup> [Deanna M. Barch](#),<sup>a,b,c</sup> [Andy Belden](#),<sup>a</sup> [Michael S. Gaffrey](#),<sup>a</sup> [Rebecca Tillman](#),<sup>a</sup> [Casey Babb](#),<sup>a</sup> [Tomoyuki Nishino](#),<sup>a</sup> [Hideo Suzuki](#),<sup>a</sup> and [Kelly N. Botteron](#)<sup>a,c</sup>

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This article has been [cited by](#) other articles in PMC.

### ABSTRACT

Go to: 

Early maternal support has been shown to promote specific gene expression, neurogenesis, adaptive stress responses, and larger hippocampal volumes in developing animals. In humans, a relationship between psychosocial factors in early childhood and later amygdala volumes based on prospective data has been demonstrated, providing a key link between early experience and brain development. Although much retrospective data suggests a link between early psychosocial factors and hippocampal volumes in humans, to date there has been no prospective data to inform this potentially important public health issue. In a longitudinal study of depressed and healthy preschool children who underwent neuroimaging at school age, we investigated whether early maternal support predicted later hippocampal volumes. Maternal support observed in early childhood was strongly predictive of hippocampal volume measured at school age. The positive effect of maternal support on hippocampal volumes was greater in nondepressed children. These findings provide prospective evidence in humans of the positive effect of early supportive parenting on healthy hippocampal development, a brain region key to memory and stress modulation.

**Keywords:** depression, parental support, nurturance, neurodevelopment

**INOLTRE** Sappiamo che una lesione vestibolare può essere causa di deficit dell'ippocampo e pertanto agire negativamente sui processi di memoria, specie spaziale.

[Neuroscience](#), 2001;105(1):1-5.

**Damage to the vestibular inner ear causes long-term changes in neuronal nitric oxide synthase expression in the rat hippocampus.**

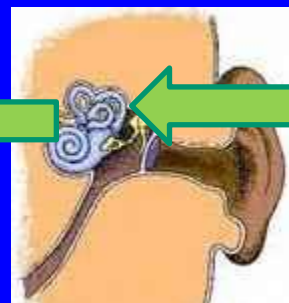
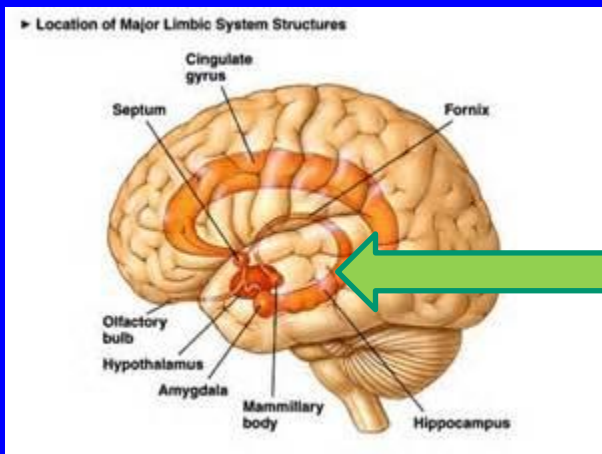
[Zheng Y<sup>1</sup>](#), [Horii A](#), [Appleton J](#), [Darlington CL](#), [Smith PE](#).

⊕ **Author information**

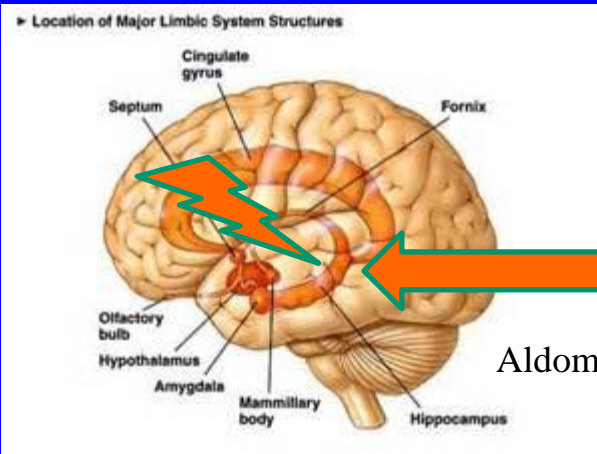
**Abstract**

The vestibular inner ear detects head acceleration and initiates compensatory eye movement and postural reflexes that help keep the visual image of the world stable on the retina, and maintain balance, during unexpected head movement. The most primitive vestibular systems are estimated to have evolved more than 500 million years ago and in mammalian and submammalian species the vestibular reflexes are mediated by basic brainstem pathways (see Wilson and Melvill Jones, 1979 for review). Although the contributions of the vestibular system to higher cognitive function have generally received less attention than its reflexive roles, vestibular sensory information is transmitted to higher centres in the brain and humans with vestibular damage are known to experience debilitating perceptual illusions (see Curthoys and Halmagyi, 1995; Berthoz, 1996 for reviews). Increasing behavioural and neurophysiological evidence suggests that the hippocampus uses information from the vestibular inner ear in order to build up maps of space that can be used in the development of spatial memory during learning tasks (McNaughton et al., 1991; Chapuis et al., 1992; Wiener and Berthoz, 1993; O'Mara et al., 1994; Wiener et al., 1995; Gavrilov et al., 1995; Stackman and Taube, 1996; Vitte et al., 1996; Taube et al., 1996; Save et al., 1998; Peruch et al., 1999; Cuthbert et al., 2000; Russell et al., 2000). However, to date, there has been no indication of the long-term neurochemical effects of the loss of vestibular input on hippocampal function. Since nitric oxide has been implicated in the mechanisms of hippocampal synaptic plasticity associated with the development of short-term memory (e.g. Schuman and Madison, 1991; Schuman et al., 1994; Arancio et al., 1996; Wu et al., 1997; Lu et al., 1999), we examined whether changes occur in the activity and expression of the enzymes responsible for nitric oxide production (nitric oxide synthases) in subregions of the rat hippocampus at different times following unilateral peripheral vestibular lesions, using western blotting and radioenzymatic assays. We found a decreased expression of neuronal nitric oxide synthase in the ipsilateral dentate gyrus at 2 weeks following the vestibular damage and not before, that may be related to the long-term effects of the loss of vestibular input on hippocampal function. These results support the hypothesis that head movement and position information derived from the vestibular inner ear may be important for the normal function of the hippocampus.

