Introduction and general Perspective of Sensorineural Hearing Loss.

IFOS International Course.

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Present and future. Aldous Huxley, 1928.

The shaking air rattled Lord Edward´s membrana tympani, the interlocked malleus incus and stirrup bones were set in motion so to agitate the membrane of the oval window and raise an infinitesimal storm in the fluids of his labyrinth. The hairy endings of the auditory nerve shuddered like weeds in a rough sea; a vast number of obscure miracles were performed in the brain and Lord Edward ecstatically whispered,***!Bach!***

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Sensory Neural loss…

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Aldous Huxley 1928.

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Sensorineural hearing loss.

Hearing loss due to damage of the neural cells of hearing is the most common physical dishabilty.

Present bilaterally and permanently between 1-3 per 1000 of aparently normal newborns.

2-4% of new borns that require intensive care).

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Sensorineural hearing loss. The most common dishability…

- Anual incidence in screening studies in the USA:
- 280 cases of fenilketonuria.
- 520 cases of hemoglobinopathy.
- 1000 cases of hypothiroidism.
- 2000 cases of cystic fibrosis.
- 24000 cases of hearing loss.

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Incidence of sensorineural hearing loss. The numbers precipitated a revolution…

- Legislation for early diagnosis of hearing loss…
- The organization of a global multidisciplinary approach oriented towards : detection, evaluation, diagnosis and early intervention.
- The development of universal screening teams for new borns, with professionals and infrastructure capable of performing adequate evaluation and diagnosis.
- Once the diagnosis is made…professional teams capable of treating patients medically, surgically (eg. cochlear implants) and of providing adequate amplification (eg. hearing aids) and rehabilitation.

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Principles of early detection and intervention and of neural plasticity…

- "The cerebral cortex is similar to a garden populated by inumerable trees -the pyramidal cells- which thanks to an intelligent treatment and care can multiply their branches, grow deeper roots and produce flowers and exquisite fruits." (Santiago Ramón y Cajal, 1894).

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Sensorineural hearing loss. Where are we?

- We are in a great moment.
- A moment of big changes, achievements and satisfactions inspite of being only at the tip of the iceberg and of not having descifered most of “the obscure miracles” described by Huxley in 1928.

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Sensorineural hearing loss.
¿What is coming up in the immediate future?

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A mayor wave is transforming our society.

A progressive increase in life expectancy.

"Developed countries."

- Before XX th Century : 40 years.
- Beginnings XX th Century: 50 years.
- Ends XX th Century: 76 years.

- By mid XXI st Century : 50% of deaths in the USA will occur after 80 years of age.

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Percentage of people over 65 years of age in "developed countries."

- 1960 : 8%.
- 1980 : 11%.
- 2000 : 13%.
- **2020 : 16%.**
- 2050 : 22%.

- *The population is turning gray. *

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Population growth in the world between 2000 and 2050.

- The proportion of the world population over 60 years will rise from 11% to 22%.
- In absolute numbers people over 60 years will rise from 605 million to 2 billion in this same period.
- People over 80 will quadruple.

(OMS. Facts about ageing. 2012.).

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Population aging in America varies significantly.

- People of 60 or more years per 100 people under 15 years.
- Bolivia 17 for every 100.
- Uruguay 70 for every 100.
- Canadá 88 for every 100.
- With the exception of Bolivia, Haití, Guatemala, Honduras and Nicaragua by 2050 the relation will be of at least 100 for every 100.

- United Nations World population prospect 2005.

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Aging and Hearing.

- Incidence and prevalence of sensorineural hearing loss.
- New Borns :0.2%
- Adolescents :1.0%
- Adults :2.0%
- Adults over 65 years : 30%
- Adults over 85 years : 50%
- **Plus :**
- Percentage of persons over 65 years in “developed” countries:

  1960: 8% 1980: 11% 2000: 13% 2020: 16%.

  (the population is getting “gray.”).

