Neuroplasticity In Blind People

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BACKGROUND

➢ It is well known that the adult brain does not have its networks static and unable to be modified. The constant change of the environmental stimuli leads the brain to remodel its neuronal connexions → **neuroplasticity**.
➢ Such changes can occur in many different situations, including the normal development and maturation of the organism, the acquisition of new skills in immature and mature organisms, after damage to the nervous system, and, as a result of sensory deprivation. In this last situation, this kind of plasticity is known with the term of **cross-modal plasticity**, where the brain area of the deprived sensory is used to process information of other senses and potentiate them.
➢ So, is really the deprivation of a sensory a big inconvenient for an organism if other senses can be potentiated? Can neuroplasticity take place in the brain of adult blind subjects?

AIMS

➢ To understand the general molecular mechanisms involved in the process of neural plasticity, focusing on the excitatory pathway of the glutamate neurotransmitter
➢ Finding out which are the anatomical and functional changes in the brain of late onset blind people
➢To figure out if late onset blind subjects have neural plasticity as has been observed in congenital or early onset blind individuals

METHODOLOGY

Scientific articles (Pubmed, Sciencedirect) → Abstracts of interest → Molecular mechanisms of neuroplasticity → **Glutamate** → Schemes made by software → ChemBioDraw

Abstracts of interest → Blind individuals → participants: late onset blind individuals

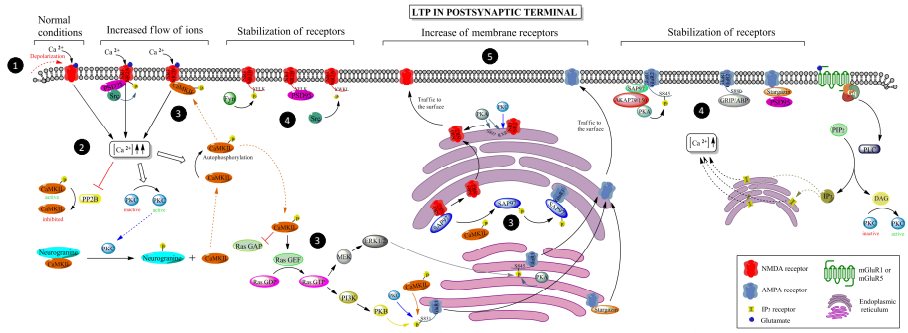
MOLECULAR MECHANISMS OF NEUROPLASTICITY

There are three main events through which neuroplasticity can be achieved: the long-term potentiation (LTP), long-term depression (LTD) and the homeostatic plasticity.

Long-term potentiation (LTP) promotes synaptic connections become stronger due continuous stimuli

1. Continuous stimuli promotes an increased release of glutamate from presynaptic terminal which interacts with NMDA receptor

2. The activation of NMDA receptor increases the intracellular calcium levels which, in turn, activates some molecules and signaling pathways



3. The activated molecules (CaMKII, PKC) and signaling pathways (Ras/MEK/ERK and Ras/PI3K/PKB) are involved in the traffic of NMDA and AMPA receptors to membrane (through phosphorylation of some specific residues) and their increased ions flux

4. Some molecules are involved in the stabilization of NMDA and AMPA receptors to membrane (PSD95, Fyn, Src and others)

5. As a result, there is an increase of NMDA and AMPA receptors to the membrane which makes neurotransmission more effective

Fig. 1. Molecular mechanisms involved in long-term potentiation in postsynaptic terminal

Long-term depression (LTD)

The lack of stimulation or lower stimulation promotes LTD, which makes synaptic connections become weaker through the internalization of glutamate receptor and /or reduction of current (reverse process of LTP).

Homeostatic plasticity (HP)

The HP promotes an equilibrium between LTP and LTD avoiding excessive excitation or inhibition ,controlling the level of activated molecules in LTP.

NEUROPLASTICITY IN LATE ONSET BLIND INDIVIDUALS

Visual stimuli are the main source of the perception of our environment. The lack of visual stimuli makes blind individuals to use other senses to perceive their surroundings and this new usage implies anatomical and functional changes in blind people's brain.