**Lo stimolo vestibolare sull'ippocampo ne determina lo sviluppo ed è pertanto fondamentale nella memoria topocinetica( Berthoz 93, Wiener 95, Stackman 96, Taube 96, Russell 2000, ecc.)**



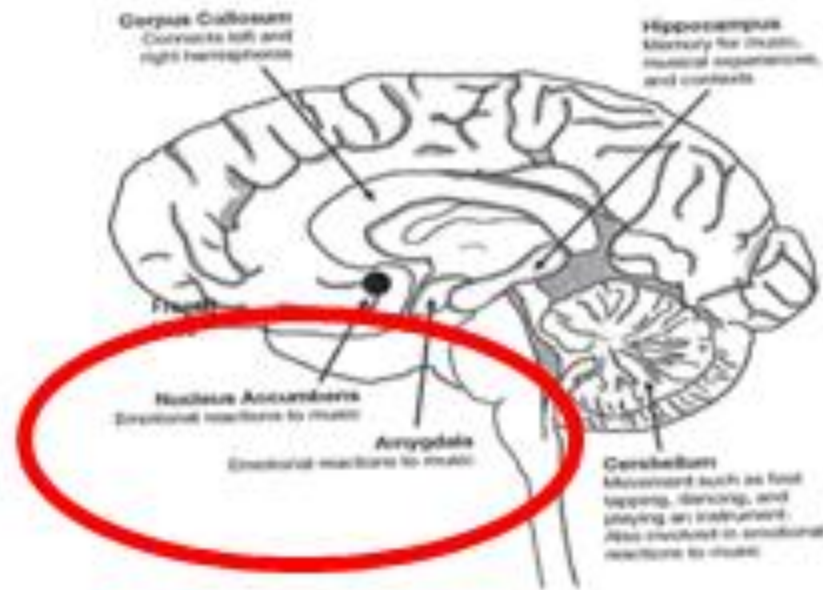
**I danni al labirinto vestibolare provocano variazioni a lungo termine nella sintesi neuronale di ossido nitrico nell'ippocampo omolaterale del ratto(Zheng, 2001)**



Aldomes 2017

# Sacculo e piacere della musica

## Where is music processed?



# PNEI E SORDITA'



# Importante il ruolo svolto dai cosiddetti ormoni sessuali femminili(estrogeno e progesterone) sul sistema Nervoso Centrale e sull'udito

[Acta Otolaryngol.](#) 2010 Feb;130(2):204-14. doi: 10.3109/00016480903016570.

## Effects of age and sex on the expression of estrogen receptor alpha and beta in the mouse inner ear.

Motohashi R<sup>1</sup>, Takumida M, Shimizu A, Konomi U, Fujita K, Hirakawa K, Suzuki M, Anniko M.

### ⊕ Author information

#### Abstract

**CONCLUSION:** Estrogen receptor (ER) alpha and beta were expressed in the inner ear, and expression decreased with increasing age. ERalpha may alter cochlear and vestibular sensory transduction, and ERbeta may have a neuroprotective function in the inner ear.

**OBJECTIVE:** Expression of ERalpha and ERbeta in the mouse inner ear and its alterations with sex and aging were analyzed.

**MATERIALS AND METHODS:** Male and female CBA/J mice aged 8 weeks and 24 months were used. The localization and the intensity of ERalpha and ERbeta immunoreactivity in the inner ear of young and old mice of both sexes were investigated by immunohistochemistry.

**RESULTS:** ERalpha and ERbeta were co-expressed in the inner ear, i.e. in the nuclei of stria vascularis, outer and inner hair cells, spiral ganglion cells and vestibular ganglion cells, vestibular dark cells and endolymphatic sac. Strial marginal cells, outer hair cells and type II ganglion cells showed less expression of ERalpha. No gender- or age-related difference was noted in the expression pattern of ERalpha or ERbeta, but fluorescence intensity of ERalpha was stronger in young female mice than in young male mice. In contrast, ERbeta revealed no significant difference. In the old mice, fluorescence intensities of both ERalpha and ERbeta were significantly decreased in both sexes.



I recettori alfa e beta dell'**estrogeno** (ER) sono stati individuati **nell'orecchio interno**. Quello ER alpha può alterare la trasduzione sensoriale cocleare e vestibolare e l'ERbeta può svolgere una funzione **neuroprotettiva** nell'orecchio interno.

[Acta Otolaryngol.](#) 2010 Feb;130(2):204-14. doi: 10.3109/00016480903016570.

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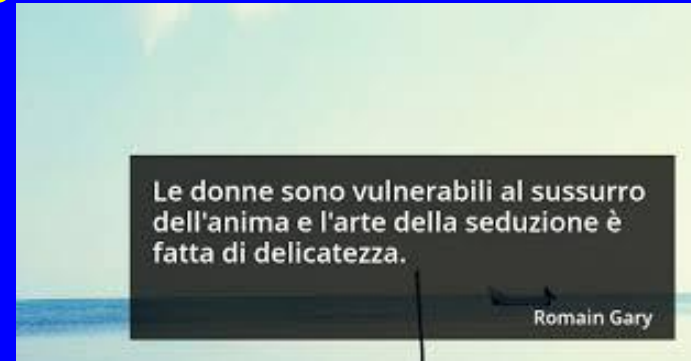
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Aldomest 2017

# Questo ruolo è finalizzato a migliorare durante la fase estrogenica la sensibilità ai richiami sessuali e l'accoppiamento



- Il ciclo ovarico può potenzialmente portare alla fluttuazione anche della funzione uditiva e di altri processi sensoriali (Parlee, 1983). Il sistema uditivo può essere più sensibile durante il picco della circolazione estrogena a causa del suo effetto eccitatorio e protettivo sul S.N.C.. Allo stesso modo, i bassi livelli di ormoni durante la fase premestruale possono riguardare una funzione uditiva meno sensibile. Uno studio recente ( Sisneros e Bass, 2003 ) ha osservato che le fibre nervose uditive di un pesce di midshipman (un pesce di allevamento vocale stagionale) sono più sensibili alle chiamate di accoppiamento maschile durante la stagione riproduttiva e non in altre occasioni. Il trattamento con estradiolo di alcuni pesci femmine durante la stagione non riproduttiva rende i loro nervi uditivi più rispondenti alle chiamate di accoppiamento maschile (Sisneros et al., 2004 ).