  Life expectancy:

  Early XX Century: 40 years Mid XX Century: 50. Ends XX C.: 76.

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In brief: Harm in central nerve fibers. Approaches.

- 1. To stimulate better those fibers that remain. Eg. Hearing Aids.
- 2. To do a “by pass” skipping the ciliated cells and stimulating directly the ganglion cells.
- Eg. Cochlear implants.
- 3. To promote regeneration of those which are damaged.
- 4. To re establish function of disfunctional cells.

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Requirements.

- Well trained and prepared professional teams.
- Hearing aids and implants.

Proportions:

By 2009 200 000 persons had been implanted.

In 2009 9 000 000 hearing aids were prescribed.

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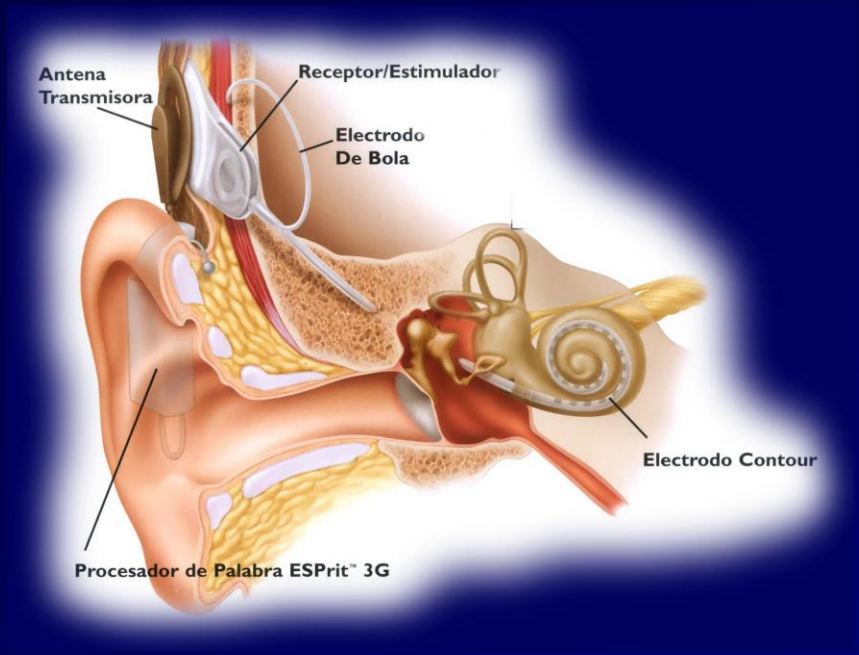

- Hearing Aids:

  Electronic devices designed to detect sounds and amplify them selectively.

- Cochlear Implants:

  Electronic devices designed to detect sounds and transform them into electrical impulses that are transmitted to the auditory nerve and are interpreted by the brain as sounds.

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¿Where are we with hearing aids?

- Radical changes have occurred in the last few years..
- Analogue traditional amplification was changed to digital processing of signals.
- Hearing aids today are beyond sole amplification and are more sound processors than amplifiers (small computers).
- The quality of sound improved radically…and the degree of user satisfaction increased from 5.5% in 2004 to 78.6% in 2008 (Don Hayes 2011).

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Where are we with hearing aids?

- The main changes have ocurred in 3 areas:
- 1. Digital processing (less noise, better hearing in noisy environments, directionality and better discrimination).