Anatomical changes

Significant differences have been reported in volume and thickness of some brain regions.
Apart from the hippocampus, which has increased and reduced volume of the anterior part and posterior part, respectively, there are other anatomical differences:

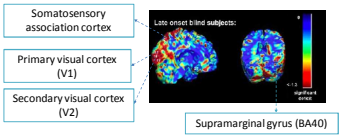


Fig. 2. Volume reduction in the brain of late onset blind subjects compared with sight controls. From *Leporé, N et al. Neuroimage 49,134-140 (2010)*

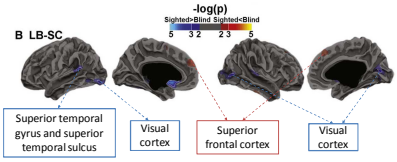


Fig. 3. Cortical thickness (red) and thinness (blue) of late onset blind brain compared to sight control. From *Park H et al. Neuroimage 47,98-106 (2009)*

Functional changes

Blind subjects show several functional differences depending on the stimulus.

Auditory stimuli

Visual cortex activation:
➢Paying attention to auditory stimulus, not when ignoring it
➢Correlates with age of onset of blindness (not years of blindness)
➢Correlates with discrimination of sound source (Congenital Blind>Late Blind>Sight Control)
➢Sound motion (also V3 and V5 activation)

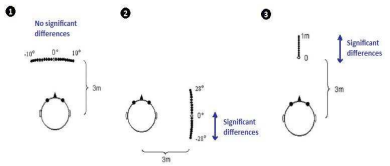


Fig. 4 Distance of sound source discrimination task of late onset blind subjects compared to sight controls. From *Voss P et al. Current Biology 14, 1734-1738 (2004).*

Tactile stimuli

Braille reading:
➢ Activation visual cortex → V1 and V2
➢ Activation non-visual areas → parietal, frontal and temporal lobes

➢ Activation of occipital cortex shortly after blindness

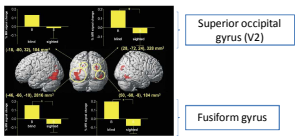


Fig. 5. Activation of visual cortex in recent LB during Braille reading. From *Sadato N, et al. Neurosci Lett 359, 49-52 (2004)*

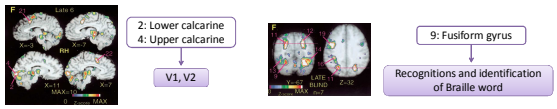


Fig. 6. Bold response in LB during Braille reading. Illustration taken from *Burton, H et al. Journal of Neurophysiology 87, 589-607 (2002)*

Language and memory

Language tasks:
➢ Verb generation to heard noun: activation of V1 and nearly regions in LB
➢ Response preparation, execution or attention → activation of right occipital cortex (congenital blind and late onset blind)

Memory abilities:
➢ Serial memory tasks: late onset blind have improved short-term and long-term auditory memory → codification of spatial information in a form of "route-like" sequential representations

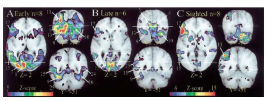


Fig. 7. Regions with significant activation during verb generation to heard words. From *Burton, H et al. Neurophysiology 88, 3359-3371 (2002)*

Blind subjects due Leber congenital amaurosis successfully treated

Gene therapy → AAV2 with RPE65 wild type gene

Subjects were able to see and there was visual cortex activation through time

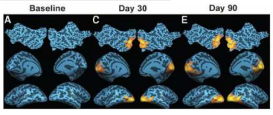


Fig. 8. Visual cortex activation after AVV2 gene therapy. From *Bennett Jet al. Sci Transl Med. 4, 120ra15 (2012)*

CONCLUSIONS

- The loss of visual sense potentiates other senses which permits to blind individuals a better perception of their environment
  - Improved sound source localization (better navigation), memory skills (remember pathways)
- Neural plasticity in adult brain is given
  - Late onset blind individuals have activation of the visual cortex with auditory and tactile stimuli and also with language and memory tasks
  - Adult congenital blind treated with gene therapy shows activation of visual cortex with visual stimuli
- Neural plasticity can take place in the adult brain but, in some cases, the plasticity would not be as wide as it is in the first's years of life where neural remodeling can be larger