**Mi spiace, non ti sento.  
Sono in fase  
progestinica!**

**L'estrogeno femminile la chiave per preservare l'udito nell'uomo??** invecchiato? Questa domanda rimane senza risposta, ma la perdita dell'udito è più profonda nei maschi anziani rispetto alle femmine. Ci sono anche differenze di sesso ben noti nella risposta uditiva del sistema cerebrale (ABR), cioè le donne hanno latenze più corte degli uomini. Inoltre, le donne in menopausa che hanno assunto la terapia ormonale sostitutiva hanno un udito leggermente migliore del gruppo controllo e le donne con **sindrome di Turner** mostrano maggiore latenza ABR e presbiacusia precoce. Questi risultati sono supportati anche da esperimenti su animali.

[Acta Otolaryngol.](#) 2006 Jan;126(1):10-4.

## Estrogen and hearing: a summary of recent investigations.

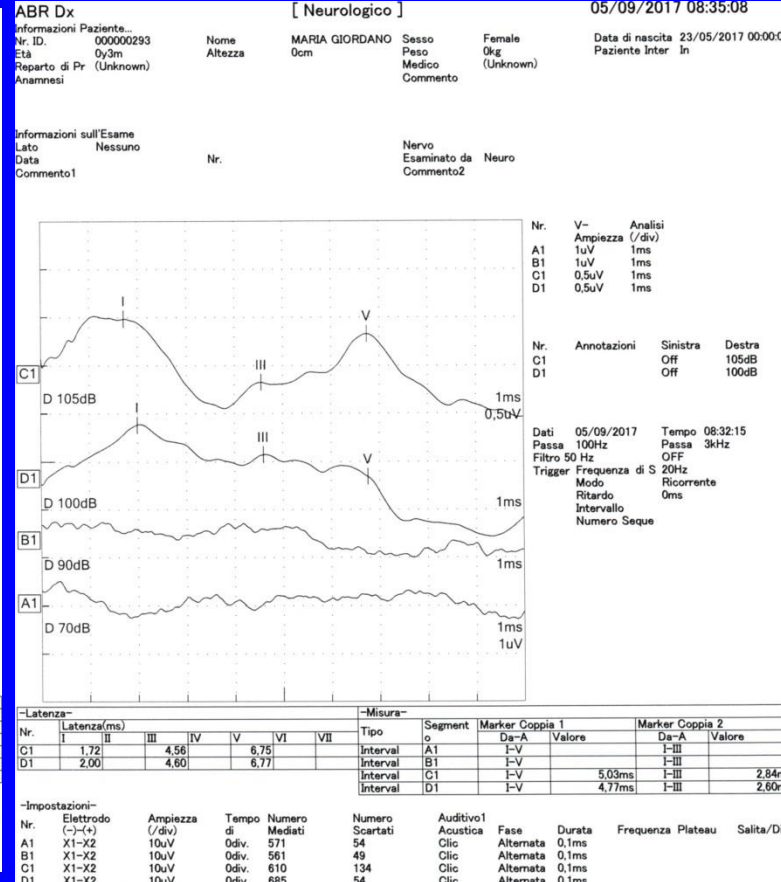
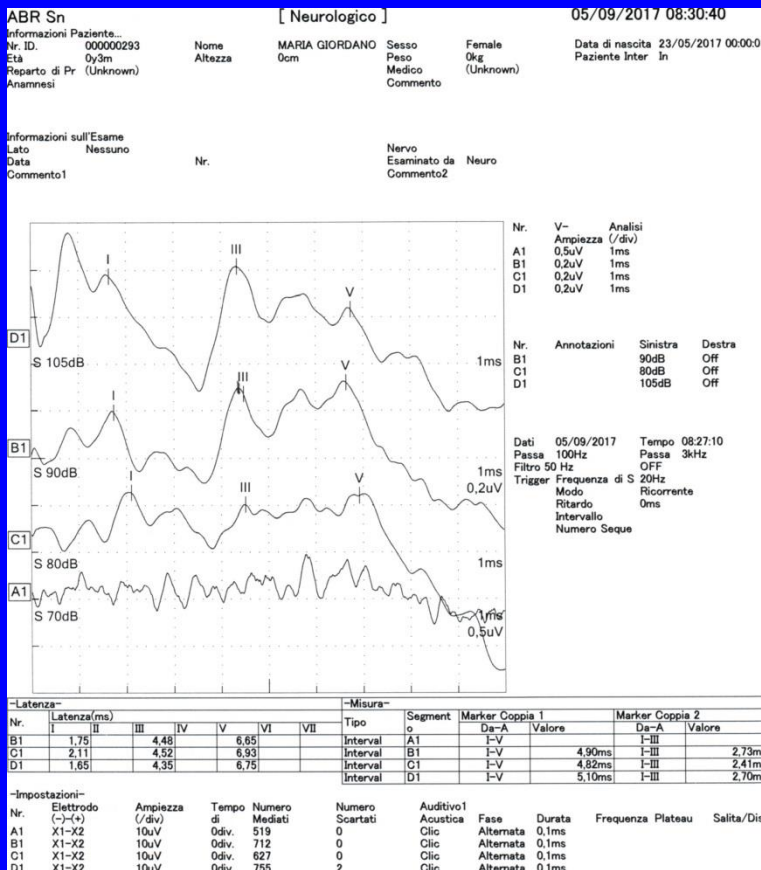
[Hultcrantz M](#)<sup>1</sup>, [Simonoska R](#), [Stenberg AE](#).

### ⊕ Author information

#### Abstract

Is the female sex steroid estrogen the key to preserved hearing in the aging human? This question remains unanswered, but hearing loss is more profound in elderly males than females. There are also well-known sex differences in the auditory brainstem response (ABR), i.e. women have shorter latencies than men. Moreover, menopausal women who are administered hormone replacement therapy have slightly better hearing than those who are not, and women with Turner's syndrome (45,X), who are biologically estrogen-deficient, show longer ABR latencies and early presbycusis. These findings are also supported by animal experiments. When boosted with estrogen or testosterone the non-reproductive female midshipman fish alters its inner ear auditory mechanism so that it can hear the male's hum-like call. If estrogen receptor beta is knocked out in mice, severe progressive hearing loss occurs, leading to early deafness. In apparent contradiction to these findings, there have been case reports suggesting that hormone replacement therapy and oral contraceptive use can lead to hearing loss, but of another type, namely acute sudden deafness. Such contradictory aspects of the action of estrogen are commonly found and may spring from the fact that there are two estrogen receptors, alpha and beta, both of which are present in the inner ear of mice, rats and humans. Knowing how sex steroids can alter hearing ability may give important clues as to how estrogen can preserve hearing in humans. In this review we present a summary of current knowledge about hearing and estrogen.