  2. Mechanics (open molds, feedback control).

  3. Inalambric transmission (connection between both hearing aids, connection with telephone, posibility of speaking by telephone using both ears, connection to TV, MP3, computer.
- Having a functional receptor is required…

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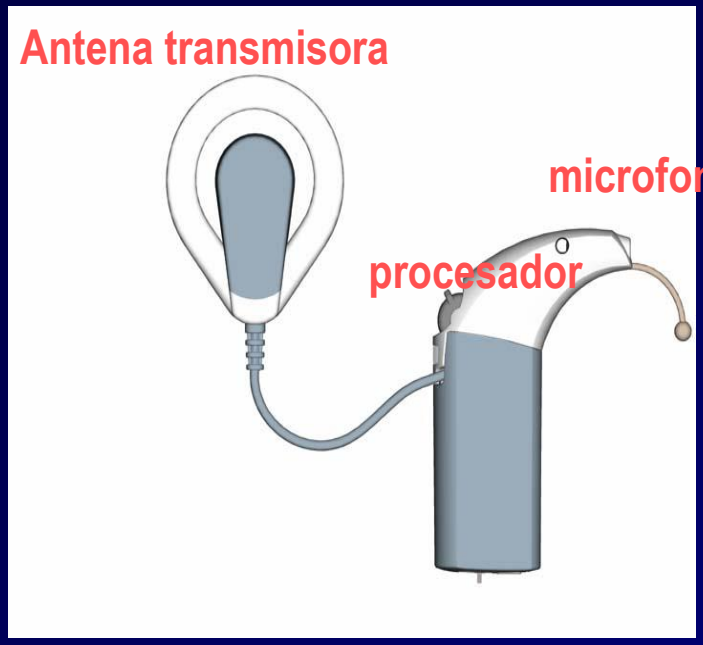
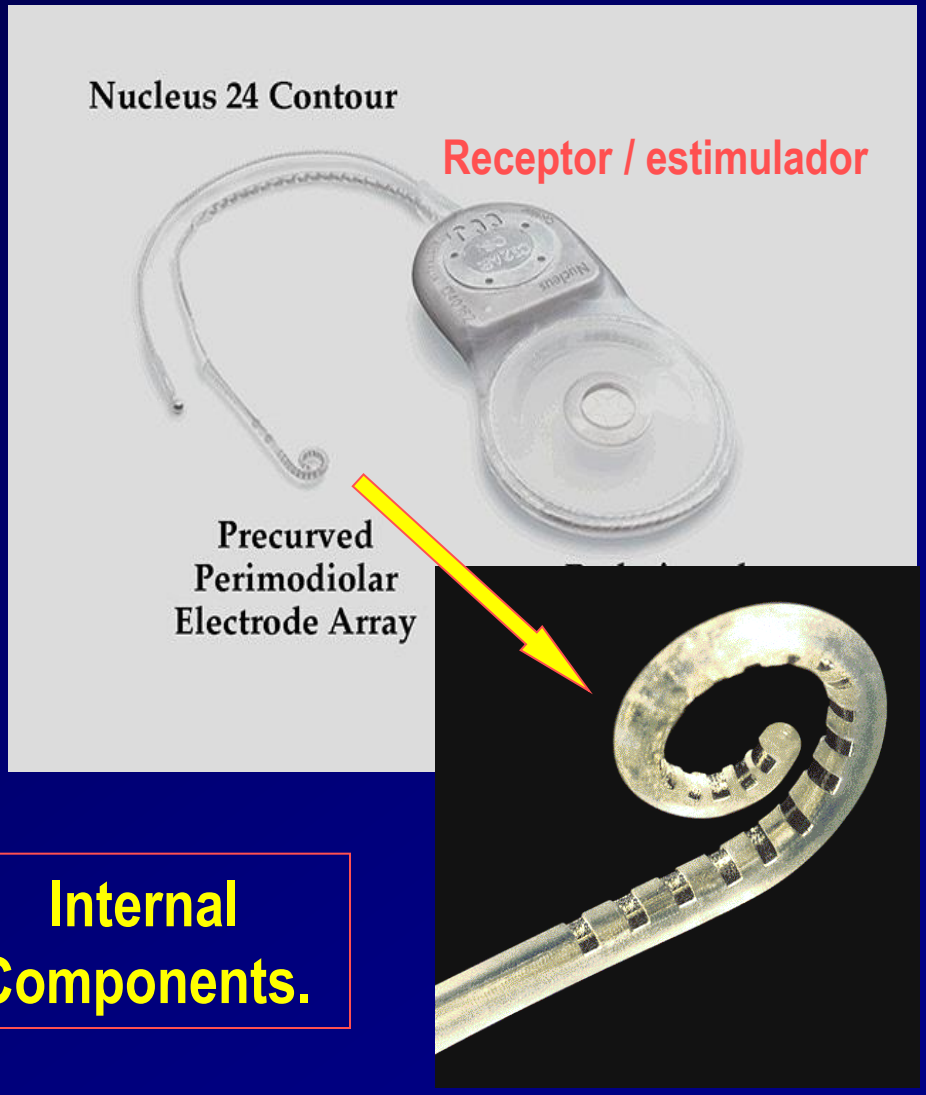
Components of a cochlear implant.





External Components.

Internal Components.

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Cochlear implants.

- Great progress has occurred since the first single channel implants by William House (eg. telephone). …
- Even if the results are wonderful…and implants are now smaller better and safer, with better materials and electrodes…we still do not understand the "obscure miracles" and language of the central nervous system and have developed no substantial conceptual changes.
- In essence…we are still abusing the extraordinary interpretation capabilities of the brain, whose circuits are used to process partial and incomplete information and make sense of it…

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To promote regeneration of those which are damaged. To re establish function of disfunctional cells.

- 1.Mielin stimulates the development of axons during development but in the adult it produces substances that inhibit growyh…neutralize inhibitors.
- 2. “Neurons of the CNS are not replaced” except in the olfactory syste. There, the glia does produce substances that stimulate neural growth...
- 3. Stimulation and/or blockage of neurotransmitters that cause disfunction. Eg. In depression.

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Where are we going in the ear? To regeneration of inner ear cells.

- 1. In mammals, the organ of Corti looses its regenerative capabilities after development.
- Birds, reptiles and fish maintain these capabilities.
- 2. The capability of inner ear cells regeneration is a latent potentiality that is regulated genetically. There are genes that promote and genes that inhibit regeneration through proteins, transcription factors and regulators of the cell cycle.

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Regeneration of inner ear cells.

- Current therapy is oriented towards modifying the stimulus but not to solve the problem itself.
- Future therapy will require an approach oriented towards the essential problem through: gene therapy, stem cell therapy, drugs and trophic factors (neorotrophins, antioxidants that could prevent damage from ototoxicity, acoustic trauma, etc.).

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Regeneration of inner ear cells.

- Genes = Regeneration:

  A. Modifying destiny (from support cell to ciliated cell).

  B. Stimulating proliferation: a. + expression.

  b. – inhibition.

  Stem cells: a. integration, differentiation.

  b. providing trophic factors.

(J. Cristóbal Maass. Atlas 2011).

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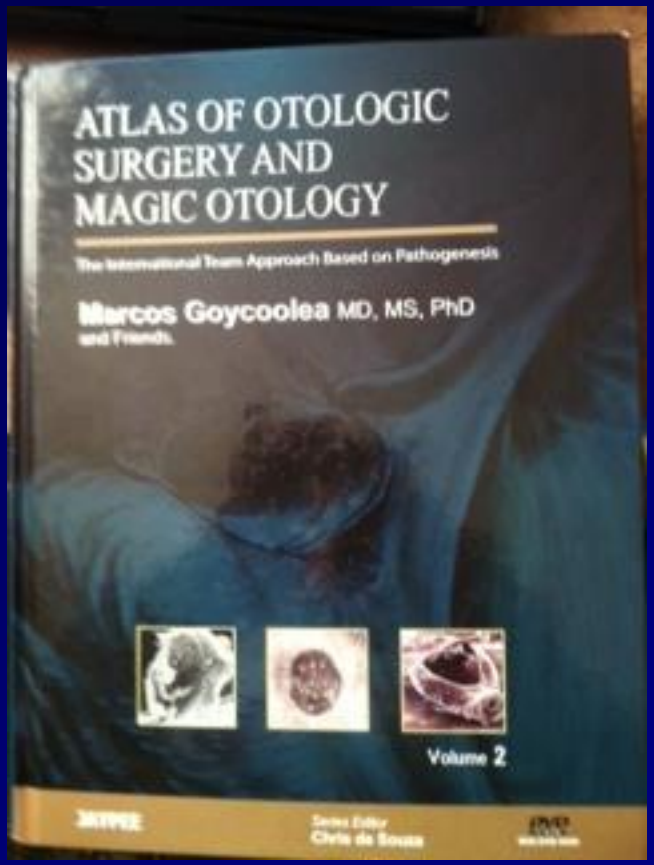