# Nostra esperienza G.MV. Mesi quattro



**Comorbilità audiologica prematurità (32,4 sett), basso peso alla nascita, ipotiroidismo congenito, anemia sideropenica,**

# Il tasso di estrogeni modifica le risposte ai potenziali evocati ed alle otoemissioni acustiche

[Front Neuroendocrinol.](#) Author manuscript; available in PMC 2014 Oct 1.

PMCID: PMC3788044

Published in final edited form as:

NIHMSID: NIHMS511423

[Front Neuroendocrinol.](#) 2013 Oct; 34(4): 285–299.

Published online 2013 Jul 31. doi: [10.1016/j.yfme.2013.07.006](https://doi.org/10.1016/j.yfme.2013.07.006)

## Estrogenic modulation of auditory processing: a vertebrate comparison


Melissa L. Caras<sup>a,b,1</sup>

[Author information](#) ► [Copyright and License information](#) ►

The publisher's final edited version of this article is available at [Front Neuroendocrinol](#)

See other articles in PMC that [cite](#) the published article.

### Abstract

Go to: 

Sex-steroid hormones are well-known regulators of vocal motor behavior in several organisms. A large body of evidence now indicates that these same hormones modulate processing at multiple levels of the ascending auditory pathway. The goal of this review is to provide a comparative analysis of the role of estrogens in vertebrate auditory function. Four major conclusions can be drawn from the literature: First, estrogens may influence the development of the mammalian auditory system. Second, estrogenic signaling protects the mammalian auditory system from noise- and age-related damage. Third, estrogens optimize auditory processing during periods of reproductive readiness in multiple vertebrate lineages. Finally, brain-derived estrogens can act locally to enhance auditory response properties in at least one avian species. This comparative examination may lead to a better appreciation of the role of estrogens in the processing of natural vocalizations and may provide useful insights toward alleviating auditory dysfunctions emanating from hormonal imbalances.

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**Keywords:** Steroid, Hormone, Estrogen, Estradiol, Comparative, Auditory, Hearing, Sensory, Seasonal

# Review Ormoni e Ipoacusia neurosensoriale anche fluttuante

| Study                  | Subjects                 | Auditory test and methodology | Documentation of ovulatory cycle        | Findings  |
|------------------------|--------------------------|-------------------------------|---|---|
| (Resende et al., 2000) | 15 ♀                     | ABR at 85 dB                  | History of changes in vaginal secretion | <ul style="list-style-type: none"> <li>• No significant difference in ABR latencies in the three testing sessions</li> </ul>  |
| (Yadav et al., 2002)   | 20 ♀                     | ABR at 70 dBnHL               | Daily BBT                               | <ul style="list-style-type: none"> <li>• A trend of ↑ in ABR wave latencies and interpeak intervals during the mid-cycle phase, but not significant.</li> </ul>   |
| (Serra et al., 2003)   | 94 ♀                     | ABR at 100 dBspl              | Ultrasonography and serum P level       | <ul style="list-style-type: none"> <li>• ABR wave latencies and interpeak intervals significantly ↓ in the periovulatory phase (cycle day not mentioned)</li> </ul>   |
| (Caruso et al., 2003b) | 94 ♀ Before and after OC | ABR at 100 dBspl              | Ultrasonography and serum P level       | <ul style="list-style-type: none"> <li>• ABR wave latencies and interpeak intervals significantly ↓ in the periovulatory phase (cycle days 13–16)</li> <li>• No significant difference in ABR wave latencies and interpeak intervals during OC</li> </ul> |

NMC, normal menstrual cycle; FA, functional amenorrhea; BBT, basal body temperature; POF, premature ovarian failure; PCOD, polycystic ovarian disease; E2, oestrogen; P, progesterone; DHEAS, dehydroepiandrosterone sulfate; T, testosterone; PP, progesterone phase ↑, increase; ↓, decrease; ♂, males; ♀, females with normal menstrual cycle.