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¿Where are we going to…?
Thanks to genetics and molecular biology…

- 1. Towards a radical change in medicine. We will switch from a passive massive medicine of detection and prevention to an individual predictive medicine.
- 2. A medicine with regeneration of tissues and eventually of organs.
- 3. A medicine that will be regenerative of the central nervous tissue not only in early stages of high plasticity Cajal…

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¿What stage are we in…?

- In the initial stages of ciliated and ganglion cell regeneration.
- In a stage in which the studies oriented towards middle and inner ear interactions are starting to give fruits.
- In the immediately previous stage to the development of routine surgical techniques to approach the neural cells of the inner ear (Atlas.)

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¿What stage are we in…?

- In a stage that is previous to approaches in which…based in genetic patterns we will be able to predict the responses to drugs and their potential benefits and toxicities (Ear drops, antimicrobials, etc.). **Routine Pharmacogenomics.**
- In a stage previous to approaches in which…based in genetic mapping we could predict the future course of sensorineural hearing losses before they occur and act in time accordingly (Eg. New born genetic screening).

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Pharmacogenomics

- Studies variations in genes and how these influence the response of the patients to medication. Purposes:1. To determine genetic variations in order to minimize adverse effects.

  2. To identify the medication that is most efficient for a particular induividual.

By means of genetics and molecular biology persons are “genotipified” for pharmacogenomics.

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Which genes have been studied?

- **A. Genes involved in metabolizing drugs.**
- (Deffective, accelerated, normal metabolization).
- Gene citocrome CYP2C9 (diclofenaco, ibopurofen.
- Gene citocrome CYP2D6 (fluoxetine).
- **B. Transporter (SLC6A4) or receptor genes.** (HTR1A) de serotonina.

- Purpose: to prescribe the most adequate medication for the most adequate patient in the most adequate dose.

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Where has our focus been pointing to? To the receptor…

- The central pathways and the central processor (cortex) will be of paramount importance in future years.

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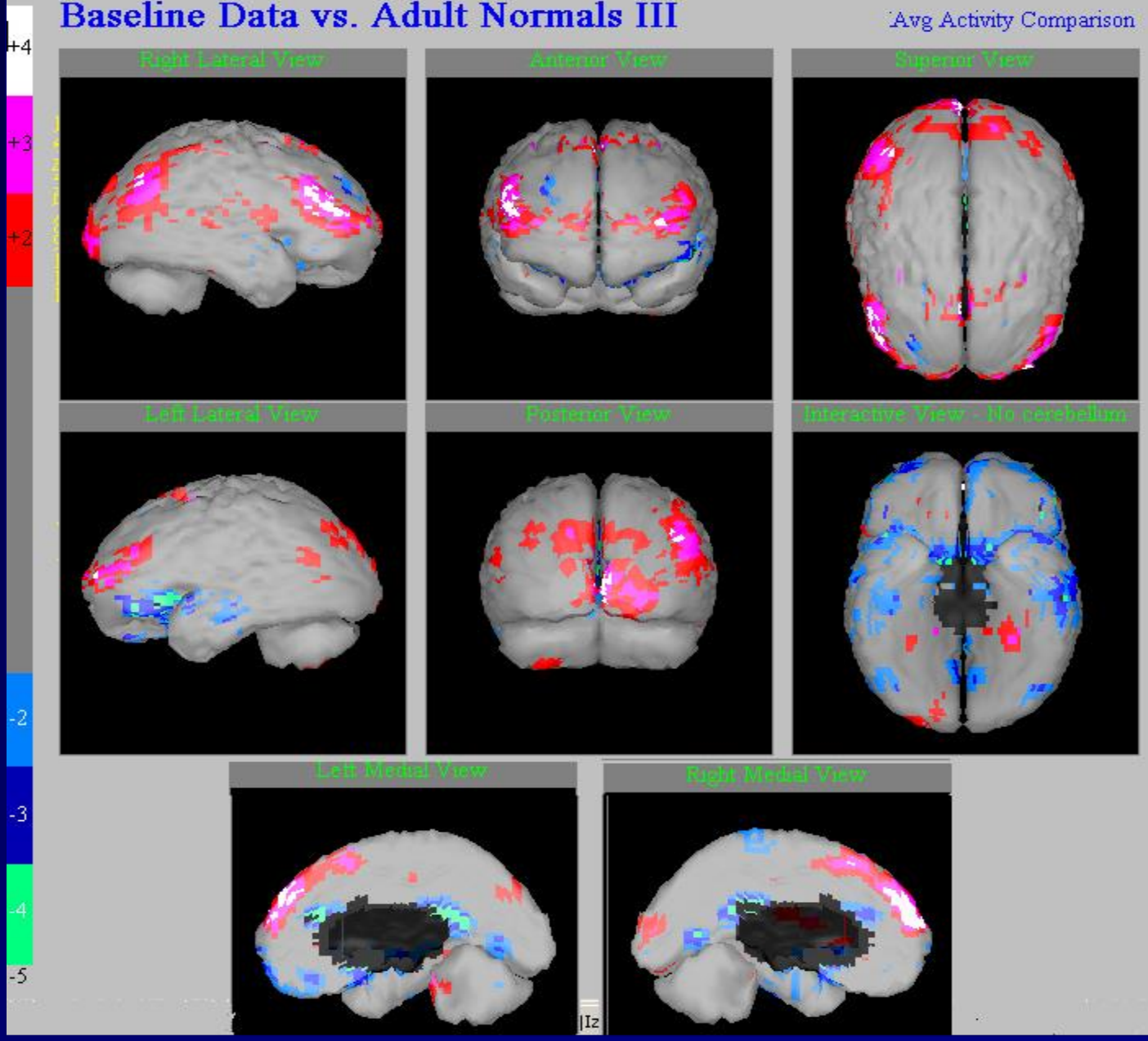
N.K. 04/06/04