**Table 2.** Studies of auditory function and menstrual cycle and the effect of reproductive hormones

| Study                         | Subjects                                    | Auditory test and methodology    | Documentation of ovulatory cycle         | Findings   |
|-------------------------------|---|----------------------------------|--|--|
| (Cox, 1980)                   | 12 ♀<br>13 ♀ OC                             | PTA (Bekesy) at 0.5, 1 and 2 kHz | Daily BBT                                | <ul style="list-style-type: none"> <li>• No significant change in auditory sensitivity between groups</li> <li>• Poorer thresholds in the menstrual phase for all</li> <li>• Negative middle ear pressure during the menstrual phase in all</li> </ul>   |
| (Swanson and Dengerink, 1988) | 10 ♀<br>10 ♀ OC                             | PTA (Bekesy) at 4 and 6 kHz      | Daily BBT                                | <ul style="list-style-type: none"> <li>• ♀ 4 kHz Threshold was lowest during ovulation (cycle days 13–14) and highest during menses (cycle days 2–3)</li> <li>• ♀ 4 kHz Threshold during ovulation was significantly lower than OC group and ♂</li> </ul>  |
|                               | 12 ♂  |                                  | Cervical mucus changes                   | <ul style="list-style-type: none"> <li>• No significant change was found in 6 kHz threshold or difference between the groups</li> </ul>  |
| (Bell, 1992)                  | 4 ♀   | SOAE                             | History and daily BBT in 2 subjects only | <ul style="list-style-type: none"> <li>• 3 Out of 4 had a clear variation in SOAE frequency</li> <li>• ↓ In the frequency before menses and ↑ time of ovulation (cycle day not mentioned)</li> </ul>   |
| (Haggerty et al., 1993)       | 8 ♀<br>2 ♂                                  | SOAE                             | History                                  | <ul style="list-style-type: none"> <li>• 6 Females had monthly variation in SOAE</li> <li>• 2 Had ↑ in frequency variation before menses</li> <li>• 5 Had ↓ in the frequency before menses and ↑ time of ovulation (cycle day not mentioned)</li> </ul>  |
| (Penner, 1995)                | 1 ♀ (NMC, FA, OC)                           | SOAE                             | Daily BBT                                | <ul style="list-style-type: none"> <li>• During NMC ↓ in the frequency of SOAE before menses and near the time of ovulation</li> <li>• Less fluctuation in SOAE frequency was noted during amenorrhea and the use of OC</li> </ul>   |
| (Yellin and Stillman, 1999)   | 13 ♀  | SOAE, DPOAE, TEOAE               | Daily BBT                                | <ul style="list-style-type: none"> <li>• SOAEs dominant early in the cycle, gradually decreased and least prevalent before menses</li> <li>• No cyclic changes in TEOAEs or DPOAEs were found</li> </ul>   |
| (Amit and Animesh, 2004)      | 15 ♀  | TEOAE                            | History                                  | <ul style="list-style-type: none"> <li>• TEOAE amplitude significantly higher during menses (cycle days 1–3) and lowest during the luteal phase (cycle days 22–25)</li> <li>• TEOAE amplitude significantly lower during midcycle (days 12–15) compared to during menses but higher than the luteal phase</li> <li>• 3 Subjects did not have TEOAE responses during midcycle and luteal phase</li> </ul> |
| (Fagan and Church, 1986)      | 10 ♀  | ABR at 50 dBnHL                  | Daily BBT                                | <ul style="list-style-type: none"> <li>• No fluctuation in ABR latencies during MC</li> </ul>  |
| (Dehan and Jerger, 1990)      | 10 ♀  | ABR at 80 dBnHL                  | Blood (E2, P, FSH and LH)                | <ul style="list-style-type: none"> <li>• Wave V latency ↑ just before ovulation and ↓ at PP and pre-menstrual period (cycle day not mentioned)</li> </ul>  |
| (Elkind-Hirsch et al., 1992a) | 9 ♀   | ABR at 70 dBnHL                  | Blood (E2, P, FSH and LH)                | <ul style="list-style-type: none"> <li>• Significant ↑ in wave III, V and I–V latency associated with ↑ E2 during mid-cycle phase (cycle days 12–15)</li> </ul>  |
|                               | 9 ♀ OC                                      |                                  |  | <ul style="list-style-type: none"> <li>• No significant changes in ABR latencies in the OC group</li> </ul>  |
| (Elkind-Hirsch et al., 1992b) | 5 ♀ POF on HRT                              | ABR at 70 dBnHL                  | Blood (E2, P, FSH and LH)                | <ul style="list-style-type: none"> <li>• HRT led to fluctuation in ABR as seen in NMC</li> <li>• Wave V and I–V latency significantly ↑ during the E2 only replacement compared to P and E2 replacement phase</li> </ul>   |
| (Elkind-Hirsch et al., 1994)  | 5 ♂<br>9 ♀<br>9 ♀ OC<br>5 ♀ POF<br>5 ♀ PCOD | ABR at 70 dBnHL                  | Blood (E2, P, FSH, LH, DHEAS and T)      | <ul style="list-style-type: none"> <li>• Wave V latency in descending order: ♀, ♀ PCOD (higher androgen levels), then ♀ POF, ♀ OC and ♀</li> </ul>   |
| (Tasman et al., 1999)         | 19 ♀  | ABR at 70 dB                     | Daily urine LH and BBT                   | <ul style="list-style-type: none"> <li>• Significant ↑ in wave V latency during E2 only replacement for POF and midcycle in ♀</li> <li>• Wave V and III–V latency ↑ in follicular phase (cycle day not mentioned)</li> </ul>   |



# Sordità fluttuante e ciclo ovarico

- Descritti in letteratura casi che documentavano alcune donne che presentavano un deficit uditivo fluttuante associato al ciclo ovarico, **in particolare con un deficit nella fase tardiva luteinica** che migliorava dopo l'inizio delle mestruazioni (Miller e Gould, 1967, Andreyko e Jaffe, 1989)



# Gravidanza e udito



- Durante la gravidanza i livelli di entrambi gli ormoni ovarici sono più alti del solito e si manifestano altri complessi cambiamenti fisiologici (Hadley, 2000 ) che possono comportare la ritenzione di liquidi che può **influenzare la circolazione nella coclea**.
- Sono stati riportati sintomi uditivi come **fulness**, i cambiamenti nella sensibilità uditiva o l'aumentare di tinnito ( Gurr et al., 1993; Tsunoda et al., 1999 ). I risultati di un questionario di Gurr et al. (1993) hanno mostrato che la prevalenza di tinnito nelle donne in gravidanza (25%) era superiore a quella delle donne non gravide (11%).

# Presbiacusia e Menopausa



- Kim et al. (2002) ha suggerito che un basso livello di estradiolo sierico riduce la sensibilità all'udito nelle donne in post-menopausa. Kilicdag e collaboratori (2004) hanno riferito che le donne in post-menopausa che usavano terapia estrogenica avevano migliori soglie rispetto al gruppo controllo. Un recente studio di Hederstierna et al. (2007) ha valutato le soglie uditive in un gruppo di donne attorno al tempo della menopausa e ha scoperto che il 40% ha avuto un certo grado di perdita uditiva. Il sottogruppo di donne che non usavano una terapia ormonale sostitutiva aveva una tendenza di livelli di soglia uditivi più basse rispetto alle donne controllo.

# UDITO E MENOPAUSA

- L'inizio della perdita uditiva legata all'età è più tardi nelle donne rispetto agli uomini ( Pearson et al., 1995 ) e sembrano coincidere con la menopausa ( Murphy e Gates, 1997 ). La differenza sessuale con la perdita dell'udito legata all'età è anche osservata nei modelli di topi di età legata all'età (topi CBA) ( Guimaraes et al., 2004 ), con una diminuzione delle ampiezze DPOAE che si verificano in precedenza nei maschi. Nei topi femminili CBA il maggior decremento delle ampiezze DPOAE si è verificato nei topi di età più recente dopo la menopausa del mouse. Questo risultato suggerisce che l'estrogeno può avere un ruolo protettivo sulla funzione di cochlea e OHC.



# Sul ruolo del simpatico

Hear Res. 1997 Mar;105(1-2):141-5.

## The tonic sympathetic input to the cochlear vasculature in guinea pig.

Laurikainen EA, Ren T, Miller JM, Nuttall AL, Quirk WS.

Kresge Hearing Research Institute, Department of Otolaryngology, University of Michigan, Ann Arbor 48109-0506, USA.

### Abstract

Vascular tone is an essential component in maintaining steady regional blood flow and dynamic responsiveness of a vascular bed. Sympathetic innervation can contribute to vascular tone. Although certain studies have reported evoked changes in cochlear blood flow (CBF) with activation of the sympathetic fibers to the cochlear vasculature, other studies have failed to show evidence of sympathetic contribution to CBF regulation when the cervical sympathetic fibers were unilaterally sectioned. We hypothesized that the bilateral 'sympathectomy of the stellate ganglia' would remove sufficient sympathetic input to the cochlea to yield a change in CBF resting level. To test this hypothesis a new technique was used to expose the stellate ganglia (SG) bilaterally and induce a chemical sympathectomy. We observed that unilateral SG blockade with 2 microliters of 4 mM lidocaine hydrochloride on either side produced a 5-10% increase in CBF, which recovered to baseline during the following 2 min. A subsequent blockade of the contralateral SG produced a rapid 25-35% increase, which then recovered partially during the following 3-4 min, remaining 5-15% above the baseline over a 20 min measurement period. Superior cervical ganglion transection did not affect CBF. Our results provide evidence for the existence of a tonic sympathetic component in the control of vascular tone in guinea pig cochlea. This neural effect is derived bilaterally from SG. This result is consistent with previous anatomical studies showing the bilateral innervation of the cochlea by the SG sympathetic fibers and with previous physiological studies on the bilaterality of evoked changes in CBF due to electric stimulation of SG.

E' tesi che l'innervazione simpatica sia la responsabile del mantenimento del flusso cocleare che deriva prevalentemente dal ganglio stellato(vedi studi di Pirodda)

# Simpatico- ipotensione e sordità giovanile

Audiology. 1997 Mar-Apr;36(2):98-108.

## **The role of hypotension in the pathogenesis of sudden hearing loss.**

Pirodda A<sup>1</sup>, Saggese D, Ferri GG, Giausa G, Grippo MC, Gaddi A.

### **⊕ Author information**

#### **Abstract**

The generic term 'sudden hearing loss' indicates the lack of knowledge about the etiology and pathogenesis of this phenomenon. In most cases it would seem feasible to consider infections or organic circulatory defects; but there are cases, generally affecting young subjects in whom the damage is often reversible, in which a functional origin is possible. We therefore investigated the possible effect of systemic arterial pressure in a retrospective study in a group of 36 patients aged not more than 40 years, treated for sudden hearing loss, comparing the mean values of their arterial pressure with those of a control group of 25 subjects, of similar age, admitted for other disorders. The significantly lower mean values of arterial pressure in the group affected by sudden hearing loss and the easier reversibility of the damage in these patients suggests that, at least in some cases, the cochlear damage may be caused by a perfusion deficit due to the combined effect of hypotension and imperfect vasomotor regulation.

# Ippocampo ed acufeni e sordità

[Neuroimage](#). 2015 Dec 19;129:80-94. doi: 10.1016/j.neuroimage.2015.12.002. [Epub ahead of print]

## Deafferentation-based pathophysiological differences in phantom sound: Tinnitus with and without hearing loss.

Vanneste S<sup>1</sup>, De Ridder D<sup>2</sup>.

### ⊕ Author information

#### Abstract

Tinnitus has been considered an auditory phantom percept. Recently a theoretical multiphase compensation mechanism at a cortical level has been hypothesized linking auditory deafferentation to tinnitus. This Bayesian brain model predicts that two very different kinds of tinnitus should exist, depending on the amount of hearing loss: an auditory cortex related form of tinnitus not associated with hearing loss, and a (para)hippocampal form associated with hearing loss, in which the auditory cortex might be of little relevance. In order to verify this model, resting state source analyzed EEG recordings were made in 129 tinnitus patients, and correlated to the mean hearing loss, the range of the hearing loss and the hearing loss at the tinnitus frequency. Results demonstrate that tinnitus can be linked to 2 very different mechanisms. In patients with little or no hearing loss, the tinnitus seems to be more related to auditory cortex activity, but not to (para)hippocampal memory related activity, whereas in tinnitus patients with more severe hearing loss, tinnitus seems to be related to (para)hippocampal mechanisms. Furthermore hearing loss seems to drive the communication between the auditory cortex and the parahippocampus, as measured by functional and effective connectivity.

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**KEYWORDS:** Auditory cortex; Bayes; Hearing loss; Parahippocampal gyrus; Parahippocampus; Tinnitus

# PNEI E FONAZIONE



Aldomes 2017



## *Un Bersaglio Unico di quasi tutte le ghiandole a secrezione interne: la laringe*

- Con la Menopausa la mucosa si assottiglia, i vasi sanguigni si riducono di numero e ricchezza di flusso, si riduce di oltre il 30% l'attività dei fibroblasti, e di conseguenza del collagene, l'elastina e i mucopolisaccaridi del connettivo cordale. Di conseguenza, le corde vocali possono diventare più rigide, meno elastiche, e perdere progressivamente quella capacità di vibrare modulando il canto.*
- L'aumento dell'ormone luteotropo (LH) può determinare ancora un aumento relativo della produzione di testosterone e questo, in carenza di estrogeni, può ulteriormente contribuire a ispessire e irrigidire le corde vocali.*



# Recettori Ormonali laringei

- **Recettori per estrogeni**, progesterone ed androgeni sono stati trovati nel citoplasma e nel nucleo delle ghiandole e nei fibroblasti all'interno della lamina propria
- **recettori per l'ormone tiroideo**, associati clinicamente a variazioni vocali. I recettori per gli ormoni steroidei fanno infatti parte di una superfamiglia che comprende anche i recettori per gli ormoni tiroidei, la vitamina D3 e l'acido retinoico. Per tale motivo alcuni ormoni possono legarsi a più di un recettore appartenente alla stessa superfamiglia
- **I progestinici**, infine, competono con gli androgeni sia a livello recettoriale che per l'utilizzazione della alfa-5-reduttasi, comportandosi quindi contemporaneamente da antiandrogeni e da antiestrogeni. I recettori per gli androgeni sono molto simili a quelli per il progesterone.



# La voce come disponibilità all'accoppiamento

- la produzione della voce (e le sue caratteristiche acustiche e sessuali) segnali al partner il periodo migliore per l'accoppiamento. Uno studio biologico inglese (Stemple e McComb, 2000) **dimostra che nei primati la voce femminile, che sembra possedere grande valenza informativa** sullo stato riproduttivo, viene percepita dai maschi ed elaborata come codice per stabilire se la femmina è pronta per l'accoppiamento.



Si consiglia ai maschi di cercare  
anche altri segnali di disponibilità  
all'accoppiamento ad evitare...



# Ciclo e voce nei professionisti

- Da ambedue i gruppi sono stati riferiti lievi problemi di voce prima della mestruazione: un lieve stato edematoso ed eritematoso delle corde vocali, oltre ad una ipostenia cordale dimostrata con la stroboscopia e l'EGG. I sintomi vocali ed i correlati strumentali sono stati prevalenti nel gruppo che ha abusato della voce, e ciò suggerisce che comportamenti di abuso vocale aggravino le leggere variazioni vocali premestruali, accrescendo così il rischio di patologie vocali, anche organiche.