Baseline Data vs. Adult Normals III

Avg Activity Comparison



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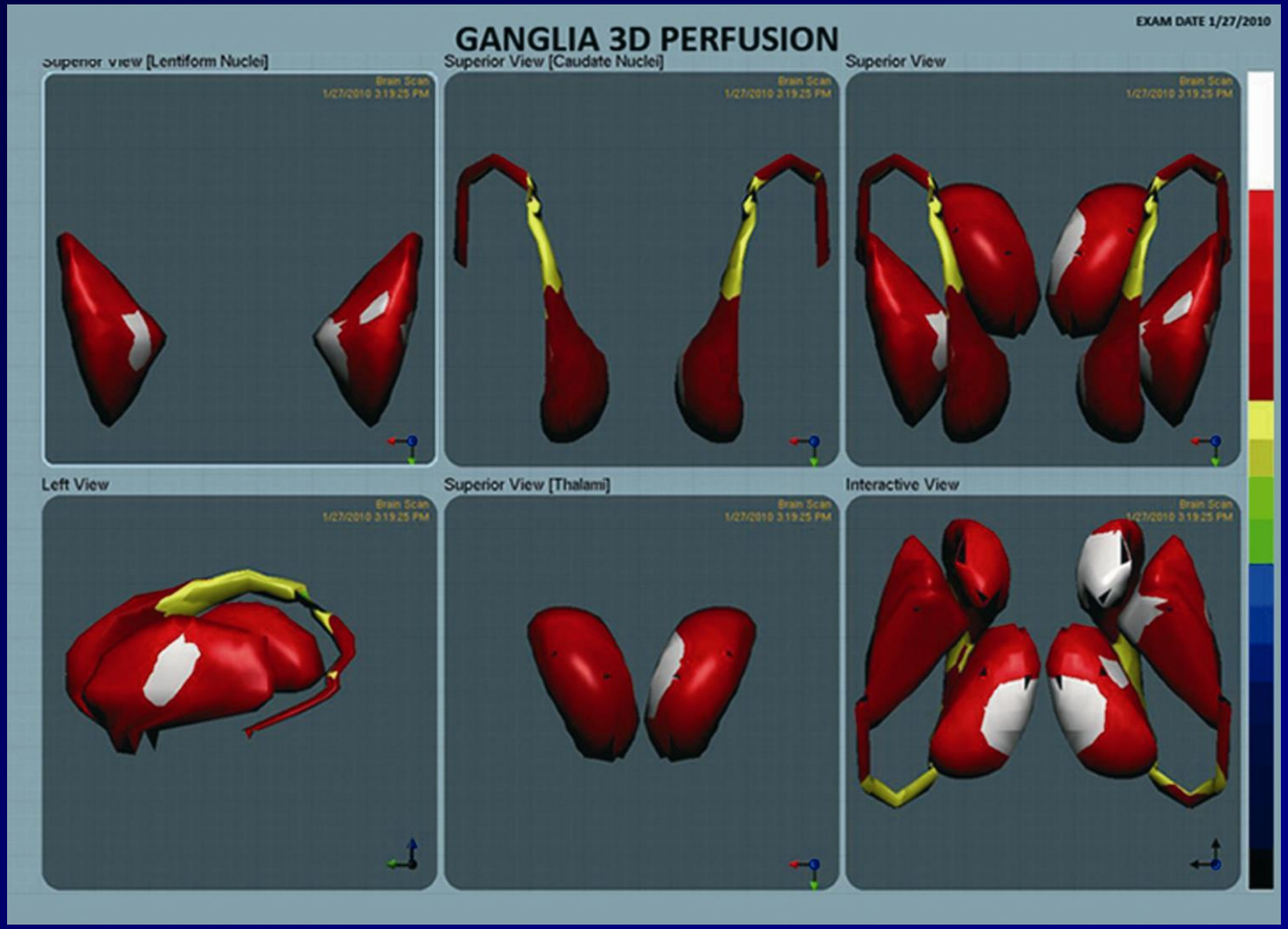