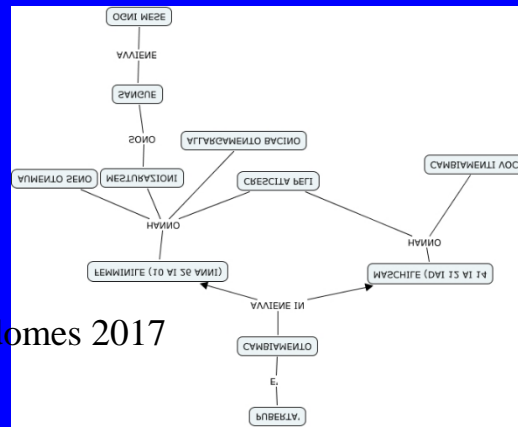
# Nel periodo premestruale

difficoltà nell'esecuzione del registro acuto, diminuzione del range vocale, perdita di potenza e riduzione dello spettro armonico) è stimata in circa il 33% tra le non professioniste ed il 41% tra le cantanti professioniste. Tali sintomi sono da attribuire ad una diminuzione sia del tono muscolare striato che dell'ampiezza della vibrazione, ad un lieve edema dello spazio di Reinke e a dilatazioni capillari variciformi nella laringe di donne con PMS.



# Puberta femminile

- Nella ragazza la laringe raddoppia le proprie dimensioni e la principale conseguenza vocale è l'abbassamento della  $f_0$  di circa una terza nei confronti della voce infantile femminile (ma può abbassarsi anche di una quinta o di un'ottava), mentre nel ragazzo la laringe quadruplica la propria dimensione e la voce può scendere di circa due ottave rispetto alla voce prepubere.
- Altre variazioni importanti sono un aumento dell'ampiezza vocale ed un aumento della perturbazione di frequenza e di ampiezza, ben valutabili con la batteria degli esami elettroacustici (la spettrografia, la fonetografia e la vocaligrafia o MDVP).



Aldomes 2017

# Voce e menopausa

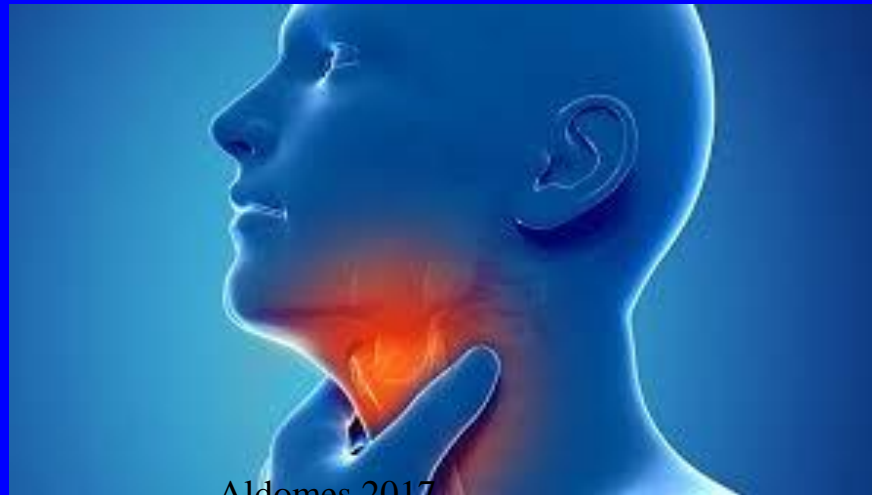
- la disfunzionalità ovarica si esprime causando **atrofia della mucosa e conseguente secchezza** evidenziabile a livello vaginale e del tratto urogenitale. In più la mancanza di estrogeni causa degradazione del tessuto connettivo e ciò colpisce la voce, la cui normalità dipende dall'integrità dello strato connettivo della corda vocale.





# «Dottore ‘mi sento’ muco in gola»

- Gli estrogeni inducono la produzione di muco abbondante, acquoso, fluido e distensibile (fenomeno della foglia di felce o spinnbarkeit).
- Il Progesterone diminuisce l'attività ghiandolare e la secrezione di muco, che diviene spesso ed opaco



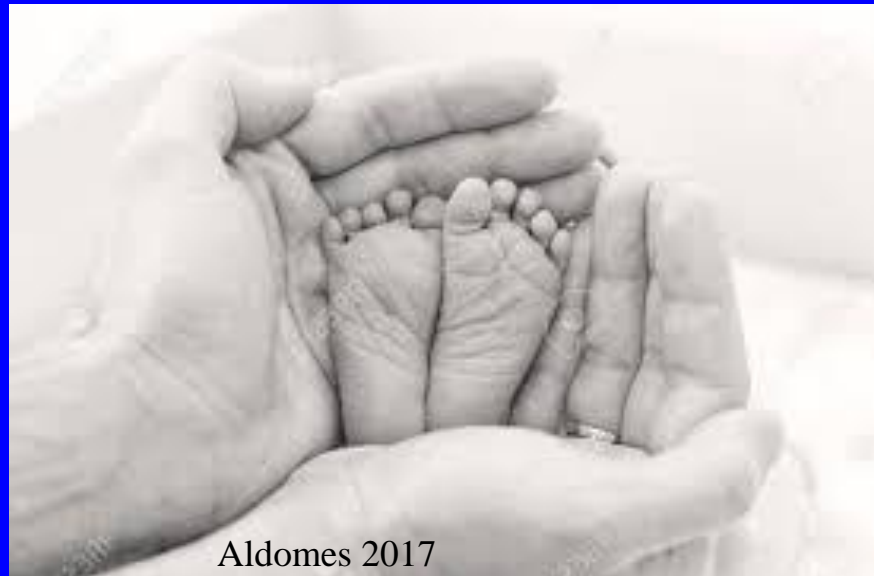
# Prosodia materna, il «maternese» motherese o baby talk (escluso lessico e sintassi)

- --tono molto alto e contorni intonazionali esagerati.
- -- Nelle frasi interrogative viene enfatizzato il tono ascendente.
- -- La produzione è lenta e fluente, le parole vengono ripetute e pronunciate più chiaramente e le pause nel discorso sono più lunghe.
- -- Le peculiarità prosodiche del motherese si registrano soprattutto nei confronti di bambini di 4 mesi, invece che di pochi giorni o più grandi (12 e 24 mesi) e sono più frequenti nell'interazione faccia a faccia. • Confrontando il linguaggio materno indirizzato a bambini di due, cinque anni e adulti, nel caso dei bambini di due anni il tono di voce è significativamente più alto rispetto a quando le madri parlano ai bambini più grandi e agli adulti.
- --Rivolgendosi ai bambini più piccoli, la tendenza ad elevare il tono di voce nella parte finale delle frasi è più frequente in un contesto di gioco piuttosto che durante il racconto di una storia. • Gli adattamenti di tipo prosodico sembrano assolvere primariamente due funzioni: una “analitica” e l'altra “socioaffettiva”.
- -- La funzione analitica aiuterebbe il bambino nel compito di elaborare il materiale linguistico ascoltato, allo scopo di meglio definire i contorni delle parole e delle frasi.
- La funzione socioaffettiva, avendo come risultato immediato quello di attirare e mantenere l'attenzione e di veicolare stati emotivi, consente al bambino di sperimentare uno scambio comunicativo efficace.



# Ed il padre?

- Caratteristiche generali simili a quelle materne, ma su base imitativa
- Diversità negli atti linguistici, perché hanno diverse intenzioni e diverse aspettative nei confronti dell'interazione



Ed il linguaggio? una diminuzione del volume della materia grigia con un aumento dei livelli di testosterone biodisponibile esclusivamente nelle aree di Broca (area corticale preposta alla espressione articolatoria del linguaggio) e Wernicke (area sensoriale linguistica per la comprensione dello stesso).

[Hum Brain Mapp](#). 2016 May;37(5):1738-48. doi: 10.1002/hbm.23133. Epub 2016 Feb 15.

### **Testosterone affects language areas of the adult human brain.**

[Hahn A](#)<sup>1</sup>, [Kranz GS](#)<sup>1</sup>, [Sladky R](#)<sup>2</sup>, [Kaufmann U](#)<sup>3</sup>, [Ganger S](#)<sup>1</sup>, [Hummer A](#)<sup>2</sup>, [Seiger R](#)<sup>1</sup>, [Spies M](#)<sup>1</sup>, [Vanicek T](#)<sup>1</sup>, [Winkler D](#)<sup>1</sup>, [Kasper S](#)<sup>1</sup>, [Windischberger C](#)<sup>2</sup>, [Swaab DF](#)<sup>4</sup>, [Lanzenberger R](#)<sup>1</sup>.

#### **⊕ Author information**

#### **Abstract**

Although the sex steroid hormone testosterone is integrally involved in the development of language processing, ethical considerations mostly limit investigations to single hormone administrations. To circumvent this issue we assessed the influence of continuous high-dose hormone application in adult female-to-male transsexuals. Subjects underwent magnetic resonance imaging before and after 4 weeks of testosterone treatment, with each scan including structural, diffusion weighted and functional imaging. Voxel-based morphometry analysis showed decreased gray matter volume with increasing levels of bioavailable testosterone exclusively in Broca's and Wernicke's areas. Particularly, this may link known sex differences in language performance to the influence of testosterone on relevant brain regions. Using probabilistic tractography, we further observed that longitudinal changes in testosterone negatively predicted changes in mean diffusivity of the corresponding structural connection passing through the extreme capsule. Considering a related increase in myelin staining in rodents, this potentially reflects a strengthening of the fiber tract particularly involved in language comprehension. Finally, functional images at resting-state were evaluated, showing increased functional connectivity between the two brain regions with increasing testosterone levels. These findings suggest testosterone-dependent neuroplastic adaptations in adulthood within language-specific brain regions and connections. Importantly, deteriorations in gray matter volume seem to be compensated by enhancement of corresponding structural and functional connectivity. *Hum Brain Mapp* 37:1738-1748, 2016. © 2016 Wiley Periodicals, Inc.

## Testosterone affects language areas of the adult human brain

[Andreas Hahn](#),<sup>1</sup> [Georg S. Kranz](#),<sup>1</sup> [Ronald Sladky](#),<sup>2</sup> [Ulrike Kaufmann](#),<sup>3</sup> [Sebastian Ganger](#),<sup>1</sup> [Allan Hummer](#),<sup>2</sup> [Rene Seiger](#),<sup>1</sup> [Marie Spies](#),<sup>1</sup> [Thomas Vanicek](#),<sup>1</sup> [Dietmar Winkler](#),<sup>1</sup> [Siegfried Kasper](#),<sup>1</sup> [Christian Windischberger](#),<sup>2</sup> [Dick F. Swaab](#),<sup>4</sup> and [Rupert Lanzenberger](#)<sup>✉1</sup>

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### Abstract

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Although the sex steroid hormone testosterone is integrally involved in the development of language processing, ethical considerations mostly limit investigations to single hormone administrations. To circumvent this issue we assessed the influence of continuous high-dose hormone application in adult female-to-male transsexuals. Subjects underwent magnetic resonance imaging before and after 4 weeks of testosterone treatment, with each scan including structural, diffusion weighted and functional imaging. Voxel-based morphometry analysis showed decreased gray matter volume with increasing levels of bioavailable testosterone exclusively in Broca's and Wernicke's areas. Particularly, this may link known sex differences in language performance to the influence of testosterone on relevant brain regions. Using probabilistic tractography, we further observed that longitudinal changes in testosterone negatively predicted changes in mean diffusivity of the corresponding


# ORGANISMO OLISTICO

[Ann Ist Super Sanita](#). 1999;35(4):335-41.

**[The evolution of the biomedical paradigm and nonconventional medicines].**

[Article in Italian]

[Bottaccioli F](#)<sup>1</sup>.

 **Author information**

## **Abstract**

At the moment, it could be possible to integrate scientific, conventional and unconventional and alternative medicine to improve the efficacy and the quality of therapies. This could be feasible thanks to the following details: a) after two centuries, the biomedical paradigm is radically changed: from mechanistic to complex, holistic vision of human physiopathology and therapeutics. This emerging paradigm enables the best assessment of unconventional medical theories and complementary and alternative therapies; b) into the diversified unconventional medicines world an open-mind to scientific debate is rising, closing the ancient contrast to conventional medicine. The pathway is crucial, it could set out the scientific quality of the conventional, complementary and alternative medicine integration.

*Possibile che per  
lavorare debba rubare  
il mestiere a neurologi,  
ortopedici, fisiatristi,  
psichiatri, psicologi...?*