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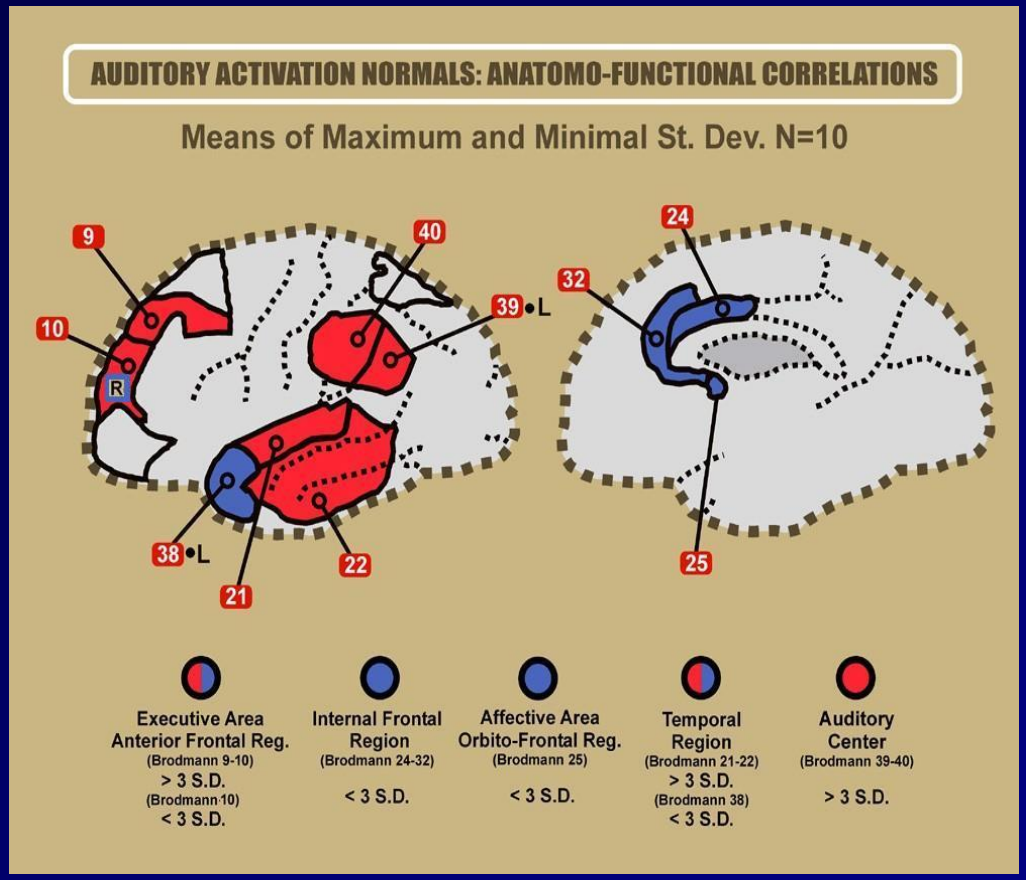
Neuronal Circuits.
Source, distance, emotions, meaning, etc.



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Where are we at this point?

1) **Central response is bilateral and the auditory pathway is ipsi and contralateral.**
   Bilateral activation of Brodmann's areas 39 and 40 regardless of the ear that is stimulated supports the concept that the central response to auditory stimuli is bilateral, therefore, that there are ipsi and contralateral routes to the auditory cortex.

2) **Central response can consist of activation or inhibition.**
   Activation of areas 39 and 40 simultaneous with inhibition of area 38 support the concept that also inhibitory and not only excitatory neuronal groups are involved in the process of hearing (central modulation process).

3) **Activation and inhibition of neuronal groups can occur simultaneously in a same Brodmann's area.**
   Eg. Brodmann's area 10.

4) **Although central response is bilateral, this does not mean that it is symmetrical.**
   A statistically significant increased activation on the left side of areas 39 and 40 regardless of the stimulated ear is suggestive that pure tones might be preferably processed in the left hemisphere.

5) **Central response to auditory stimuli involves areas other than auditory centers.**
   Central responses to auditory stimuli involve executive frontal, visual, and affective areas among many others and also involve areas of auditory memory.

6) **Central inhibition can be significantly different in the same individual, depending on which ear (side) is stimulated.**
   The significant difference in central inhibition depending on which ear (side) is stimulated is supportive of the idea of a leading or preferred ear. This difference did not occur in the centrally activated areas 39 and 40. Is the leading ear an inhibitory phenomenon?

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What do future years bring us?

- A fascinating stage in the development of otology in which knowledge and approaches will come not only from our studies but also from the integration and interaction of other scientific disciplines like electronics, engineering, mathematics as well as philosophy since these advances will bring along changes in paradigms that are beyond our imagination.

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